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CT-quantified emphysema distribution is associated with lung function decline

running title: **Emphysema distribution and lung function decline**

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ABSTRACT

Emphysema distribution is associated with COPD. It is however unknown whether CT-quantified emphysema distribution (upper / lower lobe) is associated with lung function decline in heavy (former) smokers.

587 male participants underwent lung CT-scanning and pulmonary function testing at baseline and after a median (interquartile range) follow-up of 2.9 (2.8-3.0) years. The lungs were automatically segmented based on anatomically defined lung lobes. Severity of emphysema was automatically quantified per anatomical lung lobe and was expressed as the 15^{th} percentile (HU-point below which 15% of the low attenuation voxels are distributed (Perc15)). The CT-quantified emphysema distribution was based on principal component analysis. Linear mixed models were used to assess the association of emphysema distribution with FEV_1/FVC, FEV_1 and FVC-decline.

Mean (SD) age was 60.2 (5.4) years, mean baseline FEV_1/FVC was 71.6 (9.0) % and overall mean Perc15 was -908.5 (20.9) HU. Participants with upper lobe predominant CT-quantified emphysema had a lower FEV_1/FVC, FEV_1 and FVC after follow-up compared to participants with lower lobe predominant CT-quantified emphysema (p=0.001), independent of the total extent of CT-quantified emphysema.

Heavy (former) smokers with upper lobe predominant CT-quantified emphysema have a more rapid decrease in lung function than those with lower lobe predominant CT-quantified emphysema.

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the major causes of morbidity and mortality world wide. (1) COPD consists of chronic bronchitis and emphysema, which both may lead to airflow obstruction. Emphysema is defined as an abnormal and permanent enlargement of the air spaces distal to the terminal bronchioles and destruction of bronchial walls, which in the vast majority of cases in the Western world is caused by tobacco smoking. Although emphysema is a pathological diagnosis it may also be assessed by quantitative computed tomography (CT) measuring low-attenuation areas (LAAs) of the lung. This technique has been validated against pathology (2) and has been used in multiple studies. (3) (4) (5)

Since lung cancer and COPD share smoking as a mutual risk factor, participants of lung cancer screening trials provide the unique opportunity to study the relationships between CT-quantified emphysema and lung function decline in relatively healthy smokers.(6) The results may be useful to select participants in need for more aggressive smoking cessation therapies to prevent further lung function deterioration at a fairly early stage of the disease.

Several studies have shown that subjects with similar degrees of low-attenuation areas, but with different locations within the lung show different degrees of airflow obstruction. (7) (8) However, those studies were cross-sectional and the effects of the CT-quantified emphysema distribution on disease progression, i.e. lung function decline, were not assessed. In subjects with α1-anti-trypsin (AAT)-deficiency, for instance, it was shown that emphysema distribution was associated with lung function decline. (4)

Recent advances enable automatic anatomical-based segmentation of the lungs allowing estimation of the extent of low-attenuation areas per lung lobe, in stead of per e.g. top or lower one-third of the lung. (9)

We hypothesize that, like in AAT-deficiency, distribution of low-attenuation areas in heavy smokers is associated with lung function decline. The aim of the present study was therefore to assess the effect of CT-quantified emphysema distribution, based on anatomically defined lung lobes, on lung function decline in current and former smokers participating in a lung cancer screening trial.

Methods

Participants

The study was conducted among those current and former heavy smokers taking part in the Dutch Belgian Lung Cancer Screening Trial (NELSON). In the current study only participants who underwent CT-scanning and pulmonary function tests at the University Medical Center Utrecht were included. The inclusion criteria have been described in detail elsewhere. (10) (11) In brief, the NELSON study is a population based CT-screening trial for lung cancer that studies current and former heavy smokers fit enough to undergo surgery. Both the Dutch ministry of health and the Medical Ethics Committee of the hospital approved the study protocol and informed consent was obtained from all participants. The NELSON trial is registered at www.trialregister.nl with trial number ISRCTN63545820. For this sub study, original approval and informed consent allowed use of data for future research. Participants meeting the inclusion criteria of having smoked a minimum 20 packyears were invited to participate. As fewer women in the Dutch population show the same long-term exposure to cigarettes as men, only males were included. Baseline details on smoking habits were gathered through questionnaires which included questions on duration of smoking habit, number of packyears smoked and smoking status (current or former smoker).

Pulmonary function tests

Pulmonary function tests (PFT) were performed with standardized equipment according to European Respiratory Society (ERS) and American Thoracic Society (ATS) guidelines and included forced expiratory volume in one second (FEV_1), forced vital capacity (FVC) and FEV_1 / FVC. (12) For demographic purposes we labeled participants with a FEV_1/FVC <70% and alternatively below the lower limit of normal (LLN) as having 'airflow obstruction'. Broncho dilatation was not applied (13).

CT scanning

All participants received low-dose CT, with 16-detector MDCT scanners (Mx8000 IDT or Brilliance 16P, Philips Medical Systems, Cleveland, OH). Scan data were obtained in spiral mode, with 16 x 0.75mm collimation and in full inspiration. No spirometric gating was applied since this does not improve repeatability of lung density measurements. (14)(15) Axial images were reconstructed with 1.0mm thickness at 0.7mm increment. All scans were reconstructed with a soft reconstruction filter (Philips B) at a 512x512 matrix. Exposure settings were 30mAs at 120kVp or 140kVp, depending on participant's weight, ≤80 and >80 kilograms, respectively. This low-dose CT protocol has previously been used to quantify emphysema in COPD patients and heavy smokers.(6)(16)(17)(18) The vast majority of subjects was scanned on the Brilliance 16P scanner and a very small fraction (~1%) on the Mx8000 IDT scanner, which was used a back-up scanner. We repeated the analyses with exclusion of subjects scanned on the Mx8000 IDT scanner and found no significant differences in outcome.

Segmentation of lungs and lobes

In all CT scans, the lungs and lobes were automatically segmented using previously developed and evaluated software. (9) (19) Segmentation of the lungs was performed using an algorithm based on region growing and morphological processing. Segmentation failures, for instance in case of incomplete fissures, were automatically detected based on statistical deviations from volume and shape measurements. In the cases for which failures were detected, an algorithm based on multi-atlas registration was applied to obtain the correct result. The lung segmentation software was previously evaluated on 100 scans from the same screening and performed with accuracy similar to human observers. (19) The software further subdivided the lungs into the anatomical lobes. Two lobes were segmented in the left lung (upper and lower lobe) and three in the right lung (upper, middle, and lower lobe). Lobe segmentation was initiated with a segmentation of the pulmonary fissures. Next, each voxel in the lung was assigned to one of the lobes based on its position inside the lung and relative to the fissures.

Emphysema quantification

Emphysema severity was computed for the entire lung and per lung lobe. The airways were excluded to ensure that only lung parenchyma was analyzed. (20) Severity of CT-quantified emphysema was calculated using the 15th percentile (Perc15) technique. (21) (22) (23) Perc15 provides the Hounsfield units (HU) point below which 15% of all voxels are distributed. The lower the Perc15 values are, i.e. closer to -1000 HU, the more CT-quantified emphysema is present. The use of Perc15 for emphysema quantification has been validated against pathology (24) and applied in multiple studies. (4) (6) A secondary analysis was done using the %950 HU as CT-quantified emphysema severity measure, which is defined as the

proportion of low density voxels below -950 HU. The results of these analyses are reported in the supplemental files.

Statistical analysis

Mean and standard deviation (SD) were calculated for normally distributed data and median and interquartile range for non-normally distributed data. Normal distributions were checked via Q-Q plots. Students' t-test was used to compare means of normally distributed variables and Chi-square tests for categorical variables. Correlations between the Perc15 values per lung lobe were assessed by Pearson's *r*.

The Perc15 value per lobe is expected to be highly correlated with that of the other lobes in the same participant, resulting in multicollinearity issues. Therefore, principal component analysis (PCA) with a varimax rotation was performed to obtain uncorrelated variables.

PCA is a well-known data reduction technique and is often used to convert a set of correlated variables into uncorrelated ones. (25) Multicollinearity issues are so resolved and PCA has been used recently for this purpose.(26) (27). The new variables, called 'components' in PCA terminology, are linear combinations of the original ones. There is a resemblance with linear regression: the combinations are based on 'regression coefficients', which in PCA are called 'scores' and the linear combinations are called 'components'. Every component is linked to a characteristic of the original set of variables and is often referred to as 'phenotypes'. The first component obtained is often a mean of the original variables and therefore explains the greatest proportion of variance. The second and subsequent components describe other phenotypes. The percentage of variance explained by the second component will be less than by the first component. This procedure goes on until all the variance is explained, however each next component will explain a smaller proportion. Higher components can be ignored as

the percentage of additional variance explained is minimal. Only components explaining more than 5% were retained in this case.

The values of the new variables (called factor scores) are subsequently incorporated in a random intercept, random slope linear mixed model with FEV_1/FVC, FEV_1 and FVC per time point as primary endpoint. Three separate models were created and compared. The first model contained observation time, height, BMI, age, packyears smoked and smoking status (i.e. being a continuous smoker or not). In a second model component 1 values were added and in a third model both component 1 and 2 values. The -2 restricted loglikelihood values were used to evaluate if insertion of the more components improved the fit of the model significantly. P-values ≤ 0.05 were considered as significant. A detailed description of the statistical methods is given in the supplemental files. All statistical analyses were performed using SPSS 19 (SPSS, Chicago, Illinois, USA).

Results

Baseline demographics and lung function

A total of 609 participants underwent baseline and follow-up CT-scanning and PFT. After exclusion of 22 participants because of software failure to segment the lung lobes, 587 participants were included in the current study. Mean (SD) baseline FEV_1 was 97.7 (18.1) % of predicted and FEV_1/FVC was 71.6% (9.0). Further baseline demographics and lung function values are presented in Table 1.

Smoking status

Mean (SD) packyears smoked was 41.2 (18.7) years. At enrolment of the study 305 (50.1%) participants quitted smoking and 304 (49.9%) participants not. The number of packyears

smoked did not significantly differ between current and former smokers, 38.8 and 41.1 years respectively (p=0.251).

Baseline CT-quantified emphysema: results from Principal Component Analysis

Overall mean (SD) baseline Perc15 was -908.5 (20.9) HU. Perc15 per lung lobe is given in Table 2. The Perc15 values between the five lung lobes were highly correlated (*r* ranging from 0.75 to 0.950, all p<0.0001). Two components or phenotypes were defined, which explained 94% of the variance: component 1 86.1% and component 2 7.9%. Table 2 shows the scores of the two components. Component 1 relates to the overall mean Perc15 and is interpreted as 'total lung emphysema severity (ES). Component 2 relates to 'upper / lower lobe emphysema severity' (emphysema distribution (ED)). The positive coefficients (= scores) for component 2 in Table 2 relates to a predominant upper lobe distributed emphysema, the negative coefficients to predominant lower lobe distributed. The low coefficient for the right middle lobe indicates a minor influence. In subjects with increasing 'total lung emphysema severity', the ES factor score becomes more negative, based on the multiplication with the Perc15 value (e.g. -950 HU). In subjects with predominant upper lobe emphysema the ED becomes negative as the multiplication of the Perc15 value with the positive coefficient results in a negative factor score value and positive in subjects with predominant lower lobe emphysema.

Association CT-quantified emphysema distribution and lung function after follow-up

Median (interquartile range) follow-up was 2.9 (2.8 - 3.0) years. The ES and ED values, derived from the principal component analysis, were inserted in the linear mixed model together with the other adjustment factors. The fit of the model significantly improved when

ES and ED were inserted successively ($p < 0.001$). Both ES and ED were significantly ($p<0.001$) associated with a lower FEV_1/FVC after follow-up, see Table 3. A 1 point decrement in the ES resulted in a 4.38% lower FEV_1/FVC and a 1 point decrement in the ED resulted in an additional 1.00% lower FEV_1/FVC. This shows that lower Perc15 values, i.e. more low-attenuation areas and an upper lobe predominant CT-quantified emphysema distribution are independently associated with significantly lower FEV_1/FVC values after follow-up. The effects of ES and ED on FEV_1/FVC after follow-up are illustrated in Figure 2. ES and ED were also significantly associated with lower FEV_1 and FVC after follow-up ($p<0.001$). The effect sizes for FEV_1 and FVC are given in Table 3. The effect sizes of the other covariates in the model are also presented in Table 3.

Using the %950 HU approach as measure of CT-quantified emphysema severity yielded comparable results as using the Perc15 (see supplemental files).

Discussion

In the present study we showed that upper lobe distribution of CT-quantified emphysema is associated with a lower lung function after follow-up in a large cohort of 587 former and current heavy smokers participating in a lung cancer screening trial. Knowledge of the distribution of CT-quantified emphysema thus is important with regards to the course of lung function in former and current heavy smokers.

We used principal component analysis, to solve the problem of the high correlation between the Perc15 values per lung lobe within an individual. This approach delivered two new variables (components 1 and 2). Component 1 (total lung emphysema severity, ES) characterized the total extent of CT-quantified emphysema, while component 2 (emphysema distribution, ED) characterized the difference between upper and lower lobe CT-quantified emphysema. The effect size of the emphysema distribution pattern (-1.00%) is substantially higher compared to the expected normal decline of FEV_1/FVC (-0.18%) in age matched healthy individuals. This shows that the results are of clinical importance. Ignoring the individual distribution of CT-quantified emphysema provides a less precise estimation of lung function decline.

Table 3 lists the ED and ES regression coefficients for the decline in FEV_1/FVC, FEV_1 and FVC which are the result of three separate analyses. In other words the regression coefficients for FEV_1/FVC decline were not obtained by simply dividing the regression coefficients of FEV_1 by those of the FVC. If one is tempted to such a straightforward division, one could draw the conclusion that the FEV_1/FVC ratio would increase when emphysema severity increases and that when the FEV_1/FVC ratio decreases this is due to a decrease in FVC larger

than the FEV_1. This is obviously not the case as the ED and ES coefficients for the FEV_1/FVC clearly point at a decrease. One must not forget that the ED and ES are just one of the many parameters, influencing the FEV_1/FVC, FEV_1 and FVC decline. It is not possible to isolate just the FEV_1 and FVC ED and ES coefficients to obtain the FEV_1/FVC coefficients. A more detailed explanation is given in the supplemental files.

The present longitudinal study is an extension from the previous performed cross-sectional study investigating the association between emphysema distribution and lung function. (8) However, two important methodological differences exist. Firstly, in the current study no distinction was made between mild and severe emphysema, instead the Perc15 was used as a continuous measure for emphysema severity. We preferred this measure because it was shown to be the most robust measure for the progression of low attenuation areas. (5) Secondly, in the former study segmentation of the lungs was based on a division of the lung based on volumes: top one-third and lower one-third. Other studies also used such an approach to separate upper from lower lung fields, for instance by dividing the total lung volume in two parts. (28) Inevitably parts of the anatomical lower lobe will be allocated to the upper lobe and our lobe segmentation, based on anatomical information, avoids this problem. Therefore, in the present study, three-dimensional data and the natural boundaries of the lung were used which enabled a reliable separation of the upper lung lobes from the lower lung lobes. Furthermore, the software used has shown to have an accuracy comparable to that of an independent human observer.(19)

In AAT-deficiency subjects longitudinal studies have been performed showing that lower lobe predominant emphysema was associated with a greater decline of lung function. (4) In COPD patients, without AAT-deficient only cross-sectional studies have been performed

investigating the association of emphysema distribution with lung function. Gurney et al. found that a lower lobe predominant emphysema distribution was associated with lower total lung capacity (TLC) values, however these associations were only significant for subjectively quantified emphysema and not when objectively quantified. (29) Three studies are of special interest because they quantified emphysema automatically, based on the percentage of low-attenuation areas below a specified threshold. Saitoh et al. reported that the FEV_1/FVC ratio showed the strongest correlation with lower lobe emphysema distribution, but that the carbon monoxide transfer factor (TLco) showed the strongest correlation with upper lobe emphysema distribution (30) Mair et al. showed that upper zone distribution of emphysema in COPD subjects was associated with a higher total score on the St. George's Respiratory Questionnaire. (28) A higher score on the St. George's Respiratory Questionnaire indicates more severe respiratory impairment. De Torres et al. failed to find a correlation between the distribution of emphysema and lung function parameters in subjects with mild to moderate COPD. (31) It was concluded that in mild COPD emphysema distribution is not associated with lung function. However, it should be taken in account that the sample sizes might be too small (n=115) to allow sufficient power for detecting true associations. Furthermore, in all studies classification of the emphysema distribution was not anatomically based which might have influenced the findings.

Less is known about why it is that smokers differ in emphysema distribution pattern. Like in AAT-deficiency a genetic susceptibility may play a role. (32) (33) Candidate gene studies in the National Emphysema Treatment Trial (NETT) showed that upper lobe predominant emphysema was associated with polymorphisms in two enzymes playing a role in the detoxification of smoke metabolites. (32) The authors posed that these polymorphisms alter the normal detoxification of cigarette metabolites contributing to the distribution of

emphysema. Future genome-wide association studies may further elucidate the association between genetic susceptibility and emphysema distribution in heavy smokers.

In heavy smokers upper lobe emphysema distribution is more common than lower lobe distribution (based on anatomically defined lung lobes). This is in line with the fact that emphysema in heavy smokers is mainly of the centrilobular type, which is more common in the upper lobes. It has been hypothesized that this emphysema distribution is caused by the difference in the ventilation/perfusion ratio between the upper and lower lobes. (34)

There are a number of strengths to our study. Firstly, we included a large number of participants and therefore could extensively correct for confounding factors, like age, BMI, smoking status, packyears etc., unlike most other studies. Secondly, we included relatively healthy, but heavy smoking subjects, at a high risk for developing airflow obstruction. Most previous studies examining the effects of emphysema distribution included subjects with more severe COPD only. Thirdly, all CT-scans were performed in one single center excluding possible scanner bias due to different algorithms used by different types of CT-scanners. Lastly, we used anatomical defined borders to segment the lungs which might be more accurate than using lung volumes to segment the lungs or by a visual assessment. Visual assessment has been reported to be less reliable than when determined automatically. (35) Furthermore, the severity of CT-quantified emphysema was calculated automatically which eliminates intra-observer variability between different readers of CT-scans.

The main limitation of our current study is that only males were included which is especially unfortunate because the prevalence of COPD in females is rising. Our results may not be extrapolated directly on females because it is known that males have more CT-quantified

emphysema (17) and that sex is independently associated with upper or lower lung predominant emphysema patterns. (28) Future studies should also include females to examine the association of emphysema distribution and lung function decline. Furthermore, as we included relatively healthy, but heavy smoking participants and participants with COPD GOLD stage 1, the results may not be extrapolated to more severe COPD participants straightforwardly.

In conclusion, the distribution of CT-quantified emphysema is an additional parameter, besides the total extent of CT-quantified emphysema, in predicting lung function decline. Upper lobe predominant emphysema is significantly associated with stronger lung function decline compared to lower lobe predominance emphysema in former and current heavy smokers. These findings may be of importance because they may be useful to identify subjects with greater declines in lung function and probably eligible for more intensive smoking cessation counseling.

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Table 1: Baseline participants' demographics (mean, sd) for the total cohort. * = median (interquartile range), # the severity of emphysema is expressed as the 15th percentile: HU point below which 15% of the low attenuation areas voxels are distributed (the lower the Perc15 values are, i.e. closer to -1000 HU, the more emphysema is present). LLN= lower limit of normal.

	Total cohort n=587
Age [years]	60.2 (5.4)
Height [meters]	1.78 (0.07)
BMI [kg* m $^{-2}$]	26.9 (3.6)
observation time*	2.9 (2.8 - 3.0)
Packyears smoking	41.2 (18.7)
Current smokers (%)	304 (49.9%)
FEV_1 [L]	3.36 (0.73)
FEV_1 %pred	97.7 (18.1)
FVC [L]	4.96 (0.82)
FVC %pred	107.2 (15.1)
FEV_1/FVC [%]	71.6 (9.0)
FEV_1/FVC <70%	218 (35.8%)
FEV_1/FVC <LLN	106 (17.9%)
total lung emphysema severity (15% percentile value)#	-908.5 (20.9)

Table 2: Mean (SD) **15% percentile value** (Perc15) [HU] per lung lobe (column 2) and component scores (columns 3 and 4). The two components explained 94% of the variance. Component 1 (named ES or 'total lung emphysema severity) is characterized by similar scores for each lobes and so each lobe is equally contributing to this component; component 2 (named emphysema distribution) is linked to the difference between upper and lower lobe emphysema. The component scores can be interpreted in a similar way as the regression coefficients (β) from multiple linear regression analysis.

Lung lobe	**Mean (SD) 15% percentile value**	**Scores for component 1 (=ES)**	**Scores for component 2 (=ED)**
Left upper lobe	-912.1 (21.2)	0.218	0.743
Right upper lobe	-906.6 (23.0)	0.212	0.937
Right middle lobe	-915.5 (18.5)	0.214	-0.234
Left lower lobe	-900.5 (24.7)	0.216	-0.680
Right lower lobe	-899.9 (24.2)	0.217	-0.759
Variance explained		**86.15%**	**7.93%**

Table 3: Results of the linear mixed models analysis: the table depicts the effect (β with 95% CI) of a unit change in each of the listed parameters on the FEV_1/FVC, FEV_1 and FVC values.

The e.g. FEV_1/FVC at a time point can be calculated using the following general equation: $FEV_1/FVC = \alpha + (x_1 * \beta_1) + (x_2 * \beta_2) + (x_3 * \beta_3) + \ldots + (x_i * \beta_i)$ and this results in the following equation for the FEV_1/FVC = 75 + (age*-0.15) + (height*0.03) + (BMI*0.18) + (observation time*-0.58) + (packyears*-0.05) - 3.68 (if continuous smoker) + (emphysema score*-4.38) + (distribution score*-1.00).

Parameter	**Unit change in parameter**	**Effect (β) on FEV_1/FVC [%] (CI 95%)**	**Effect (β) on FEV_1[mL] (CI 95%)**	**Effect (β) on FVC [mL] (CI 95%)**
Age [years]	increment: 1 year	-0.15 (-0.27 – -0.03)$^{\#}$	-36 (-45 – -27)$^{\wedge}$	-44 (-54 – -35)$^{\wedge}$
Height [cm]	increment: 1 cm	+0.03 (-0.12 – 0.07)^{NS}	+39 (32 – 47)$^{\wedge}$	+55(47 – 63)$^{\wedge}$
BMI [kg* m^{-2}]	increment: 1 $kg.m^{-2}$	+0.18 (0.02 – 0.38)^{NS}	+4.6 (-11 – 20)^{NS}	-8(-25 – 7)^{NS}
observation time	increment: 1 year	-0.58 (-0.71 – -0.45)$^{\wedge}$	-74 (-81 – -67)$^{\wedge}$	-20 (-33 – -6)*
packyears	increment: 1 packyear	-0.05 (-0.08 – -0.01)*	-5 (-8 – -3)$^{\wedge}$	-4 (-7 – -1)*
Smoking status	if continuous	-3.68 (-5.00 – -2.35)$^{\wedge}$	-134 (-238 – -31)$^{\#}$	-47 (-60 – 153)^{NS}
Emphysema severity (ES)	decrement: 1 point	-4.38 (-3.73 – -5.03)$^{\wedge}$	- 64 (-105 – -13)*	-165 (-217 – -112)$^{\wedge}$
Emphysema	decrement: 1 point	-1.00 (-0.37 – -1.64)*	-13 (-33 – -2)$^{\#}$	-50 (-90 – -10)$^{\#}$

distribution (ED)

[#] = p <0.05, * = p <0.01, ^ =p<0.001 and [NS] = p>0.05.

Figure 1: Illustration of a random CT scan with the lobe segmentation as it was performed by the software. The top row shows the original scan and the lower row the segmentation of the anatomical lobes.

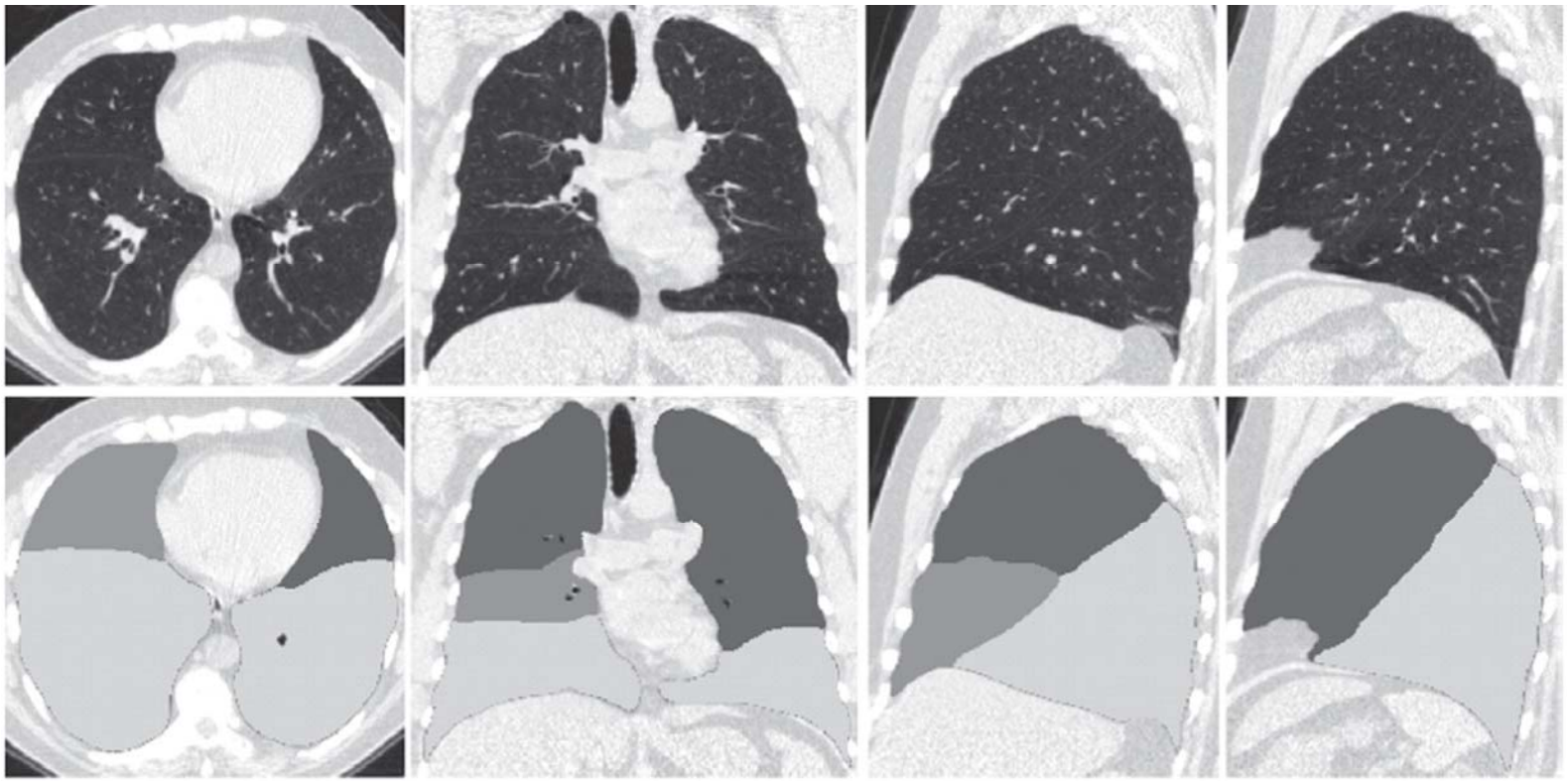
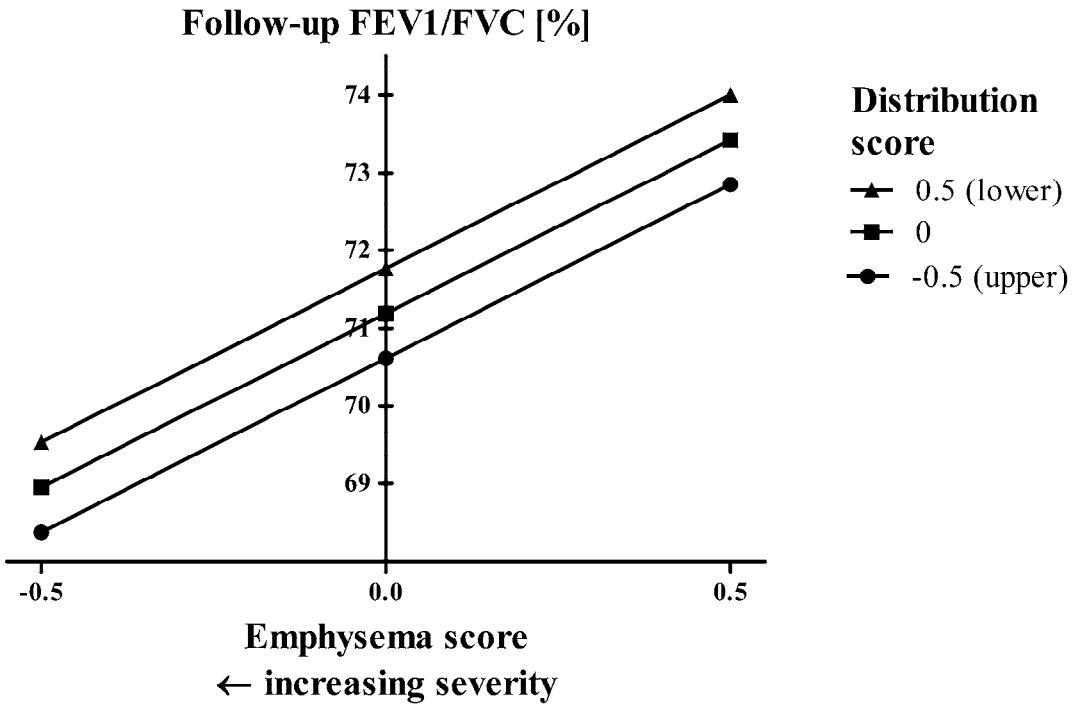


Figure 2: An illustration of the FEV_1/FVC [%] after 3-year of follow-up in a participant with a starting age of 60 years, height of 1.78 meters and 41 packyears, being the mean values of the cohort. The emphysema severity (ES) is depicted on the x-axis and the FEV1/FVC [%] after 3 years on the y-axis. It can be seen that a lower ES value results in a lower FEV_1/FVC [%] after follow-up. The graph is stratified by the value of the emphysema distribution (ED): -0.5; 0 and 0.5, being the first, second and third quartile, respectively. It shows that a lower ED value results in a lower FEV_1/FVC [%] after follow-up. For instance an individual with upper lobe emphysema (the line with the black circles) has a lower FEV1/FVC after follow-up than the individual with lower lobe emphysema (the line with the black squares) despite having a similar emphysema score (x-axis).


Follow-up FEV1/FVC [%]
74
73
72
71
70
69
-0.5
0.0
0.5
Emphysema score
← increasing severity
Distribution score
0.5 (lower)
0
-0.5 (upper)