Normal Range of Emphysema and Air Trapping on CT in Young Men

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OBJECTIVE. The purpose of our study was to assess the normal range of CT measures of emphysema and air trapping in young men with normal lung function.

MATERIALS AND METHODS. A cohort of 70 young men with high-normal spirometry and body plethysmography underwent paired inspiratory and expiratory CT. Visual and quantitative scores of emphysema and air trapping were obtained. On CT, emphysema was defined as the 15th percentile of the attenuation curve ($Perc_{15}$), and as the percentage of inspiratory voxels below −950 (IN_{-950}) and below −960 (IN_{-960}) HU. On CT, air trapping was defined as the expiratory-to-inspiratory ratio of mean lung density ($EI\text{-}ratio_{MLD}$), and the percentage of voxels below −856 HU in expiration (EXP_{-856}). Means, medians, and upper limits of normal (ULN) are presented for the total population and for smokers and nonsmokers separately.

RESULTS. The mean age (± SD) of the subjects was 36.1 ± 9.3 years. Smoking history was limited (range, 0–11 pack-years). Spirometry was high normal, ranging from 113% to 160% of predicted for vital capacity (VC), and from 104% to 140% of predicted for forced expiratory volume in 1 second (FEV_1). The ULN was 2.73% for IN_{-950}, 0.87% for IN_{-960}, −936 HU for $Perc_{15}$, 89.0% for $EI\text{-}ratio_{MLD}$, and 17.2% for EXP_{-856}.Visual CT scores showed minimal emphysema in eight (11%), > 5 lobules of air trapping in five (7%), and segmental air trapping in three (4%) subjects. CT measures were similar for never- and ever-smokers.

CONCLUSION. We report the normal range of CT values for young male subjects with normal lung function, which is important to define pulmonary disease.

Keywords: air trapping, CT, healthy subjects, pulmonary emphysema, quantitative assessment

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Visual and quantitative CT are increasingly used in research and clinical practice—including young individuals—and it is important to understand the range of normality to diagnose disease [1]. Quantitative CT has matured since it was introduced two decades ago [2], and it is commonly used in the assessment of emphysema and air trapping [3–5]. However, air trapping and emphysema can also be seen in nonsmokers and individuals without disease [6–9].

Furthermore, a limited bilateral subpleural reticular pattern, cystic airspaces, and increased bronchial wall thickness have been described as related to increasing age and independent of smoking history [10]. Parenchymal changes are also present in never-smoking men [11]. All these CT features may be part of the normal spectrum in smokers and lung aging. The normal spectrum of CT features in young men is not well known, and we had the opportunity to retrospectively analyze paired inspiratory and expiratory volumetric CT scans obtained in a population of young male subjects with normal lung function. Therefore, the purpose of this study was to assess the range of visual and commonly used quantitative CT measurements of emphysema and air trapping in a population of young men.

Materials and Methods

This study retrospectively evaluated clinically obtained CT data and was approved by the local ethical review board of the University Medical Center Utrecht. Written informed consent was waived.

Study Population

Recently, the Diving Medical Center (DMC) of the Royal Netherlands Navy, Ministry of Defense in The Netherlands treated six pulmonary barotraumas in professional military divers and submarine personnel. These subjects shared high-normal spirometric and body plethysmographic values, together with abnormalities found on chest CT (i.e., air trapping, blebs, and bullae). This initiated the clinical protocol as part of the annual diving examination, decided by the national military board, to evaluate all military divers and submariners with high-normal lung function values with inspiratory and expiratory chest CT to identify possible lung abnormalities and possibly prevent future pulmonary barotraumas.

For this descriptive study, we retrospectively collected the first 77 consecutive subjects who had been referred to our hospital by the DMC. Clinical examinations (i.e., CT and pulmonary function tests) were postponed when acute illness was present, and all investigations were performed in clinically stable subjects. The inclusion criteria for our analysis were an available volumetric inspiratory and expiratory chest CT, pulmonary function test results, demographic patient characteristics, and smoking history. Two subjects were excluded because of a failed expiratory CT. Another five subjects were excluded because of lung segmentation errors (described later). The final study population consisted of 70 subjects.

CT Protocol

Volumetric paired inspiratory and expiratory CT was performed in all subjects. CT examinations were performed using the same scanner (Brilliance 16P, Philips Healthcare) in a single center. Settings were 120 kVp at 130 mAs for inspiratory CT and 90 kVp at 20 mAs for expiratory CT in all subjects. Images were reconstructed with a slice thickness of 1 mm at 0.7-mm increments using a sharp reconstruction kernel (L- and E-filters, Philips Healthcare, for inspiratory and expiratory CT, respectively).

Quantitative CT Analysis

Quantitative measures were obtained after fully automatic segmentation of the lungs [12]. The segmentation process was visually checked in all subjects. As mentioned earlier, five subjects were excluded because of errors in the lung segmentation. Quantitative CT measures of pulmonary emphysema and air trapping were calculated in the segmented lung volumes. CT emphysema was defined as the percentage of voxels below −950 HU in inspiration (IN_{-950}) [13, 14], the percentage of voxels below −960 HU in inspiration (IN_{-960}) [15], and the 15th percentile of the attenuation curve in inspiration ($Perc_{15}$) [16, 17]. CT air trapping was defined as the expiratory-to-inspiratory ratio of mean lung density ($EI\text{-}ratio_{MLD}$) [18, 19] and the percentage of voxels below −856 HU in expiration (EXP_{-856}) [20]. Perc 15 is expressed in HU, all other quantitative measurements were expressed as a percentage. Calculations were performed after application of a noise reduction filter [21] to decrease the influence of image noise on the quantitative CT measurements.

Visual Assessment

All CT examinations were scored in consensus for the presence and extent of emphysema and air trapping by two observers with 10 and 2 years of experience in chest radiology. Emphysema was defined as focal regions of low attenuation [22], and scored as the percentage of lung parenchyma involved. Air trapping was defined as sharply demarcated areas of lung tissue with a lower than normal increase in attenuation and lack of volume reduction after expiration [22]. Air trapping extent was scored as the absolute number of secondary pulmonary lobules, segments, or lobes involved.

Pulmonary Function Testing

Pulmonary function was measured by qualified respiratory technicians using the Vmax Encore pulmonary function testing system (Cardinal Health), and performed according to the European Respiratory Society guidelines [23]. Calibration of the Vmax Legacy was performed according to the manufacturer's guidelines before every measurement. Reference values were calculated using validated prediction equations [24]. Vital capacity (VC), forced expiratory flow in 1 second (FEV_1), ratio of FEV_1 over forced vital capacity (FEV_1/FVC), forced expiratory flow at 50% of expiration (FEF_{50}), total lung capacity (TLC), and ratio of residual volume over TLC (RV/TLC) were measured. VC, FEV_1, FEF_{50}, and TLC were presented as percentage of predicted values and FEV_1/FVC and RV/TLC as percentages.

Data Analysis

The mean ± SD, median (25th–75th percentile), and 95th percentile (i.e., upper limit of normal) of the quantitative CT measures were calculated for the total study population as well as for smokers and never-smokers separately. The difference in visual emphysema presence between smokers and never-smokers was tested with the Fisher exact test. The difference in visual air trapping presence between smokers and never-smokers was tested with the chi-square test. The difference in extent of air trapping according to smoking status was tested with the Fisher exact test. A Mann-Whitney *U* test was used to test for differences in age between subjects with and without CT abnormalities. The association between smoking status and quantitative CT measurements was tested using the Mann-Whitney *U* test. A p value < 0.05 was considered significant. All statistical analyses were performed using SPSS statistical software version 15.0. Data are presented as mean ± SD unless indicated otherwise.

TABLE 1: Characteristics of the 70 Male Divers and Submariners

Parameter	Value
Age (y)	36.1 ± 9.3
Length (cm)	183 ± 6.6
BMI (kg/m^2)	26.2 ± 2.0
Smoking status	
Never-smokers	47 (67)
Smokers	23 (33)
Pack-years	
Never-smokers	
Smokers[a]	4.4 (interquartile range, 2.2–8.3)
Days between PFT and CT[a]	14 (interquartile range, 7–30)
Pulmonary function	
VC (% predicted)	129 ± 9
FEV_1 (% predicted)	125 ± 8
FEV_1/FVC %	76.6 ± 5.6
FEF_{50}, (% predicted)	105 ± 20
TLC (% predicted)	118 ± 10
RV/TLC (%)	21 ± 4

Note—Data are mean ± SD. Except where indicated otherwise, data in parentheses are percentages. BMI = body mass index, PFT = pulmonary function test, VC = vital capacity; FEV_1 = forced expiratory flow in 1 second, FEV_1/FVC = ratio of FEV_1 to forced vital capacity, FEF_{50} = forced expiratory flow at 50% of expiration, TLC = total lung capacity, RV/TLC ratio of residual volume to total lung capacity.
[a]Median (25th–75th percentile).

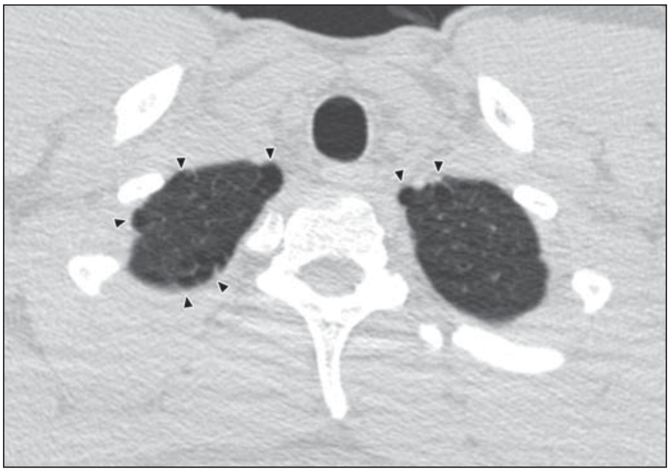

Fig. 1—Inspiratory CT scan of chest shows bilateral paraseptal emphysematous lesions in lung apices (*arrowheads*) seen as focal regions of low attenuation in 35-year-old man who is current smoker with 4.4 pack-years of smoking history.

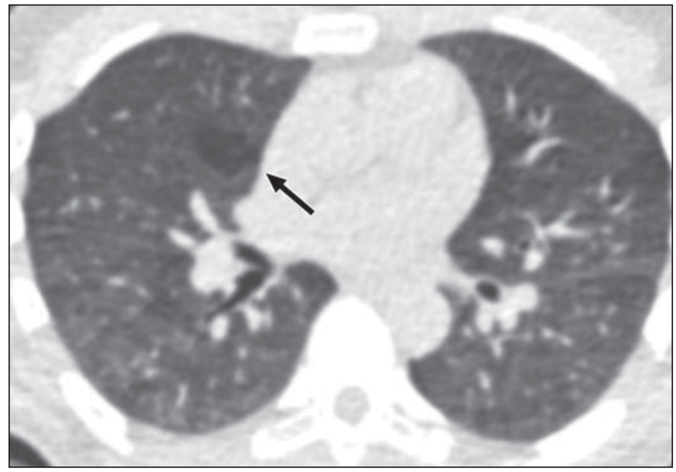

Fig. 2—Expiratory CT image of chest shows lobular air trapping in right upper lobe (*arrow*) in 45-year-old man who is never-smoker.

Results

Study Population

Our study population contained 70 male subjects, with a mean (± SD) age of 36.1 ± 9.3 years (range, 19–53 years). Forty-seven (67%) were never-smokers, and 23 (33%) were current or ex-smokers, with a median of 4.4 pack-years (range, 0.2–11.0 pack-years). Study population characteristics and pulmonary function data are presented in Table 1.

Visual Assessment

Eight subjects (11%) had a few lobules with minimal centrilobular or paraseptal emphysema; less than 1% of total lung parenchyma was involved in all (Fig. 1). The prevalence of emphysema was similar between smokers and never-smokers ($p = 0.42$). Air trapping was detected in 56 subjects (80%), of whom 55 (98%) showed lobular air trapping (Fig. 2). Three subjects showed segmental air trapping (Fig. 3), which was additional to lobular air trapping in two. The median number of lobules involved was two, with 14 subjects showing more than three lobules and five subjects showing more than five lobules. The presence and amount of lobular air trapping were not different between smokers and nonsmokers ($p > 0.26$). Segmental air trapping was only found in smokers ($p = 0.03$). We did not find an association between age and CT abnormalities. The complete results of visual scoring are summarized in Table 2.

Fig. 3—Expiratory CT image of chest shows segmental air trapping in right middle lobe (*arrowheads*) in 47-year-old man who is former smoker with 3.0 pack-years of smoking history.

Quantitative Analysis

Results for the quantitative assessment of CT emphysema and CT air trapping are summarized in Table 3. The upper limits of normal for CT emphysema are 2.73% for IN_{-950}, 0.87% for N_{-960}, and −936 HU for $Perc_{15}$. The upper limits of normal for CT air trapping are 89.0% for $EI\text{-}ratio_{MLD}$ or 17.2% for EXP_{-856}. Results for quantitative CT measurements were not significantly different according to smoking status. A possible pattern of higher lung density values in smokers was seen, although this did not reach statistical significance.

Discussion

In this study, we present the range of visual and quantitative CT emphysema and CT air trapping measurements in a population of young men. Because little is known regarding the normal range of imaging in such a population, reporting the range of CT features in these subjects is important. Knowledge of the results of visual and quantitative CT measures may be useful in establishing the normal spectrum and help in the detection of disease at an early stage.

Quantitative CT emphysema and air trapping are surrogate measures of disease. On the basis of the correlation between disease parameters and lung density, a continuous radiologic measure is calculated. Therefore, there is not a strict binominal distribution of presence and absence. Accordingly, we showed that in a healthy population a low percentage of lung voxels show attenuation below the CT emphysema threshold. The presence of disease can be regarded as a value beyond the upper limit of normal in the healthy population. However, it is important to note that densitometry values can be affected by biologic and technical factors—for example, interstitial lung disease, contrast medium injection, reconstruction algorithm, CT scanner, and radiation dose. Ideally, with current technology, quantitative reference values should be obtained for each CT protocol individually.

TABLE 2: Visual Scoring for Emphysema and Air Trapping in Young Male Subjects With Normal Spirometry

Parameter	All ($n = 70$)	Never-Smokers ($n = 47$)	Smokers ($n = 23$)	p
CT emphysema				
Extent < 1%	8 (11)	4 (9)	4 (17)	NS
CT air trapping				
Present	56 (80)	37 (79)	19 (83)	NS
Lobular air trapping	55	37	18	NS
Lobules involved[a]	2 (interquartile range,1–4)	2 (interquartile range, 1–4)	1 (interquartile range, 1–3)	NS
Segmental air trapping	3	0	3	0.03

Note—Except where indicated otherwise, data in parentheses are percentages. NS = not significant.
[a]Median (25th–75th percentile).

Regarding quantitative CT measures, no studies were found that assessed the range of quantitative CT air trapping measures in healthy men, and few studies were found on the normal range of quantitative emphysema measures. Marsh et al. [25] evaluated 185 never-smoking subjects without respiratory disease (age 25–75 years) and calculated IN_{-950} in three slices in the upper part of the lungs. They found a median of 1.4% (interquartile range 0.6–2.9) for all three slices, which is somewhat higher than our 0.59% (interquartile range 0.28–1.30). Irion et al. [26] evaluated 30 young nonsmoking subjects (age 19–41 years) who were scanned to rule out lung disease and calculated IN_{-950}. They found a mean and 95th percentile of 0.19% and 0.35%, respectively. These values are lower than our 0.97% and 2.73%, even though they performed low-dose scanning without noise filtering. Differences in study populations, slice thicknesses, and CT protocols may have contributed to the differences in results. Nevertheless, the observed differences are small, and all studies, including ours, indicate that a low percentage of CT emphysema is found in healthy subjects.

Regarding visual scores, several studies in healthy subjects have been reported; however, none of these studies obtained volumetric CT data. Nevertheless, our finding that lobular air trapping is visually present to some extent in the majority of healthy subjects is in line with previous results [6–9], and we correspondingly did not find a difference in the presence of lobular air trapping between nonsmokers and smokers [6, 8]. In 250 volunteers, Mastora et al. [6] showed that segmental air trapping is more frequently seen in smokers, a finding that is supported by our data. One finding we could not replicate was a significant increase in air trapping extent with increasing smoking history [6, 7, 9]. This difference may be explained by the very low smoking history of our subjects, which is different from previous studies in which smoking history was substantial.

Smoking has to be taken into account when studying chest CT abnormalities. Apart from its association with air trapping and emphysema, smoking has other effects in the lung. It has been shown that areas of ground-glass attenuation and ill-defined micronodules are related to smoking and are common findings in smokers [11, 27, 28]. These inflammatory changes of the lung may raise the lung density and thereby mask pulmonary emphysema, a process that is supported by the fact that smoking cessation leads to a paradoxical decrease in lung density (increase of emphysema) [29]. In the current study, we found slightly higher lung density in smokers, although it did not reach statistical significance. This may well be due to the minimal smoking history and relatively small number of subjects in our study population.

Recently the effect of aging on the lung has received considerable attention, and aging has been shown to induce lung changes. Copley et al. [10] showed significant differences in CT features between younger and older individuals. Those authors showed that bronchial dimensions, air cysts, and limited subpleural reticular patterns were significantly more frequent in subjects more than 75 years old. Vikgren et al. [11] correspondingly showed that bronchial altera-

TABLE 3: Quantitative CT Measures for Emphysema and Air Trapping in Young Male Subjects With Normal Spirometry

Parameter	IN_{-950}	IN_{-960}	$Perc_{15}$	EXP_{-856}	$EI\text{-}Ratio_{MLD}$
All ($n = 70$)					
Mean ± SD	0.97 ± 1.10	0.35 ± 0.33	−919 ± 13	5.12 ± 7.98	76.2 ± 7.3
Median	0.59	0.25	−921	3.22	76.4
25th–75th Percentile	0.28–1.30	0.13–0.51	−913 to −929	0.69–6.23	70.1–81.3
95th Percentile	2.73	0.87	−936	17.2	89.0
Never-smokers (n = 47)					
Mean ± SD	1.11 ± 1.26	0.38 ± 0.36	−921 ± 12	5.86 ± 9.13	76.5 ± 7.4
Median	0.68	0.27	−921	3.57	76.4
25th–75th Percentile	0.28–1.98	0.14–0.57	−915 to −930	0.79–6.25	70.2–81.2
95th Percentile	3.21	1.13	−937	28.2	90.5
Smokers ($n = 23$)					
Mean ± SD	0.69 ± 0.62	0.27 ± 0.22	−917 ± 13.7	3.62 ± 4.68	75.6 ± 7.0
Median	0.52	0.19	−920	1.12	76.3
25th–75th percentile	0.15–1.13	0.08–0.35	−909 to −928	0.17–5.21	69.9–81.4
95th Percentile	2.31	0.80	−933	17.6	89.1
p[a]	0.18	0.24	0.12	0.18	0.65

Note—IN_{-950} = emphysema score below −950 HU in inspiratory scan, IN_{-960} = emphysema score below −960 HU in inspiratory scan, $Perc_{15}$ = emphysema score as 15th percentile of attenuation distribution curve on inspiratory scan, EXP_{-856} = air trapping score below -856 HU in expiratory scan, E/I-$ratio_{MLD}$ = expiration-to-inspiration ratio of mean lung density,
[a]Comparison between smokers and never-smokers.

tions, septal lines, areas of ground-glass attenuation, and subpleural and parenchymal nodules are to some extent considered normal in men approximately 60 years old and that apart from emphysema none of the CT features was pathognomonic for smoking-induced disease [11].

That we did find emphysema in both smokers and nonsmokers, in contrast to previous reports, is likely due to our volumetric scanning technique. Lesions were often single and all very small. Thus, they can be easily missed when nonvolumetric scanning is applied. Lee et al. [7] showed that, in addition to parenchymal changes, the frequency and extent of air trapping also increase with age. We did not find a relationship between age and CT abnormalities, which is most likely due to the age-distribution of our study population, with more than 75% of the subjects under 45 years old.

The strength of our study is that it provides reference values for several quantitative CT measures in young men and we used a single CT scanner to perform volumetric scanning in both inspiration and expiration. A limitation of our study is that the study population consists of healthy military divers and submariners with high-normal lung function, representing the healthy worker employed by the military. The larger lung volumes may produce lower density values, and therefore our measurements might overestimate, but certainly do not underestimate, the normal limits. Furthermore, inherent to current CT technology, the quantitative measures can differ according to the noise-filtering, data reconstruction, and CT scanner used. Differences in scanning parameters should be carefully ascertained before generalizing quantitative results.

In conclusion, we have shown the normal spectrum for visual and quantitative CT measurements of emphysema and air trapping in a population of young male subjects with normal pulmonary function tests. These data are important to define disease in subjects with corresponding age and sex.

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