Distribution of Lung Density and Mass in Patients With Emphysema as Assessed by Quantitative Analysis of CT*

Manadou Haua Hann Diallo, MD; Hervé Guénard, MD; François Laurent, MD; Pierre Carles, MD, FCCP; and Jacques Giron, MD

Study objective: To assess the effects of emphysema on the apex-to-base gradient of lung density (D) and lung mass (M) and to explore the relationship between M and lung function.

Methods: CT scans of whole lungs were performed in 12 healthy subjects and 29 patients who were breathing at functional residual capacity, after which lung function tests were performed. Whole D and M and regional D (RLD) and M (RLM) were calculated. The degree of emphysema was scored.

Results: The RLM for each height did not differ significantly between patients with disease and healthy subjects, while RLD was significantly lower in the patients with disease. A less marked nonlinear, increasing, craniocaudal gradient of D was observed in the group with disease, suggesting that the distension increases progressively from the apex to the base. RLD and RLM in the 40 to 90% lung height differed significantly among patients in the emphysema group with normal, high, and low M compared to the healthy subjects. M did not differ significantly between patients with centrilobular and panlobular emphysema, which was thought to stem from the marked variations in the results. Vital capacity was lower in the patients with low M.

Conclusions: The lower RLD in the group with low M was due to both lung overinflation and to tissue loss, while in the groups with high or normal M, it was due only to lung overinflation.

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Key words: emphysema; lung density; lung mass; pulmonary function

Abbreviations: CLE = centrilobular emphysema; Cqs = quasistatic compliance; D = lung density; Dlco = single-breath diffusing capacity of the lung for carbon monoxide; Do = predicted lung density at predicted functional residual capacity; Dv = density of biological material as measured by water displacement; Ed = degree of emphysema; FRC = functional residual capacity; FRCo = predicted functional residual capacity; HRCT = high-resolution CT; HU = Hounsfield units; M = lung mass; MANOVA = multivariate analysis of variance; ME = mixed emphysema; Mref = predicted lung mass at predicted functional residual capacity; Mw = mass of biological material as measured by water displacement; NS = not significant; PLE = panlobular emphysema; Raw = airway resistance; RLD = regional lung density; RLM = regional lung mass; RV = residual volume; SLD = severity of lung destruction; TLC = total lung capacity; Vair = regional lung air volume; VC = vital capacity; Vlw = volume of biological material as measured by water displacement; Vtiss = lung tissue volume; Xt = extent of emphysema

Emphysema is an anatomic disorder. Morphologic and functional changes develop in relation with the severity of the disease and affect the four major components of the lung, mainly pulmonary air and tissue volumes, but also interstitial fluid and blood volumes. At the onset of the disease, the mean linear intercept increases with lung distension, whereas lung tissue volume (Vtiss) and lung mass (M) change little. In an animal model of emphysema, M was only observed to increase sharply after a long interval, exceeding baseline M by 26%. CT scans of the lung have revealed an increase in whole M in cases of human emphysema, although subsequent analyses of subgroups of patients indicated that normal M or even loss of M was not uncommon in this condition. The decrease in lung density (D) may be related to a change in the volume of air, or in the mass of tissue, or a combination of

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both. Thus, there appears to be a wide range of alterations in M and D in these patients, reflecting variations in lung structure in emphysema. In view of the interdependence of M and mechanical behavior of the lung,7 alterations in regional D (RLD) or whole D may well have an impact on lung function.

In the lung, the craniocaudal gradient of D has been attributed to differences in regional blood volume and gas volume, which in turn are determined by gravity, mechanical stresses, and intrapleural pressures.7,8 The gradient of D is higher when the subject is in the vertical rather than in the supine position. In emphysematous lungs, in addition to the redistribution of lung air and blood content, the severity of the tissue destruction may be an important additional factor of this posture-related gradient of D. From a study of regional lung compliance,9 it has been shown that the vertical gradient of D observed in emphysematous lungs is related to a change in local compliance, indicating that this gradient has both tissue and hydrostatic components. Although there are numerous reports on the ventrodorsal gradient of D, few studies have been devoted to the craniocaudal density gradient of human lungs in subjects with emphysema.9 To our knowledge, the interrelationship between both the severity and extent of emphysema (Xt) and the distributions of tissue mass and air volume in this gradient have not been investigated previously.

The aims of the present study were the following: (1) to assess the craniocaudal distribution of D as well as its determinants as measured in patients with emphysema while in the supine posture and in a group of healthy subjects; (2) to relate alterations in D to either distension or to changes in M; and (3) to correlate these alterations with lung function as well as with indexes of the degree of emphysema (Ed).

**Materials and Methods**

**Patient Selection**

Twenty-nine patients in stable condition (27 men, 2 women) with mild-to-severe emphysema (mean age, 55 years; age range, 40 to 70 years) and 12 healthy subjects (mean age, 38 years; age range, 26 to 50 years) devoid of pulmonary disease who gave their informed consent were included in the study. Only patients showing macroscopic emphysematous lesions on high-resolution CT (HRCT) images were retained for the study. Screening clinical and functional examinations preceded CT studies of the lungs. Those examinations showing reversible airflow (eg, an increase in FEV1 of >15% during bronchodilator tests) were excluded.

**Pulmonary Function Testing**

Thoracic gas volume at functional residual capacity (FRC) was measured by means of a body plethysmograph (constructed in the laboratory) using the occlusion technique, followed by full inspiration to total lung capacity (TLC) and subsequent expiration to residual volume (RV). Vital capacity (VC), TLC, RV, and the RV/TLC ratio were computed. The study was completed by three FVC maneuvers with display of flow-volume loops. The best loop based on the best sum (FEV1 + FVC) was retained. The FEV1/FVC ratio was calculated. Airway resistance (Raw) during panting, and quasi-static, transpulmonary pressure-volume curves were obtained using the integrated signal from a pneumotachograph at the mouth, while esophageal pressure was measured by an esophageal balloon, during slow exhalation from TLC. Quasi-static compliance (Cqs) was taken as the slope of the quasi-static transpulmonary pressure-volume curve between FRC and FRC + 0.5 L. Measurements of the single-breath diffusing capacity of the lung for carbon monoxide (DLco) yielded values of the lung transfer factor for carbon monoxide (MasterLab; Jaeger; Wurzberg, Germany). All results were expressed as percent predicted, using the reference values (Table 1).11 PaO2 and PaCO2 were measured on a sample of arterial blood (Corning 168; Chiron; East Walpole, MA).

**CT Study**

**Physical Parameters and Procedures:** Lungs were all scanned lengthwise in both conventional (ie, 120 kV, 100 mA) and high-resolution mode (ie, 137 kV, 255 mA) using a fourth-generation rotating device (Somatom DRH; Siemens; Erlangen, Germany) with a 4-s scanning time. The device was calibrated every 7 h using an air phantom. The ability of this system to accurately measure D, volume, and mass was ascertained by scanning standard phantoms of various densities ranging between air and water (Appendix I).

The subjects underwent scanning at their FRC using a homemade gating device. Contiguous 8-mm-thick scans were obtained from the apex to the base of the lungs by incremental movement of the scanning table, the position of which could be specified and read with an accuracy of ±0.5 mm (SD). Scans of 1-mm thickness were obtained at the same imaging session at 10-mm intervals. Images were analyzed using a 350-mm field of view and a 256 × 256 reconstruction matrix in conventional mode. In high-resolution mode, a 240-mm field of view, 512 × 512 reconstruction matrix, and a high spatial-frequency algorithm were used. All images were obtained at window widths and levels for the appropriate enhancement of parenchymal structures. The type of emphysema was determined by the results of previous studies from the HRCT images12 and was referred to as centrilobular emphysema (CLE), panlobular emphysema (PLE), or mixed emphysema (ME), when both types were present in the lung.

**Data Analysis and Regional Parameters:** For the calculation of individual scan density and mass, thick scan images were displayed on the screen and were processed via a computer linked on-line with the display screen. A fast contour detection program using a high-frequency algorithm automatically rejected high-density hilar structures and isolated pulmonary tissue on each individual scan. The regional radiologic density and volume of the enclosed area on individual images were determined using the dedicated software. Twenty-five to 35 images were processed in this fashion for the left and right lungs. Regional Hounsfield units (HU) were converted later into regional physical density from the linear relationship between density and HU12,13,14 over the range between air (−1,000 HU) and water (0 HU). Regional M (RLM) was calculated from each individual scan image as RLD times every 7 h using an air phantom. The ability of this system to accurately measure D, volume, and mass was ascertained by scanning standard phantoms of various densities ranging between air and water (Appendix I).

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assuming that the density of the parenchyma alone was equal to unity; ie, that the regional Vtiss was equal to the RLM irrespective of units:

\[ V_{airr} = V_{tissr} \left(1 - \frac{RLD}{RLD}\right), \]

where \( V_{airr} \) is regional lung air volume and \( V_{tissr} \) is regional lung tissue volume. To allow comparison of the distributions of RLD and RLM over total lung height between healthy subjects and patients, 8-mm-thick scans were sampled from apex to base at approximately 10% height spacings. Therefore, only about 30% of the scans were taken into account. The first and the last scans were added to the previous nine scans so as to fit the total height of the lungs. The origin of the left pulmonary artery was used as an anatomic marker to divide the lungs into apex and base scans. This corresponded closely to the 50% of the apex-to-base distance of the lungs in patients with emphysema. Therefore, the scans between 0% and 50% apex-to-base distance were assigned to the apex, and those between 60% and 100% were assigned to the lung base.

**Analysis of the Patient Groups**

Patients were classified into three groups according to the ratio of total M to predicted M at predicted FRC (FRCo) (\( M_{ref} \)) (ie, the M that a subject should have with FRCo and with the predicted D at FRCo [Do]): The Do was determined from the mean D at FRCo in healthy subjects, and the FRCo was determined from reference values.\(^1\)\(^1\) Using the Do and the FRCo, we calculated the \( M_{ref} = \left[FRCo \left(Do/(1 - Do)\right)\right] \) (see Appendix 2). Patients were assigned to one of three groups according to their \( M/M_{ref} \) ratio. Patients with \( M/M_{ref} \) ratios > 1.12 were considered to have high M, those with \( M/M_{ref} \) ratios of < 0.92 were considered to have low M, and those with \( M/M_{ref} \) ratios within the 1.12 to 0.92 range were considered to have a normal M. These \( M/M_{ref} \) ratios were chosen so as to obtain three groups of nearly equal size. The RLD, RLM, and \( V_{airr} \) in patients with high, low, and normal M and in the healthy subjects were plotted against lung height at 10% spacing from apex to base.

**Quantification of the Ed**

To calculate the Ed, the severity of lung destruction (SLD) and the Xt were quantified on the basis of the previously selected 8-mm-thick scans, using a small grid and the direct observational method of Sakai et al.\(^1\)\(^8\) Both SLD and Xt were quantified by two observers. Twenty-two scans of the right and left lung were read for SLD and Xt in each patient. Briefly, the Xt on each scan was measured by overlaying a small plastic grid on the CT images as the count of the squares falling on emphysematous surface area relative to the surface area of the whole scan under consideration. The data were expressed as the percentage of lung involvement and were converted later to numeric values of \( 1 \) (< 25% involvement), \( 2 \) (25 to 50% involvement), \( 3 \) (50 to 75% involvement), and \( 4 \) (> 75% involvement). The SLD was read directly from the CT images and also was scored on four levels (0 to 3). Final scores were recorded by consensus between the two readers. The SLD and the Xt were mixed according to the method of Sakai et al\(^1\)\(^8\) to provide an index of the Ed.

**Data Analysis**: Data were analyzed using a standard statistical package (NCSS6.0; Statistical Solutions Lim; Cork, Ireland). Whole M, D, and lung function were tested and compared between healthy subjects and patients with emphysema using the nonpaired \( t \) test. Intragroup and intergroup differences in lung function and also differences in the Ed, RLD, RLM, and \( V_{airr} \) in the three groups of patients with emphysema and in healthy subjects were assessed by multivariate analysis of variance (MANOVA) for two factors; first, for the craniocaudal lung height and second, at each given 10% level of this craniocaudal distance. Once the MANOVA test found a term significant, a univariate analysis of variance was used to determine which of the variables and factors were responsible for the significance. The differences among the groups then were assessed using Fisher’s Exact Test least significant difference multiple-comparison procedure. The correlations between whole D and whole M, and between whole M and RLM for a given lung height, were analyzed to assess the specific effect of M found on apex or base scans on the increase or decrease in M. The correlations between the radiologic and the functional data and between RLM and Ed were tested in the total patient population. In all cases, the level of significance was set at 0.05.

**Results**

\( M \) and \( D \)

Patients had CLE (\( n = 15 \)), PLE (or base-dominant lesions in one ZZ patient \( n = 10 \)), or ME (\( n = 4 \)). There were seven patients with CLE and four patients with PLE in the group with high M; six patients with CLE, one patient with PLE, and three patients with ME in the group with normal M; and two patients with CLE, five patients with PLE, and one patient with ME in the group with low M. The mean (± SD) M was greater in patients with CLE than in those with PLE both in the group with high M (CLE, 1,302 ± 148 g; PLE, 1,273 ± 196 g) and in the group with low M (CLE, 906 ± 277 g; PLE, 813 ± 175 g) without reaching a significant level.

The mean D was significantly lower in the group with emphysema (0.209 ± 0.048 g/mL; \( p < 0.001 \)) than in healthy subjects (0.322 ± 0.062 g/mL). The mean M, although higher in the group with emphysema (1,084 ± 238 g), did not differ significantly from that in healthy subjects (987 ± 202 g). Of the 29 emphysema patients, 11 had normal M, 10 had high M, and 8 had low M. The right lung was heavier than the left lung, although the difference was not significant (NS) either in the group of healthy subjects or in the group of patients with emphysema.

The correlation between D and M was significant in the group of patients with emphysema (\( D = 0.074 \times M [kg] + 0.128 \) \( r = 0.379; \ p < 0.05 \) but was not in healthy subjects.

RLM did not differ significantly between the healthy subjects and the patients with emphysema (Fig 1, top, a). However, RLDs at each 10% of lung height of the apex-to-base distance were significantly lower in the group of patients with emphysema (Fig 1, bottom, b) than in the healthy subjects.

Excluding the first scan, the gradient of D vs height from the apex to the base could be split into the following two parts: one part nearly flat, and the other part steeper in the bases (Fig 1, bottom, b).
The slope of the regression line of RLD as a function of lung height (percentage) was significantly (p < 0.05) different from zero in the group of healthy subjects but not in the group of emphysema patients in the upper two thirds of the lung (0 to 70% height). In the lower third (70 to 100% height), the gradient of RLD was 20% higher in the healthy subjects compared to the group of emphysema patients, and the slopes of the regression lines, RLD as a function of lung height percentage, differed significantly from zero both in the group of emphysema patients (p < 0.05) and in the group of healthy subjects (p < 0.02). The absolute difference in D between the healthy subjects and the emphysema patients (right-side axis) was shown as a linear regression line of increasing gradient of D toward the bottom of the lung.

To discern the position in the lung in which differences in RLM might account for the overall differences in whole M between patients, linear regression between RLM for a given height and whole M were calculated. The slopes of the regression lines increased from top to bottom, as shown at 20% and 60% lung height (Fig 2, bottom, b, and top, a, respectively). Slopes were different from zero from 30 to 90% lung height and increased significantly and progressively from 1.6 to 4.9% at 30% and 90% lung height, respectively.

**RLM, RLD, and Vairr**

The mean differences of RLM (Fig 3, top, a), RLD (Fig 3, middle, b), and Vairr (Fig 3, bottom, c) between healthy subjects and patients with emphysema, and among the emphysema patient groups, at each 10% spacing level in the overall lung height can be seen in Figure 3. The shape of the distributions of RLM, RLD, and Vairr over the total lung height was similar in the healthy subjects and in the three groups of emphysema patients. The maximal values of RLM were observed at 80% height in the three groups of emphysema patients; the maximum volume of Vairr was observed at about 50% lung height (Fig 3, top, a, and bottom, c, respectively).

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The Ed in the Apex-to-Base Distance

The average Ed was significantly (p < 0.05) lower in the group with high M (1.065 ± 0.66) than in the groups with low M (1.41 ± 0.63) and normal M (1.49 ± 0.66). There were significant (p < 0.001) negative correlations between Ed and the percent of lung height in the groups with high and normal M (Fig 4), while a positive correlation was noted in the group with low M. At each height, regression equations of RLM and RLD vs Ed were calculated in the total patient population. All regression equations, except the one for the first apex scan, had negative and significant slopes (p < 0.001). Slopes increased from the apex to the base, although the data were more scattered at the base. There was no significant correlation between RLD and Ed.

Functional Data

In healthy subjects, there were significant correlations between M and height (r = 0.692; p < 0.05) and between D and Raw (r = −0.609; p < 0.05). In the whole group of patients with emphysema, M was correlated significantly with height (r = 0.468; p < 0.02) and FEV₁ (r = 0.393; p < 0.05), while D was correlated with FEV₁ (r = 0.476; p < 0.01), FEV₁/FVC ratio (r = 0.608; p < 0.01), and RV/TLC ratio (r = −0.495; p < 0.02). The striking difference among the groups of patients with emphysema (Table 2) was in VC. There were significant differences in VCs among the three groups (Table 2). The group with low M had lower than normal VC, while VC was close to normal in the group with high M and was in

Figure 3. Plot of the distributions of RLM, RLD, and regional air volume in the three groups of emphysema patients and in healthy subjects for overall lung height. Data and mean (± SD) values of RLM (top, a), RLD (middle, b), and regional air volume (bottom, c) are indicated for the groups of emphysema patients with high M (○), normal M (◇), and low M (□) and for healthy subjects (●). * = significance (p < 0.05) determined by the MANOVA test when at least one group differs from the others (see “Data Analysis” section).

Figure 4. Relationship between the Ed and lung height with the regression lines to the data in the groups of emphysema patients with high M (○, dotted line), normal M (◇, long dashed line), and low M (□, solid line). Note that all the regression lines were significant but with negative slopes for the groups with high M and normal M and with a positive slope for the group with low M.
the normal range in the group with normal M. Distension (high RV) and obstruction (low FEV1/FVC ratio) were more marked in patients in the group with low M, who had, however, normal pulmonary compliance. The decrease in VC was correlated significantly with the resultant following four factors: low FEV1/VC ratio and body weight; and high RV and Raw. DLCOsb and PaO2 did not differ among the groups. The group with low M thus appeared to exhibit a stepwise trend in the alteration of lung function.

**DISCUSSION**

The main findings of this study are the following: (1) the significant positive correlation between D and M in patients with emphysema, the average M not being different from that in the healthy subjects; (2) an increased difference in the apex-to-base gradient of D in patients with emphysema compared to the healthy subjects; (3) the lower RLD observed in patients with normal and high M compared to the healthy subjects was a result of distension (i.e., an increase in regional air content), whereas in the patients with low M, lower RLD stemmed from both distension and loss of lung tissue; (4) the alterations in whole M in the patients with low and high M were a result of alterations in RLM in the bases but not in the apices; and (5) Ed was more severe in the patients with low M, which is in agreement with the fact that RLM, regardless of height, was negatively correlated with Ed.

Table 2—Anthropometric, Radiologic and Lung Function Data in Groups of Patients With Emphysema*

<table>
<thead>
<tr>
<th>Data</th>
<th>Low M</th>
<th>Normal M</th>
<th>High M</th>
<th>p Value</th>
</tr>
</thead>
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<tr>
<td>Age, yr</td>
<td>63 ± 19</td>
<td>52 ± 13</td>
<td>52 ± 13</td>
<td>NS</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>52 ± 10</td>
<td>67 ± 11</td>
<td>58 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>Height, cm</td>
<td>168 ± 7</td>
<td>170 ± 7</td>
<td>170 ± 9</td>
<td>NS</td>
</tr>
<tr>
<td>M, g</td>
<td>822 ± 126</td>
<td>1,051 ± 181</td>
<td>1199 ± 205</td>
<td>&lt; 0.05</td>
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<tr>
<td>D, g/mL</td>
<td>0.196 ± 0.065</td>
<td>0.198 ± 0.037</td>
<td>0.234 ± 0.023</td>
<td>NS</td>
</tr>
<tr>
<td>Raw, kPa/Ls/s</td>
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<td>0.27 ± 0.08</td>
<td>0.38 ± 0.24</td>
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</tr>
<tr>
<td>FEV1/FVC % pred</td>
<td>61 ± 22</td>
<td>65 ± 14</td>
<td>72 ± 20</td>
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<tr>
<td>FRC, % pred</td>
<td>129 ± 37</td>
<td>141 ± 30</td>
<td>137 ± 33</td>
<td>NS</td>
</tr>
<tr>
<td>RV, % pred</td>
<td>160 ± 58</td>
<td>155 ± 55</td>
<td>141 ± 39</td>
<td>NS</td>
</tr>
<tr>
<td>VC % pred</td>
<td>66 ± 24</td>
<td>117 ± 22</td>
<td>85 ± 22</td>
<td>&lt; 0.02</td>
</tr>
<tr>
<td>L</td>
<td>2.66 ± 0.69</td>
<td>5.11 ± 1.26</td>
<td>3.44 ± 0.99</td>
<td>&lt; 0.005</td>
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<tr>
<td>Gs, L/kaPa</td>
<td>2.61 ± 0.69</td>
<td>5.67 ± 2.70</td>
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<td>NS</td>
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<tr>
<td>DLCOsb, % pred</td>
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<tr>
<td>PaO2, kpa</td>
<td>5.43 ± 0.63</td>
<td>5.30 ± 1.39</td>
<td>5.36 ± 0.66</td>
<td>NS</td>
</tr>
<tr>
<td>PaCO2, kpa</td>
<td>5.43 ± 0.63</td>
<td>5.30 ± 1.39</td>
<td>5.36 ± 0.66</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Values given as mean ± SD. See Table 1 for abbreviations not used in text.
**Whole M and D**

In a previous study including 24 patients, we found a slightly but significantly greater M in patients with emphysema than in healthy subjects. In the present study, which includes more patients, the difference in M between the group of patients with emphysema and the healthy subjects was NS. The interesting point is that M was not reduced in most patients with emphysema, which might be expected from the definition of emphysema as a destructive process, which suggests a loss of tissue (i.e., a loss of mass). Overall M in patients with pulmonary emphysema results from the balance between lung destruction and secondary healing or remodeling.\(^{16,17}\) This would indicate that lung remodeling outweighs lung destruction in the emphysema patients with relatively high M, and vice versa for the patients with low M. Therefore, M might represent a useful index of the following two types of emphysema: one that is mostly destructive with little remodeling and light lungs (low M); and the other dominated by the remodeling process with heavy lungs (high M). In healthy subjects, at a given lung volume (i.e., at FRC), D is constant regardless of M (i.e., the volume of air is directly proportional to M). In patients with emphysema, the decrease in D with M cannot be wholly attributed to the decrease in M, as the slope of the D = f(mass) relationship was too low, but, rather, it suggests that patients with low M have lungs that are relatively more distended than those in patients with high M. Since D depends directly on lung volume, our emphysema patients and healthy subjects all underwent CT scanning at end-expiratory level (i.e., at FRC).

With the subject in the supine position, FRC tends to be lower than when the subject is in the sitting position by several hundred milliliters in healthy individuals, depending on the displacement of the abdominal contents toward the thorax. In emphysema patients, FRC in the supine position is less likely to change, owing to their distension and/or obstruction. This would have enhanced slightly the observed difference in D between the healthy subjects and the emphysema patients.

**RLD and RLM as a Function of Lung Height Percentage (Healthy Subjects vs Emphysema Patients)**

The means of the distributions of RLM with lung height were comparable in the healthy subjects and in the group of patients with emphysema, suggesting that the balance between destruction and remodeling was the same throughout the emphysematous lungs. The shape of the distribution of RLD with lung height (Fig 1, top, a) in emphysema patients resembled that of healthy subjects, albeit shifted downward. Excluding the uppermost part of the apex, the distribution of RLD in healthy subjects in the craniocaudal axis appeared nonlinear, increasing slightly from the top to the hilum, and sharply from the hilum to the base. This increase in RLD with height in the base could be due to alterations in parenchymal or blood masses. In the supine position, as when standing, the lung is subjected to gravity,\(^{7,9}\) and the weight of the posterior parts of the bases will stress both the anterior part of the bases and the apices. Furthermore, in the supine position, the stress in the bases will be reduced by the abdominal mass, displacing the lung toward the apex, thereby reducing the volume of air in the bases and increasing its density. Blood volume also would be expected to be greater in the underhanging part of the lung (i.e., the posterior parts of the bases).\(^{18,19}\) Independently of the greater vascularization and higher capillary density of basal lung regions compared to the apex,\(^{19,20}\) distension in the supine position would tend to attenuate the gradient in patients with emphysema (Fig 1, bottom, b), as it would in healthy subjects during inspiration. This interpretation is supported by the fact that Vairrs were increased in all compartments in the three diseased groups (Fig 3, bottom, c). Whereas static compliances were in the normal range in most emphysema patients, the lower gradient of D in these patients suggests a severe loss of elasticity in their lung bases, especially in the group with low M.

The difference in D between healthy subjects and the group of patients with emphysema increased with lung height, suggesting either a greater loss of tissue or a greater distension in the lung bases of the patients. As there was no difference in the distribution of RLM between the two groups, distension would appear to be the major factor in the increasing difference in RLD with height.

**Differences Between the Patient Groups**

The overall analysis of a rather heterogeneous population tended to obscure differences between the patients with high, low, or normal M. Thus, the patients were allocated into three groups as a function of their M/Mref ratios. Threshold values of the M/Mref ratio of 0.92 and 1.12 were chosen to obtain groups with equal numbers of patients. Patients also could have been split up by taking the mean value of M of the healthy subject group ± 1 SD as the normal range or by using a clustering statistical analysis. However, our healthy group was too small to define the SD of a healthy population accurately, and clustering would need a larger series of patients. Furthermore, M is dependent on the size of the lung, which in turn depends on height. Therefore,
we thought it more appropriate to calculate the M that the patients should have had if they had a normal FRC and a normal D, as D has been shown to be independent of age,6,21,22 and to classify patients according to this Mref. The groups of emphysema patients with high M and normal M had a slightly positive but nonsignificant craniocaudal gradient of D between the apex and 80% lung height, whereas the group with low M had an absence of gradient (Fig 3, middle, b). Although the gradient of D observed at low lung volume9,10,23 in healthy subjects as well as in emphysema patients has been shown to be reduced with lung inflation at TLC, our observations indicated that this gradient might be abolished even at FRC in emphysema patients who have severe, destructive losses of lung tissue.

There were significant differences in absolute regional lung air volume between all diseased groups and healthy subjects, except at 0% and 10% lung height. The absolute values of regional lung air content were lower in the patients with low M compared with the patients with normal and high M, although the values were consistently higher than in the healthy subjects, indicating that the low D in the group with low M was due not only to the loss of lung tissue but also to lung distension.

**Ed Score and RLM**

The slope of the relationship between the RLM of a given compartment and the whole M of the group of patients with emphysema showed an increasing slope between 20% and 90% lung height, except for the end scan at the base. Therefore, the increase or decrease in M observed in the groups of patients with emphysema was mostly due to changes in M in the bases and was not evenly distributed, as was suggested by the analysis of the emphysema patients as a whole. Such differences could be accounted for in terms of the anatomic differences between the apex and the lung base. Blood and relative tissue volumes are greater in the bases19,21 and would be expected to be more sensitive to structural alterations like the loss of tissue or to the diffuse inflammation commonly found in emphysema.24,25 This was supported by the findings from our three groups of emphysema patients that, whereas RLM was related to Ed in the apex and in the base, only a high score of Ed in the base, as reported in the group patients with low M, was followed by severe loss of tissue.

The average regression equation of RLM vs Ed in the overall group of patients with emphysema indicated that with increasing severity of emphysema there was significant loss of lung tissue. Since M did not differ between the two types of emphysema in either of the patient groups having high M or low M, it could be argued that the increase or loss of M stemmed more from the localization than the type of the emphysema. Coxson et al26 studied the relationship between whole M and the Ed assessed from the lower –910-HU level of the D curve. The lack of a significant correlation between ≤910-HU level and M in their results was partly related to the fact that the low D areas that are assumed to quantify the extent of emphysema reflected lung overdistension rather than true loss of tissue. The present results are in agreement with those of Coxson et al26 as no significant correlation was observed between X and RLM, although we did observe a correlation between the SLD indexes with both RLM and Ed (which is a pool of both indexes). The lack of correlation between RLD and Ed indicates that RLD depends on both RLM and Vairr and that the overdistension observed in many patients in the disease group was not directly related to the Ed.

The dissimilar pattern of distribution of emphysema between the patient groups with high M and normal M compared to the patient group with low M was related to the type of emphysema in each group. Among the 21 patients of the groups with high M and normal M, 13 had CLE, 5 had PLE, and emphysema was more severe in the apex; in the group with low M, 2 patients had CLE, 5 patients had PLE, and emphysema was more severe in the base. As the remaining patients had a mixed form of emphysema, the variation in emphysematous involvement noted in our three groups was consistent with the recognized distribution pattern of the disease according to the type of emphysema.27

**Lung Function in the Diseased Groups**

The present data indicate that the group with low M with the most severe forms of obstruction and distension had lower D and M. Previous studies based on a lung model have established the important role played by M on lung mechanics and function.7,10 The present findings extend these observations and indicate that severe loss of M up to 20%, as observed in our group of emphysema patients with low M, may occur in patients with emphysema and would be accompanied by a marked alteration in lung function. It would be of interest to make a longitudinal study of lung function and alterations in M in individual patients. This might indicate whether patients with low M were previously in the group of patients with high M and normal M. Indirect evidence that the preservation of M has a beneficial effect on lung function is supported by a study undertaking the pathologic examination of bronchioles and bronchiolar wall thickness.
in patients suffering from emphysema. These authors found that the patients with the greatest increase in bronchiolar tissue volume were the least obstructed. In contrast, the patients with losses of bronchiolar tissue volume, which were akin to those in our group of patients with low M, had more severe obstruction, lending support to the idea that the mechanical behavior of the lung in emphysema is related to whole M.

The lower VC in the group of emphysema patients with low M than in groups with high M and normal M may derive from several factors acting alone or in combination. Our patients with low M (1) were leaner than those with normal M (52 ± 10 kg vs 67 ± 11 kg, respectively); (2) had lower FEV1/FVC; (3) had higher Raw; and (4) had higher RV. Although these four factors did not differ individually among the patient groups, their combined effect on VC limitation was statistically significant. As it has been shown that lung function was better related to the lung base than to the lung apex, it is likely that the location of the severe loss of tissue in the lung base in patients with low M contributed to the marked functional alterations observed in this group. It would be of interest to know whether the low M observed in the patients with low M corresponds to a particular form of emphysema with low remodeling or whether it is the result of a general process of becoming more lean, as suggested by the lower body weight of these patients.

CONCLUSION

In conclusion, the M of emphysematous lungs is, on average, not different from normal. In the patients with emphysema, the mean of the distribution of M appeared to be normal, although D was lower and the apex-to-base gradient of D was lower than that in the healthy subjects. However, there were considerable differences among the groups of patients. Tissue mass in the lung base appeared to be the main determinant of the alteration in whole M in patients with emphysema. In the patient group with high M, the decrease in D can be attributed to a distension overshadowing the overweight, while in the group with low M, the loss in D was due both to distension and to loss in lung weight. The patients with low M appeared to be the most functionally impaired.

APPENDIX 1

To check the ability of CT scanning to determine density displacement (Dw), volume (Vlw), and mass (Mw), as measured by water displacement, of material and to determine the calibration curve of our scanner, we performed a companion study of various phantoms. Seven parallelepipeds constructed from polystyrene (0.0340 g/mL), chestnut (0.664 g/mL), poplar (0.396 g/mL), oak (0.602 g/mL), framire (0.602 g/mL), iroko (0.635 g/mL), and niangon (0.727 g/mL) were scanned lengthwise using contiguous 8-mm scans. The results of the end-most slices were discarded to exclude voxels averaging at the wood-air interface. Air and water phantoms were scanned later to cover the overall density range of pulmonary tissue. The true densities of the phantoms were determined from the ratio of their Mw to their volumes Vlw, as determined by weighing and water displacement, respectively. Taking into account the exclusion of the end slices, CT underestimated Dw, Mw, and Vlw of the wood phantoms by 4 ± 5%, 6 ± 7%, and 8 ± 6%, respectively. A plot of HU vs Dw gave a regression line very close to the identity line over the range of densities between air (1 mg/mL) and water (1 g/mL). Some scatter was observed but only toward the higher densities (ie, > 0.80 g/mL) and still with a < 3% error.

APPENDIX 2

The relationship between the Vtiss and M of a subject breathing at FRC could serve to determine the Mref from the FRCo and the Do at FRCo:

\[ Vtiss \times dtiss = (FRCo + Vtiss) \times Do \]

where dtiss is lung tissue density (air excluded). If dtiss = 1

\[ Vtiss = FRCo[Do/(1 - Do)] = Mref \]

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