Effect of Chronic Hyperinflation on Diaphragm Length and Surface Area

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We have used three-dimensional reconstructions obtained with spiral computed tomography to measure total diaphragm length (L_{di}) and surface area (A_{di}), the length (L_{do}) and surface area (A_{do}) of the dome, and the length (L_{ap}) and surface area (A_{ap}) of the zone of apposition in 10 hyperinflated patients with severe chronic obstructive pulmonary disease, or COPD (FEV_1 = 27% predicted: FRC = 225% predicted) and 10 normal subjects matched for age, sex, and height. Measures of L_{di}, A_{di}, L_{ap}, and A_{ap} decreased linearly between FRC and TLC in the two groups, but L_{do} and A_{do} did not change. On average, patients' A_{di} and A_{ap} at FRC were reduced to 73% and 54% of normal values, whereas A_{do} was unaffected. When compared at similar absolute lung volumes, mean diaphragm dimensions were similar in patients with COPD and normal subjects, but individual values were very variable in both groups. This variability was partly accounted for by differences in body weight: i.e., the greater the weight, the longer the diaphragm. We conclude that (*1*) patients with COPD have marked reductions in A_{di} and A_{ap} at FRC but have diaphragm dimensions similar to those of normal subjects when compared at similar absolute lung volumes, and (*2*) normal subjects and patients with COPD show substantial intersubject variability in diaphragm dimensions that is partly explained by differences in body weight. Cassart M, Pettiaux N, Gevenois PA, Paiva M, Estenne M. Effect of chronic hyperinflation on diaphragm length and surface area. AM J RESPIR CRIT CARE MED 1997;156:504–508.

In patients with chronic obstructive pulmonary disease (COPD), hyperinflation of the lungs decreases the operating length of the diaphragm. As a result, the inspiratory function of the muscle is impaired. The magnitude of diaphragm shortening increases with the degree of hyperinflation, and it is generally assumed that, at a given absolute lung volume, diaphragm length and surface area are similar in patients with COPD and normal subjects.

However, very few studies have investigated the effect of chronic hyperinflation on diaphragm dimensions. In two early studies using chest radiographs, Sharp and colleagues (1) reported that the diaphragm was 40% shorter at FRC in patients with COPD than in normal subjects, and Rochester and Braun (2) showed that diaphragm length was reduced by 28% in patients with COPD at residual volume (RV) compared with normal subjects at their RV; this difference, however, disappeared when diaphragm lengths were compared at similar absolute lung volumes. Interpretation of these results is difficult because measurements of diaphragm dimensions were obtained from two-dimensional analysis of chest radiographs, were generally performed at a single lung volume, and were not always compared with measurements obtained in adequately matched controls.

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In a previous study (3), we have described a technique of three-dimensional (3D) diaphragm imaging using spiral computed tomography (CT) that allowed accurate measurements of diaphragm length and surface area. In the present work, we have used this technique to compare diaphragm dimensions at different lung volumes in 10 hyperinflated patients with severe COPD and 10 normal subjects matched for age, sex, and height.

METHODS

Patients

The study was performed on 10 patients (2 females) with a well-established history of chronic airway disease and 10 control subjects matched for sex, age, and height. Details of the subjects are given in Table 1: the patients were severely obstructed and hyperinflated, whereas the control subjects had normal pulmonary function tests (4). All 10 patients were smokers or exsmokers and had predominant emphysema as indicated by severe hyperinflation, low diffusing capacity, and extended areas of low attenuation on chest CT. It is worth stressing that the patients had no history of asthma and that each of them had been clinically stable for at least 6 wk before the study. All but one patient had a body mass index greater than 18 (mean $\pm$ SD, 20.5 $\pm$ 2.5), suggesting that their nutritional status was not grossly altered. The patients' chest films did not reveal any thoracic or parenchymal abnormalities other than those consistent with the diagnosis of COPD. All subjects gave oral informed consent to the procedures as approved by the Human Studies Committee of the Institution.

Technique

The technique used has been previously described in detail (3). Before taking the spiral CT acquisitions, we fixed a metallic bullet on the xiphoid process and a flexible metallic wire around the costal margin;

TABLE 1

ANTHROPOMETRIC AND FUNCTIONAL CHARACTERISTICS OF 10 PATIENTS WITH COPD AND 10 CONTROL SUBJECTS

	Control Subjects	Patients with COPD
Age, yr	54.8 ± 12.9	54.7 ± 11.1
Sex, M/F	8/2	8/2
Height, cm	168 ± 12	168 ± 10
Weight, kg	66 ± 11	59 ± 12
BMI	23.3 ± 2.1	20.5 ± 2.5
TLC, % predicted	114 ± 13	141 ± 12*
FRC, % predicted	117 ± 26	225 ± 29*
FEV_1, % predicted	95 ± 14	27 ± 6*
FEV_1/VC, % predicted	88 ± 6	46 ± 8*

Values are means ± SD. All lung volumes were measured seated. Predicted values are from the ECCS Working Party (4).
BMI = body mass index.
* $p < 0.001$.

the bullet was used as a reference point and the wire was used to identify the loci of origin of costal diaphragmatic fibers.

While wearing a noseclip and lying supine with their arms at their sides, the patients were asked to breathe to total lung capacity (TLC), functional residual capacity (FRC), or FRC plus one-half inspiratory capacity (FRC+), where the acquisitions were performed. To attain this last volume, the subjects were connected to a spirometer and instructed to breathe in to TLC and slowly expire until FRC+ was reached. At each volume, the subjects were asked to hold their breath and relax against a closed airway. Before the actual acquisitions, a few practice trials were always performed to familiarize the subjects with the procedures and with the sensation of respiratory muscle relaxation. In addition, the acquisition was always preceeded by a 2–3 min period of increased tidal breathing, which made breath-holding more comfortable and facilitated relaxation; supplemental oxygen was provided to the patients during the period of hyperventilation. During the acquisitions, one of the investigators encouraged the subjects to appropriately relax the respiratory muscles.

The acquisitions were made using spiral CT and extended from 1 cm above the diaphragmatic dome to 1 cm below the metallic wire at the costal margin. On the axial slice that included the xiphoid marker, we defined 20 coronal and 30 sagittal reconstructions at each volume. The reconstructed images, as well as their positions relative to the xiphoid marker, were transferred to a Pentium PC and diaphragm contours were digitized in three contiguous segments that corresponded to the dome and to the right and left (coronal view) or anterior and posterior (sagittal view) portions of the zone of apposition. A 3D reconstruction of the muscle was obtained using the coronal and sagittal digitized contours (Figure 1).

In addition to the acquisitions centered on the diaphragm, we performed a spiral CT at TLC that extended from the lung apex to the lung base. On images reconstructed axially every 10 mm, lung contours were digitized and the value of supine TLC was calculated using slice thickness and the surface covered by lung parenchyma on each slice. This method had been previously validated on three phantoms; the difference between the actual volume of the phantoms and the volume calculated by the CT was less than 5%. Values of supine FRC and FRC+ were calculated using CT values of TLC and a spirogram obtained in the supine posture.

Data Analysis

Total diaphragm length (L_{di}), the length of the zone of apposition (L_{ap}), and the length of the dome (L_{do}) were measured on coronal and sagittal digitized silhouettes. However, we chose to restrict these measurements to slices that had an orientation close to that of diaphragm muscle fibers. Inspection of diaphragms in cadavers indicated that these slices were positioned slightly anteriorly to the midcoronal section in the coronal plane and were centered on the right and left hemidiaphragm in the sagittal plane. We also calculated muscle fiber length in the coronal orientation (L_{mu}) by subtracting the length of the central tendon from coronal L_{di}; we used the value of 10.7 cm reported by Arora and Rochester (5).

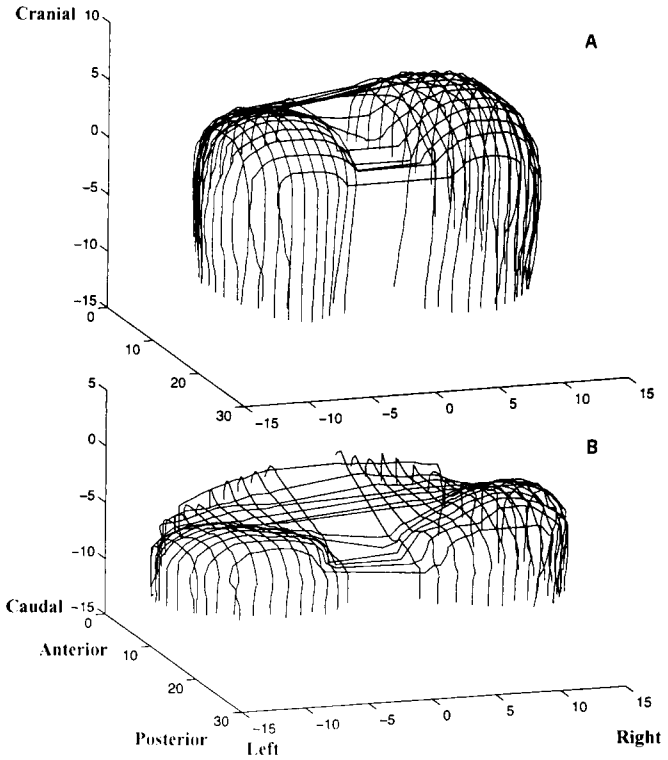

Figure 1. Three-dimensional reconstruction of diaphragm in one control subject (*A*) and one patient with COPD (*B*) at FRC. Reconstruction is shown from posterior-superior left lateral perspective. Units = cm. There is marked reduction in muscle surface area in the patient.

For surface measurements, we created small triangular surfaces on 3D reconstructions obtained at each lung volume (3, 6), and we calculated total diaphragm area (A_{di}) as the sum of the area of the dome (A_{do}) and the area of the zone of appositions (A_{ap}). To calculate the muscular surface of the diaphragm (A_{mu}), we subtracted 143 cm^2 from A_{di} (5).

Statistical analysis was performed using paired *t* tests and analysis of variance (ANOVA) when appropriate. Values of $p < 0.05$ were considered statistically significant.

RESULTS

The procedure was well tolerated by the subjects. The duration of the acquisitions varied from 15 to 25 s according to the height of the subject and the volume studied.

Diaphragm Length

Table 2 gives average values of L_{di}, L_{do}, L_{ap}, and L_{mu} obtained in the patients with COPD and the normal subjects at the three lung volumes studied. In both groups, coronal and sagittal L_{di} and L_{ap} and coronal L_{mu} decreased linearly as lung volume increased ($p < 0.001$), with the changes between FRC and TLC being greater in the normal subjects than in the patients. At the three lung volumes studied, L_{di}, L_{ap}, and L_{mu} were smaller in patients with COPD than in normal subjects, but differences were greater at FRC than at higher lung volumes. At FRC, coronal L_{di}, L_{ap}, and L_{mu} in the COPD patients were reduced to 79.8%, 51.5%, and 75.3% of the values in the normal subjects, respectively. On the other hand, L_{do} did not

TABLE 2

AVERAGE VALUES OF DIAPHRAGM LENGTH IN 10 PATIENTS WITH COPD AND 10 CONTROL SUBJECTS AT FRC, FRC+, AND TLC

	Lung Volumes					
	FRC		FRC+		TLC	
Diaphragm Length	Control	COPD	Control	COPD	Control	COPD
L_{di}, cm						
Coronal	56.9 ± 2.0	45.4 ± 1.6‡	50.4 ± 2.0	43.4 ± 1.6†	44.1 ± 1.6	38.9 ± 1.7†
Sagittal right	40.4 ± 1.4	30.6 ± 1.0‡	33.7 ± 1.1	29.6 ± 0.9†	29.3 ± 0.9	27.3 ± 0.9
Sagittal left	36.7 ± 1.7	28.3 ± 1.1‡	32.1 ± 1.8	27.6 ± 1.0†	28.0 ± 1.4	26.7 ± 1.1
L_{do}, cm						
Coronal	29.7 ± 0.5	31.5 ± 1.0	32.7 ± 0.6	30.9 ± 0.7*	32.6 ± 0.7	29.8 ± 0.0*
Sagittal right	20.0 ± 0.4	18.9 ± 0.7	20.6 ± 0.7	19.0 ± 0.7*	20.3 ± 0.6	18.6 ± 0.5*
Sagittal left	19.0 ± 0.9	18.8 ± 0.8	19.4 ± 0.7	18.7 ± 0.8	19.6 ± 0.8	18.8 ± 0.7
L_{ap}, cm						
Coronal	27.2 ± 1.7	14.0 ± 1.1‡	17.7 ± 1.7	12.3 ± 1.1†	11.6 ± 1.0	9.1 ± 1.1*
Sagittal right	20.5 ± 1.2	11.7 ± 1.1‡	13.1 ± 0.8	10.6 ± 0.9*	8.9 ± 0.5	8.8 ± 0.9
Sagittal left	17.5 ± 1.6	9.5 ± 0.9‡	12.7 ± 1.8	8.9 ± 0.8*	8.4 ± 0.8	7.9 ± 0.9
L_{mu}, cm						
Coronal	46.2 ± 2.0	34.8 ± 1.6‡	39.4 ± 1.8	32.7 ± 1.6†	33.4 ± 1.6	28.2 ± 1.7†

Values are means ± SE.
* $p < 0.05$, † $p < 0.01$, ‡ $p < 0.001$ patients versus control subjects.

change significantly with lung volume, and differences in L_{do} between the two groups were generally small and statistically nonsignificant.

Diaphragm Surface Area

Table 3 shows average values of A_{di}, A_{do}, A_{ap}, and A_{mu} in the patients with COPD and the normal subjects. As expected from length measurements, A_{di}, A_{ap}, and A_{mu} decreased linearly in both groups as lung volume increased ($p < 0.002$). Changes in surface area were less pronounced in the patients than in the normal subjects due to their smaller inspiratory capacity, but changes per unit lung volume were similar in the two groups. At FRC, FRC+, and TLC, measures of A_{di}, A_{ap}, and A_{mu} were smaller in patients with COPD than in normal subjects; at FRC, A_{di}, A_{ap}, and A_{mu} in the patients with COPD represented 73.0%, 53.8%, and 69.5% of the normal values, respectively. As observed for L_{do}, A_{do} did not change significantly with lung volume and there was no significant difference in A_{do} between groups. Table 3 also shows that the proportion of muscular surface area (A_{ap}/A_{mu}) and of total surface area (A_{ap}/A_{di}) apposed to the rib cage was significantly smaller in the patients than in the controls at FRC and FRC+. On the other hand, the proportion of muscular surface area in the dome ($A_{mu}–A_{ap}/A_{do}$) was similar in the two groups, whatever the lung volume studied.

Figure 2 displays average values of A_{di}, A_{ap}, and A_{do} in the 10 COPD patients and the 10 normal control subjects as a function of supine lung volume. As expected, data from the patients were displaced toward higher lung volumes, but the relationships between diaphragm surface area and lung volume in the two groups fitted almost a single line. This indicated that a similar absolute lung volume, A_{di}, A_{ap}, and A_{do} were similar in the normal subjects and the COPD patients. A similar observation was made for A_{mu}. When looking at individual data, however, diaphragm dimensions were very variable in the two groups. This is illustrated in Figure 3, which shows individual values of A_{di}, A_{do}, and A_{ap} obtained at FRC as a function of supine lung volume.

DISCUSSION

Two previous studies have assessed diaphragm length from chest radiographs in patients with COPD. Sharp and colleagues (1) studied 21 patients with COPD (results of pulmonary func-

TABLE 3

AVERAGE VALUES OF DIAPHRAGM SURFACE AREA IN 10 PATIENTS WITH COPD AND 10 CONTROL SUBJECTS AT FRC, FRC+, AND TLC

	Lung Volumes					
	FRC		FRC+		TLC	
Diaphragm Surface Area	Control	COPD	Control	COPD	Control	COPD
A_{di}, cm^2	1,198 ± 68	876 ± 50‡	1,018 ± 72	834 ± 48†	851 ± 55	776 ± 52†
A_{do}, cm^2	490 ± 22	495 ± 30	518 ± 28	491 ± 26	515 ± 27	493 ± 31*
A_{ap}, cm^2	708 ± 51	381 ± 28‡	499 ± 46	343 ± 28‡	336 ± 31	284 ± 29
A_{mu}, cm^2	1,055 ± 69	733 ± 50‡	875 ± 72	691 ± 48†	708 ± 55	633 ± 52
A_{ap}/A_{mu}	0.67 ± 0.11	0.52 ± 0.21‡	0.57 ± 0.11	0.50 ± 0.18†	0.47 ± 0.12	0.45 ± 0.22
$A_{mu}–A_{ap}/A_{do}$	0.70 ± 0.15	0.70 ± 0.18	0.72 ± 0.16	0.70 ± 0.16	0.72 ± 0.15	0.70 ± 0.19
A_{ap}/A_{di}	0.59 ± 0.12	0.43 ± 0.17‡	0.48 ± 0.13	0.41 ± 0.17‡	0.39 ± 0.14	0.36 ± 0.19

Values are means ± SE.
* $p < 0.05$, † $p < 0.01$, ‡ $p < 0.001$ patients versus control subjects.

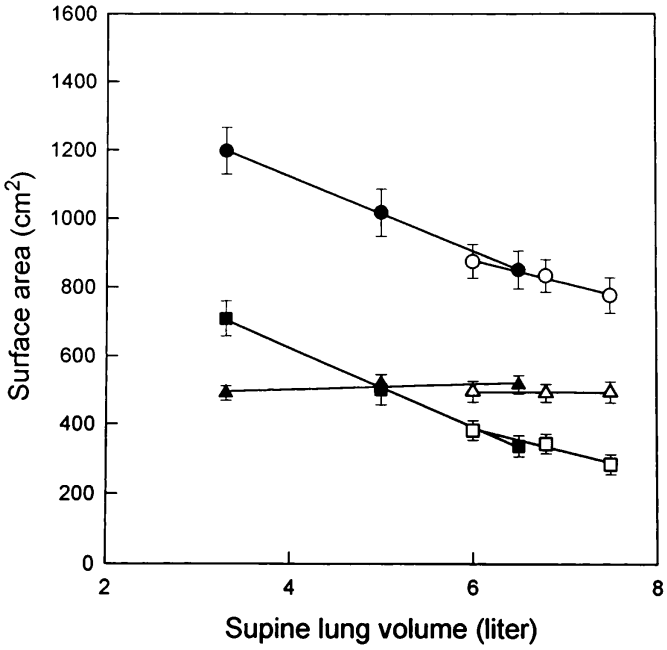

Figure 2. Average surface area of the diaphragm (*circles*), the dome (*triangles*), and the zone of apposition (*squares*) in 10 normal subjects (*closed symbols*) and 10 patients with COPD (*open symbols*) as a function of supine lung volume measured by CT. Data were obtained at FRC, midinspiratory capacity, and TLC in the two groups. Bars = SE. Data in the normal subjects and the patients almost fitted single lines.

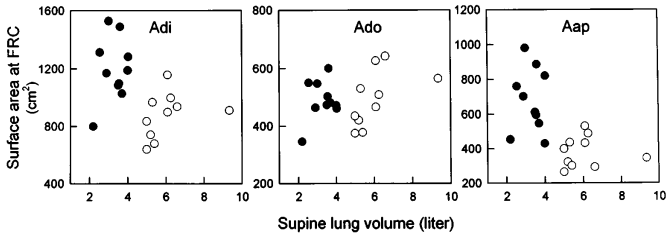

Figure 3. Individual surface area values of the diaphragm (A_{di}) the dome (A_{do}), and the zone of apposition (A_{ap}) measured at FRC in 10 normal subjects (*closed symbols*) and 10 patients with COPD (*open symbols*) as a function of supine lung volume. In both groups, diaphragm surface area showed a large intersubject variability.

tion tests were not provided) and 23 normal subjects and found that the patients' diaphragms at FRC were about 32% shorter than normal. More recently, Rochester and Braun (2) compared diaphragm length in 32 patients with COPD (TLC, 112% predicted; FEV_1, 35% predicted) and 22 healthy subjects and found that, on average, the muscle at RV was 28% shorter in the patients than in the normal subjects. It is difficult to compare these results with those of the present studies because Sharp and colleagues (1) and Rochester and Braun (2) made measurements from chest radiographs obtained in the upright posture, whereas we performed CT measurements in the supine posture. However, the 20–24% reduction in the patient's coronal or sagittal L_{di} observed here at FRC is in keeping with the changes reported in these previous works.

Our studies have demonstrated that changes in diaphragm dimensions produced by chronic hyperinflation occurred exclusively in the zone of apposition. In fact, the dimensions of the dome were not significantly altered in the patients, so that reductions in L_{ap} and A_{ap} were greater than reductions in L_{di} and A_{di}. This pattern of changes could be anticipated because the dimensions of the dome are relatively insensitive to changes in lung volume. In two previous studies (3, 6), we found that L_{do} and A_{do} in four normal subjects increased by less than 15% on going from FRC to TLC; in the present study, normal subjects increased L_{do} and A_{do} by less than 10% over the inspiratory capacity.

Figure 1 and Tables 2 and 3 show that the zone of apposition was not eliminated in the supine posture at TLC, even in the hyperinflated COPD patients. From anatomic considerations, we regarded a flexible metallic wire attached to the skin at the lower costal margin and continuing along the subject's back as a valid indicator of diaphragm insertions on the ribs and vertebrae. For reasons discussed in our previous study (6), this assumption presumably overestimated our measurements of L_{ap} and A_{ap}. This error, however, was probably small and does not make comparison between patients and control subjects less meaningful.

When compared at similar absolute lung volumes, mean diaphragm dimensions were identical in COPD patients and matching normal controls. For example, at volume corresponding to the patient's FRC, the dimensions of the diaphragm, dome, and area of apposition were similar in the two groups (Figure 2). However, there was a marked intersubject variability in diaphragm dimensions in both the normal subjects and the patients with COPD (Figure 3).

Diaphragm dimensions might be influenced by contraction of the muscle itself or by contraction of other respiratory muscles. Although the subjects of this study underwent a few practice trials before the actual acquisitions, they were asked to hyperventilate an oxygen-enriched gas mixture before the breath-holds, and were encouraged to relax their respiratory muscles, we cannot ensure that complete relaxation was actually achieved. So subjects with a longer diaphragm might have contracted the rib cage inspiratory muscles and/or the abdominal muscles during the acquisitions and conversely, subjects with a shorter diaphragm might have contracted the rib cage expiratory muscles and/or the diaphragm itself.

Contraction of the diaphragm reduces the proportion of surface area apposed to the rib cage, or A_{ap}/A_{di} (7). Therefore, if contraction of the muscle were responsible for the intersubject difference in muscle length and surface area, one would expect A_{ap}/A_{di} to be smaller in the subjects with a shorter diaphragm, and vice versa. As a matter of fact, in each group A_{ap}/A_{di} showed little intersubject variability. Furthermore, in this study, as in our previous works (3, 6), diaphragm dimensions showed linear relationships with lung volume, suggesting that adequate relaxation was achieved during the acquisitions. Involuntary contraction of respiratory muscles would be expected to produce variable changes in diaphragm dimensions with substantial alinearity between lung volumes.

When values of A_{di}, A_{do}, and A_{ap} at FRC were normalized for subject's height, the range of values shown in Figure 3 did not narrow, suggesting that the intersubject variability in diaphragm surface area was not due to differences in height. Similarly, the observation that in each group diaphragm surface area at FRC was not correlated with FRC values (expressed either in liters, as in Figure 3, or as a percentage of predicted FRC) suggested that the variability in diaphragm dimensions was not due to differences in FRC. That is, subjects with larger FRC did not have smaller diaphragm dimensions, and vice versa.

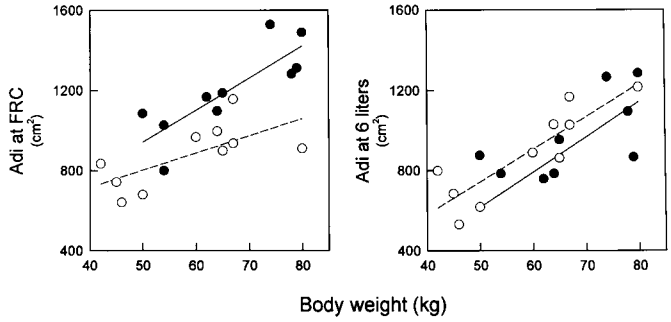

Figure 4. Individual values of diaphragm surface area (A_{di}) measured at FRC (*left panel*) and at an absolute volume of 6 L (*right panel*) in 10 normal subjects (*closed symbols*) and 10 patients with COPD (*open symbols*) as a function of body weight. In both groups the relationships were statistically significant, and they were superimposed on each other when A_{di} was measured at a volume of 6 L.

On the other hand, weight appeared to be a significant factor. Figure 4 (*left panel*) displays values of A_{di} obtained in each subject at FRC as a function of body weight; the relationships were significant in both the patients ($r = 0.67$, $p < 0.05$) and the normal subjects ($r = 0.83$, $p < 0.01$) and had a positive slope; i.e., the greater the weight, the greater the surface area of the diaphragm. As expected, the relationship in the patients was displaced toward smaller A_{di} values; however, when A_{di} was measured or computed by linear extrapolation at an absolute volume of 6 L (Figure 4, *right panel*), the relationships in the patients ($r = 0.87$, $p < 0.001$) and the normal subjects ($r = 0.69$, $p < 0.05$) were superimposed (the difference was nonsignificant by covariance analysis). This indicated that, at a given absolute lung volume, diaphragm dimensions are similar in normal subjects and patients with COPD and are largely determined by body weight.

This effect of body weight on diaphragm dimensions has been previously studied by Rochester and colleagues (2, 5). From measurements obtained at necropsy in subjects without chronic respiratory disease, Rochester and Arora showed that diaphragm length and surface area were markedly reduced when nutritional status was compromised (5). Furthermore, in their study of diaphragm dimensions from chest radiographs, Rochester and Braun (2) showed that the muscle was more shortened in underweight than in well nourished patients with COPD. Although the subjects studied here had a reasonably well-preserved nutritional status, the trends shown in Figure 4 are in keeping with these observations. The mechanisms underlying this effect of body weight on diaphragm dimensions is unknown; it is possible that when body weight increases (and abdominal compliance decreases), more volume is accommodated by the rib cage than by the diaphragm-abdomen compartment, so that diaphragm surface area tends to be greater at a given absolute lung volume.

In conclusion, the present studies have demonstrated that (*1*) COPD patients have marked reductions in A_{di} and A_{ap} at FRC; (*2*) when compared at similar absolute lung volumes, however, diaphragm dimensions are similar in patients with COPD and normal subjects; and (*3*) normal subjects and patients with COPD show substantial intersubject variability in diaphragm dimensions that are partly explained by differences in body weight. Undernutrition in patients with COPD might thus alter diaphragm function not only by decreasing muscle mass but also by amplifying the decrease in muscle length produced by the hyperinflation.

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