Structure of the latissimus dorsi muscle and respiratory function

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Orozco-Levi, Mauricio, Joaquim Gea, Jaume Sauleda, Josep M. Corominas, Joan Minguella, Xavier Aran, and Joan M. Broquetas. Structure of the latissimus dorsi muscle and respiratory function. *J. Appl. Physiol.* 78(3): 1132–1139, 1995.—The aim of this study was to evaluate whether respiratory function influences the structure of the latissimus dorsi muscle (LD). Twelve patients (58 ± 10 yr) undergoing thoracotomy were studied. Lung and respiratory muscle function were evaluated before surgery. Patients showed a forced expired volume in 1 s (FEV_1) of 67 ± 16% of the reference value, an FEV_1-forced vital capacity ratio of 69 ± 9%, a maximal inspiratory pressure of 101 ± 21% of the reference value, and a tension-time index of the diaphragm (TT_{di}) of 0.04 ± 0.02. When patients were exposed to 8% CO_2 breathing, TT_{di} increased to 0.06 ± 0.03 ($P < 0.05$). The structural analysis of LD showed that 51 ± 5% of the fibers were type I. The diameter was 56 ± 9 μm for type I fibers and 61 ± 9 μm for type II fibers, whereas the hypertrophy factor was 87 ± 94 and 172 ± 208 for type I and II fibers, respectively. Interestingly, the histogram distribution of the LD fibers was unimodal in two of the three individuals with normal lung function and bimodal (additional mode of hypertrophic fibers) in seven of the nine patients with chronic obstructive pulmonary disease. An inverse relationship was found between the %FEV_1-forced vital capacity ratio and both the diameter of the fibers (type I: $r = -0.773$, $P < 0.005$; type II: $r = -0.590$, $P < 0.05$) and the hypertrophy factors (type I: $r = -0.647$, $P < 0.05$; type II: $r = -0.575$, $P = 0.05$). The increase in TT_{di} when the subjects breathed CO_2 directly correlated with the diameter of all the LD fibers ($r = 0.636$, $P = 0.05$). These results strongly suggest that the structure of the LD can be influenced by changes in respiratory function. Thus, it does not appear to be the most appropriate control for structural studies of the respiratory muscles.

respiratory muscles; type I fibers; type II fibers

IN MANY of the structural studies of the respiratory muscles (10, 22, 38, 39), the latissimus dorsi muscle (LD) has been included as the control because it was thought not to participate in ventilation (13). The LD is a thoracic muscle, and its main function is the adduction of the arm (17, 30, 42). However, LD could also have a potential role in the respiratory movements of the rib cage if its insertions into the ribs are considered. It could participate in either inspiration or expiration, depending on the direction of contraction and the areas implicated in such. In fact, these actions have been suggested by some anatomists (17, 30, 42). Likewise, recent electrophysiological studies have clearly demonstrated an increase in the activity of LD during breathing movements when resistive inspiratory loads are applied (8, 32, 40). In summary, although some reports have appeared, the relationships between this muscle and respiratory function have not been fully studied (9, 11, 12, 33). If LD actually does participate in ventilation, particularly under mechanical overloads, then structural changes could be expected in patients with chronic pulmonary diseases (37). The aim of this study was to investigate the potential relationships between respiratory function and the structure of the LD.

MATERIALS AND METHODS

Patients

Twelve male patients (mean age 58 ± 10 yr) undergoing thoracotomy for small lung neoplasms were studied (Table 1). None was treated with drugs known to modify muscle structure (i.e., steroids). All of them were sedentary individuals, and their daily physical activities were similar. The study was approved by the Research Committee on Human Investigation at our institution. Consent was obtained after the purposes and potential risks of the investigation were fully explained and understood by each patient.

Pulmonary Function Tests

Forced spirometry and inspiratory capacity (Datospir 92, Sibel, Barcelona, Spain) and thoracic gas volume and single-breath pulmonary diffusing capacity of carbon monoxide (Masterlab, Jaeger, Würzburg, Germany) were measured in each patient. Reference values were those from a mediterranean population (34, 35). Blood samples were obtained from the radial artery and were analyzed for arterial P_{O_2}, arterial P_{CO_2}, and pH with standard polarographic techniques (ABL 330, Radiometer, Copenhagen, Denmark).

Throughout the study of the respiratory muscle function, patients breathed through a low-resistance two-way valve (Hans Rudolph, Kansas City, MO). Breathing pattern [tidal volume (V_T), respiratory rate (RR), inspiratory time (T_I), and total respiratory time (T_T)] was obtained from a pneumotachometer (Screenmate, Jaeger) inserted in the inspiratory circuit and connected to a multichannel recorder (Beckman R-611, Sensormedics, Anaheim, CA).

Respiratory Muscle Function Tests

Respiratory muscle strength was assessed through transdiaphragmatic pressure and maximal inspiratory pressure (MIP) measured at the mouth. The former was quantified with the classic esophageal and gastric balloons technique (26). The balloon catheters were connected to pressure transducers (Transpac II, Abbott, Chicago, IL), and the signal was registered using the above-mentioned polygraph. Calibrations were always performed at the beginning and at the end of each study. Transdiaphragmatic pressure was determined

TABLE 1. *Individual and mean values for age, nutritional characteristics, and both lung and diaphragmatic functions of the patients*

	Patient No.												
	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	Mean ± SD
Age, yr	59	59	58	51	78	69	47	67	46	53	63	46	58±10
%IBW	123	104	102	88	104	115	77	86	55	68	101	98	105±11
BMI	28	24	24	20	24	27	27	27	20	25	23	23	24±3
FVC, %ref	53	92	69	87	64	66	65	63	85	55	83	78	72±13
FEV_1, %ref	51	89	71	91	61	53	46	62	64	55	87	79	67±16
$\%FEV_1/FVC$	70	71	76	79	66	58	54	71	57	75	76	77	69±9
TLC, %ref	90	98	89	107	94	92	93	102	99	116	117	90	99±10
DL_{CO}, %ref	71	71	73	94	87	80	94	115	90	74	83	62	83±14
Pa_{O_2}, Torr	81	88	85	80	82	78	88	80	75	80	100	87	84±10
Pa_{CO_2}, Torr	42.1	45.0	44.0	44.9	43.0	44.8	44.8	43.9	47.9	38.1	34.6	45.0	42.9±3.3
MIP, cmH_2O	−56	−77	−81	−93	−46	−66	−96	−89	−91	−79	−104	−118	−83±20
$\bar{P}di$, cmH_2O	5.2	10.3	10.7	5.8	7.0	2.3	5.5	6.6	9.8	5.7	10.5	7.6	7.3±2.6
$\bar{P}di/Pdi_{max}$	0.006	0.14	0.15	0.07	0.11	0.03	0.03	0.06	0.08	0.06	0.17	0.09	0.09±0.04
TT_{di}	0.03	0.06	0.06	0.03	0.04	0.02	0.02	0.02	0.03	0.03	0.07	0.04	0.04±0.02

IBW, ideal body weight; BMI, body mass index; FVC, forced vital capacity; FEV_1, forced expired volume in 1 s; TLC, total lung capacity; DL_{CO}, lung diffusing capacity of carbon monoxide; Pa_{O_2}, arterial PO_2; Pa_{CO_2}, arterial PCO_2; MIP, maximal inspiratory pressure; $\bar{P}di$, transdiaphragmatic pressure during quiet breathing; Pdi_{max}, transdiaphragmatic pressure during maximal maneuver; TT_{di}, diaphragm tension-time index; %ref, percentage of reference value.

during quiet breathing ($\bar{P}di$) and when a maximal maneuver was performed (Pdi_{max}). For the latter, the sniff technique at functional residual capacity was chosen because it appears to be more reproducible and easily performable by patients with chronic obstructive pulmonary disease (COPD) (1). In each situation, the tension-time index for the diaphragm [$TT_{di} = (\bar{P}di/Pdi_{max})(TI/TT)$] was also calculated (2).

Hyperventilation Induced by CO_2

Patients were studied breathing both room air and 8% CO_2-enriched synthetic air. The latter came from a Douglas bag (Collins, Braintree, MA) connected to the external inspiratory circuit. Two washouts of the bag were always performed before the studies. Respiratory pattern, $\bar{P}di$, and TT_{di} were evaluated after ≥30 s of CO_2 breathing.

Nutritional Assessment

The nutritional status of the patients was evaluated with anthropometric and biochemical parameters. The former included weight (kg), height (cm), body mass index (weight/height^2), and the percentage of ideal body weight (IBW). This was calculated using the predicted values of the World Health Organization (16) [%IBW = (actual wt/ideal wt)100]. Blood analysis included hemoglobin, serum cholesterol, triglycerides, total protein, albumin, globulins, the albumin/globulin index, and prothrombin consumption time.

Morphometric Analysis of the Muscle

Relatively large biopsies (~1 g) from LD were obtained during thoracic surgery. Samples were taken at the sixth intercostal space on the posterior axillary line. Each biopsy was immediately plunged into isopentane cooled over liquid nitrogen. They were then stored at −70°C until they were processed. Transversal cuts 10 μm thick were performed in cryostat at −20°C. Types I, II, IIa, and IIb fibers were identified by adenosinetriphosphatase stains (5, 6). The diameter of the fibers was assessed using a morphometric semiautomatized system (Videoplan-II, Zeiss, Kontron Electronics, Munich, Germany). At least 100 fibers were measured in each case. The shorter diameter was chosen in preference to the alternative cross-sectional area or mean diameter because it is less affected by the angle of the cut and fiber kinking (15). With use of previous studies as a reference, diameters between 40 and 80 μm were considered normal (39). Atrophy and hypertrophy factors were calculated for each sample according to the method of Brooke and Engels (4). Both factors score the fibers proportionally to their diameter. This method has been fully described elsewhere (4, 39). The frequency histogram of the diameters of the fibers was also considered for assessing the overall heterogeneity of the muscle. For this, the morphology of the curve and the means ± SD of the distribution were used. The range of possible values for the diameter of the fibers was divided on a scale into 15 compartments. For practical reasons our scale began at 0 μm and finished at 150 μm. When the frequency diagram was completed, a smoothed curve that covered the entire diameter range was drawn. This method makes it possible to best identify additional modes of fibers (29).

Study Design

First day. When informed consent was obtained, patients performed conventional pulmonary function tests and their nutritional status was assessed.

Second day. Twenty-four to 48 h later, respiratory muscle strength was evaluated. As previously described, patients were tested both at room air and when breathing 8% CO_2.

Third day. Biopsies from the LD were taken at the beginning of the surgical procedure and were subsequently processed for morphometric studies.

Statistical Analysis

All data are presented as means ± SD. Each variable was tested for normal distribution with Kolmogorov-Smirnov's test. As usual, the percent change between different interventions for a variable was defined as [(final value − previous value)100]/previous value.

Student's paired *t*-test was used to compare variables from different interventions. Pearson's coefficient was used to as-

TABLE 2. *Breathing pattern and diaphragmatic function with subjects breathing air or 8% CO_2*

Diaphragmatic Function	RR, cycles/min	V_T, ml	$\dot{V}_E$, liters	T_I, s	T_T, s	T_I/T_T	V_T/T_I, l/s	$\bar{P}di$, cmH_2O	$\bar{P}di/Pdi_{max}$	TT_{di}
Room air	19±6	769±235	13.9±4.9	1.4±0.4	3.6±1.2	0.39±0.04	0.567±0.181	7.3±2.6	0.09±0.04	0.04±0.02
8% CO_2	23±7	1,233±287	28.6±7.1	1.1±0.3	2.7±0.6	0.42±0.04	1.127±0.285	13.7±6.4	0.14±0.09	0.06±0.03
P value	<0.05	<0.001	<0.001	<0.01	<0.05	NS	<0.001	<0.01	0.06	<0.05

Values are means ± SD. RR, respiratory rate; V_T, tidal volume; $\dot{V}_E$, minute ventilation; T_I, inspiratory time; T_T, total respiratory time.

ɜess correlation, and linear regression analysis was used when appropriate. $P \leq 0.05$ was considered significant.

RESULTS

Function Tests

Respiratory function. CONVENTIONAL LUNG FUNCTION TESTS. Three patients (*subjects 2, 4,* and *11*) had normal lung function, and the others showed a light to moderate obstructive or combined ventilatory pattern [forced expired volume in 1 s (FEV_1) ranged from 46 to 91% of the reference value (%ref)]. No individual exhibited lung hyperinflation (defined as a total lung capacity of >120% ref), but total lung capacity was >100%ref in four subjects. Arterial blood gases were normal except for two subjects with light to moderate hypoxemia. Individual values and means are expressed in Table 1.

BREATHING PATTERN (ROOM AIR AND CO_2-INDUCED HYPERVENTILATION). At room air, the breathing pattern variables (both respiratory times and volumes) were normal. Comparisons between these data and those obtained during 8% CO_2 appear in Table 2. In the latter situation minute ventilation, V_T, RR, and V_T/T_I increased. In contrast, respiratory times (T_I and T_T) significantly decreased with no changes in T_I/T_T.

Respiratory muscle function. ROOM AIR. Different variables expressing either the strength or the functional reserve of the respiratory muscles against fatigue were normal (Table 1).

CO_2-INDUCED HYPERVENTILATION. Under this ventilatory overload, TT_{di} increased (Table 2) and, interestingly, this change was inversely correlated with the ratio of %FEV_1 to forced vital capacity (FVC) ($r = -0.599$, $P < 0.05$).

Nutritional Status

Three patients showed an IBW of <80%. The different analytic variables were normal in all the subjects (Table 1).

Morphometric Analysis of the Muscle

Percentage of fibers. All muscle samples showed the typical mosaic pattern with the two different types of fibers, and no clusterings were observed. Type I accounted for 51 ± 5% of the fibers, and the rest were type II. The latter were subtyped as IIa (51 ± 5%) and IIb (49 ± 5%).

Mean least fiber diameter. The global diameter of the LD fibers was 58.7 ± 8.4 μm. If considered separately, the diameter was 56.1 ± 9.4 and 61.3 ± 8.6 μm for type I and II fibers, respectively. A direct correlation was found between the diameter of the two types of fibers ($r = 0.728$, $P < 0.05$). When type II fibers were subtyped, mean diameter was 55.7 ± 7.4 μm for type IIa and 59.4 ± 7.2 μm for type IIb. Because each subtype of fibers was measured separately, small discrepancies exist between the means of diameters in overall and subtyped II fibers. Individual values (mean value from each patient) are shown in Table 3.

Atrophy and hypertrophy factors: heterogeneity of the distributions of fiber diameters. Although the mean values of the atrophy and hypertrophy factors were normal (<200) (5), individual values were widely scattered (Table 3). The distribution of type I fibers was unimodal in six subjects (*subjects 2–4, 7, 8,* and *12*) and bimodal in the remaining individuals. The distribution for type II fibers was unimodal in five individuals (*subjects 2,*

TABLE 3. *Individual and mean values from the morphometric analysis of latissimus dorsi muscle*

	Patient No.												
	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	Mean ± SD
Diameter													
Fiber type I	59.2	52.4	49.6	36.0	61.9	67.0	65.0	45.5	67.6	60.0	55.2	53.9	56±9
Fiber type II	55.2	55.9	62.7	52.1	58.1	73.4	65.5	48.8	77.4	64.0	55.4	67.3	61±9
Hypertrophy factor													
Fiber type I	113	20	0	0	229	288	100	0	123	113	49	10	87±94
Fiber type II	57	24	139	0	86	536	117	14	611	319	0	160	172±208
Atrophy factor													
Fiber type I	57	190	175	986	129	27	20	330	0	65	172	206	196±267
Fiber type II	151	12	139	194	100	18	0	183	0	83	115	30	85±72
Standard deviation													
Fiber type I	14.0	11.9	10.6	8.9	16.2	16.2	11.5	10.1	10.6	13.5	11.5	13.2	12.3±2.3
Fiber type II	11.6	10.1	16.5	12.0	13.4	16.6	11.7	10.2	14.5	17.8	11.7	13.2	13.3±2.6

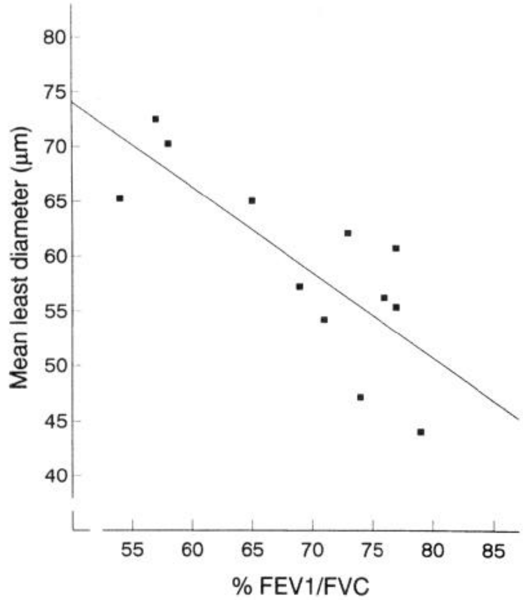

FIG. 1. Plots between diameter of all latissimus dorsi fibers and ratio of percent forced expired volume in 1 s (%FEV_1) to forced vital capacity (FVC). Solid line, regression line. $r = -0.737$, $P < 0.01$.

4, 7, 8, and *11*) and bimodal and even trimodal in the others. Whereas the main mode corresponded to fibers of normal size, the additional mode was formed by hypertrophic fibers. A direct correlation was observed between the mean diameter and the SD of the distributions in each type of fibers (type I: $r = 0.635$, $P < 0.05$; type II: $r = 0.639$, $P < 0.05$).

Relationships Between Muscle Structure and Respiratory Function

Percentage and size of the fibers. No significant correlations were found between data from respiratory function and the percentage of either type I or type II fibers. In contrast, %FEV_1/FVC inversely correlated with the diameter of the fibers ($r = -0.737$, $P < 0.01$; Fig. 1) and also showed a tendency to correlate with FEV_1 ($r = -0.560$, $P = 0.06$). If considered separately, the diameter of type I fibers showed an inverse relationship with both functional variables (FEV_1: $r = -0.669$, $P < 0.05$; %FEV_1/FVC: $r = -0.773$, $P < 0.005$). The diameter of type II fibers did disclose an inverse correlation only with the %FEV_1/FVC ratio (-0.590, $P < 0.05$).

Atrophy and hypertrophy factors: heterogeneity of the fiber distributions. The global hypertrophy factor was inversely correlated with the FEV_1/FVC ratio ($r = -0.637$, $P < 0.05$) and showed a tendency to correlate with FEV_1 ($r = -0.530$, $P = 0.06$). If considered separately, an inverse relationship was observed between the type I fiber hypertrophy factor (H_I) and both FEV_1 ($r = -0.608$, $P < 0.05$) and the %FEV_1/FVC ratio ($r = -0.647$, $P < 0.05$) and between the type II fiber hypertrophy factor (H_{II}) and the %FEV_1/FVC ratio ($r = -0.575$, $P = 0.05$).

Interestingly, those patients with normal lung function showed unimodal distributions for both type I and type II fibers (Fig. 2*A*). In contrast, those subjects with an obstructive pulmonary disease generally disclosed heterogeneous distributions with additional modes of hypertrophic fibers (Fig. 2*B*). This phenomenon was evident for type II fibers when considered both in an overall sense and, interestingly, when fibers were subtyped into IIa and IIb.

Relationships Between Muscle Structure and the Respiratory Muscle Function

Percentage and size of the fibers. Data from respiratory muscle function breathing room air did not show significant relationships with either the diameter or the percentage of each type of fiber. However, when ventilatory effort was induced by 8% CO_2, the resulting increase in TT_{di} showed a direct correlation with both the global ($r = 0.636$, $P < 0.05$; Fig. 3*A*) and type II fiber diameters ($r = 0.634$, $P < 0.05$). The diameter of type I fibers showed the same tendency ($r = 0.551$, $P = 0.06$).

Atrophy and hypertrophy factors: heterogeneity of the fiber distributions. Regarding the activity of the respiratory muscles of subjects breathing room air, the MIP directly correlated with both the SD for fiber type I ($r = 0.608$, $P < 0.05$) and H_I ($r = 0.636$, $P < 0.05$; Fig. 3*B*) and $\bar{P}di$ showed a tendency to inversely correlate with the latter ($r = -0.563$, $P = 0.06$). The $\bar{P}di/Pdi_{max}$ ratio and the TT_{di} index showed no relevant relationships with data from the structural study.

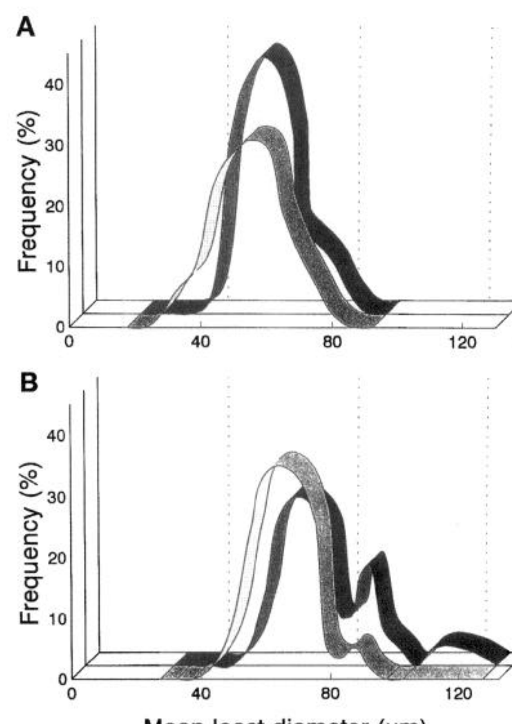

FIG. 2. Representative distribution of latissimus dorsi fibers in patient with normal lung function (*subject 2*, FEV_1 = 89% of reference value; *A*) and subject with chronic obstructive pulmonary disease (*subject 9*, FEV_1 = 64% of reference value; *B*). Light ribbon, type I fibers; dark ribbon, type II fibers.

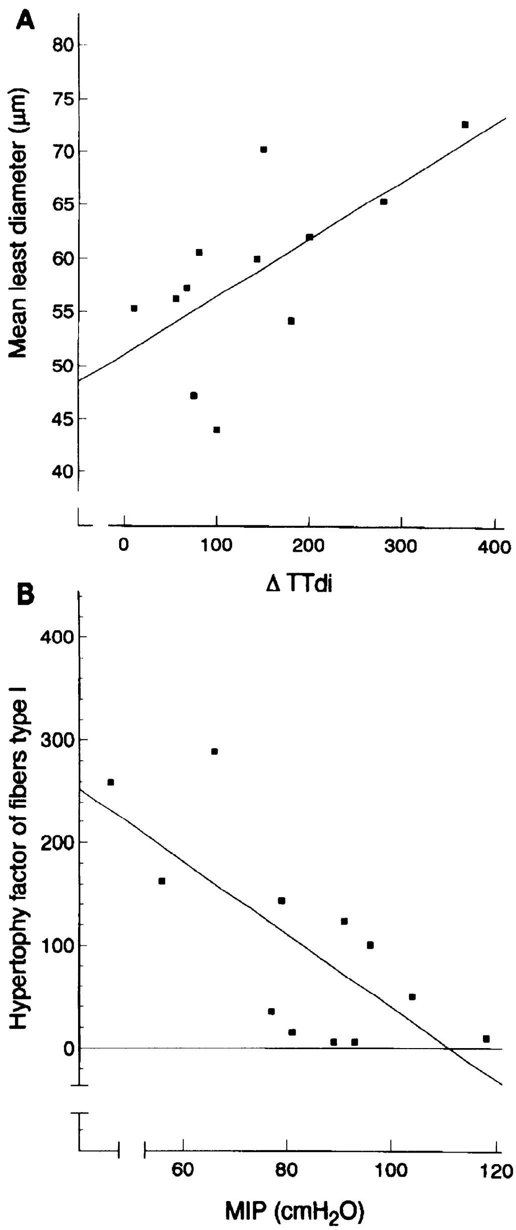

FIG. 3. *A*: relationship between diameter of all latissimus dorsi fibers and changes in diaphragm tension-time index (ΔTT_{di}) (room air vs. 8% CO_2). $r = 0.640$, $P < 0.05$. *B*: relationship between hypertrophy of LD type I fibers and maximal inspiratory pressure (MIP). $r = -0.636$, $P < 0.05$. Solid line, regression line.

When subjects breathed 8% CO_2, the amount of the change in TT_{di} directly correlated with the global hypertrophy index ($r = 0.640$, $P < 0.05$) and H_{II} ($r = 0.706$, $P = 0.01$). Interestingly, most of the patients with a higher increase in TT_{di} during CO_2 breathing (*subjects 5–7, 9,* and *10*) were those whose hypertrophic mode in the distributions of the LD fibers was more evident.

Relationships Between Muscle Structure and Nutrition

Percentage and size of the fibers. No relationships were found between nutritional items and the percentage of the fibers. In contrast, the diameter of type II fibers directly correlated with serum albumin ($r = 0.662$, $P < 0.05$).

Atrophy and hypertrophy factors: heterogeneity of the fiber distributions. No relationships were found between nutritional variables and the different morphological items from type I fibers. However, H_{II} directly correlated with the serum albumin ($r = 0.652$, $P < 0.05$) and the SD for fiber type II correlated with serum proteins ($r = 0.602$, $P < 0.05$).

DISCUSSION

Lung Function and Structure of LD

The most relevant findings in this study are the relationships observed between respiratory function and the structure of the LD, particularly the direct correlation found between the degree of airway obstruction and the size of the fibers of the LD. The same phenomenon is expressed by complimentary correlations obtained between other spirometric parameters and "dystrophy" (atrophy, hypertrophy, and heterogeneity) variables. Thus, some relationships between respiratory function and the structure of the muscle were present. Various comments can be made regarding these findings.

First, the method used in this study to assess the structure of the fibers (see APPENDIX) has not only made it possible to identify a shift in fiber size in COPD patients but also to understand that this shift is mainly due to the presence of additional populations of hypertrophic fibers. In other words, the behavior of the fibers was not homogeneous. Some became hypertrophic, whereas some remained normal in COPD patients. Furthermore, the distribution of the fibers in healthy subjects is probably similar to that observed in the present study in individuals with normal lung function: unimodal and relatively narrow, with a mean close to 60 μm (Fig. 2*A*). It is possible to hypothesize that as airway obstruction appears and progresses the distribution broadens and finally becomes bimodal (Fig. 2*B*). Further studies, however, are needed to clarify these points.

Second, this study was not designed to compare healthy subjects with COPD patients. In fact, only three subjects with normal lung function were included. Thus, it was not possible to make statistical comparisons between groups. On the contrary, this is a correlation study where both functional and structural variables have been considered as continuous. Interestingly, it is evident from the correlation figures (i.e., Fig. 1) that those subjects with normal lung function showed lower values for their LD fiber diameters.

This study included only patients submitted to thoracotomy. This model has been used by other authors in previous studies of respiratory muscles (10, 23, 38, 39). However, it certainly has its limitations: severe COPD patients cannot be submitted to thoracotomy, and it is difficult to obtain a control group of subjects with normal lung function. In addition, ethical reasons exclude alternative methods for obtaining LD biopsies (i.e., ambulatory biopsies in a general population). Thus, a correlation design was preferred for the present study.

It is not possible to conclude from the results of this study that LD directly participates in the development of respiratory work. In other words, correlations found between functional and structural data do not necessarily mean that a cause-effect relationship exists. However, it is well known that a chronic overload acting on a systemic skeletal muscle may account for the increase in the size of its fibers (18, 37). Although no comparable data are available on respiratory muscles, similar behavior under training conditions has been proposed (3, 7, 28). Moreover, structural changes in LD have been observed during chronic electrical stimulation in animal models (31).

The work of breathing is augmented in COPD. This augmentation can result in higher muscle activity to maintain an adequate level of ventilation (19, 41). If these increased loads were to act as a training, one could expect hypertrophy of the respiratory muscles (37). However, just the opposite has been described: the main respiratory muscles appear to be atrophic (10, 22, 39) in severe COPD patients, and their strength is reduced (14, 25, 36). A similar behavior (atrophy resulting in the impairment of the strength) has been described in other skeletal muscles (27). Different reasons have been given for the atrophy: malnutrition (22), the chronic increase in mechanical impedance of the respiratory system (14, 39), the absence of rest periods between ventilatory efforts (18), and the effect of hyperinflation on the respiratory muscles of the rib cage (neurogenic atrophy; Ref. 10). Thus, the atrophy of the main respiratory muscles could be added to other factors determining strength impairment (20). Then, additional muscles (such as LD) could be recruited to achieve the necessary level of pleural pressure.

Some potential mechanisms could be evoked to explain structural changes in LD. It has been suggested that LD could act as an accessory muscle for ventilation (17, 30, 42). Its actions could be implicated in holding thoracic elements in their place and/or collaborating in forced ventilation (11, 13, 30). In fact, it has been recently demonstrated (8, 32) that the activity of this muscle linearly increases when progressive inspiratory loads are applied in healthy subjects. Thus, as mentioned above, LD could be intermittently recruited in COPD patients, depending on the request and loads. Interestingly, Gronbaek and Skouby (21) observed inspiratory activity in LD during quiet breathing in 40% of the patients with chronic airflow obstruction vs. 0% of the control subjects. Moreover, the inspiratory activity was also noted in LD during forced breathing in 88% of the patients and in 46% of the control subjects. In other words, action of LD appears to be necessary when other respiratory muscles are surpassed during those situations where the mechanic loads of ventilation are strongly increased (e.g., airflow obstruction, bronchial infections, or exercise; Ref. 40). Additionally, LD could be recruited during sprint activations of the respiratory muscles during defensive mechanisms (e.g., cough). If these events frequently occur, then the intermittent activation of the muscle could emulate training or conditioning with the resultant hypertrophy of fibers (24). This is probably the situation even in patients with just mild to moderate airflow obstruction.

Unfortunately, because this study was not designed to evaluate functional properties of the LD muscle, no specific measures of its strength were included. However, with reference to the relationship found between lung function and LD structure, it would be interesting to design further studies that could establish a link between muscle use and changes in fiber size. This would make it possible both to elucidate the mechanism implicated in the structural changes and to evaluate the physiological relevance of the observed "hypertrophy." Previous electrophysiological studies support the hypothesis of a temporary recruitment of this muscle in healthy subjects when respiratory loads are applied (8, 32). Although few studies have been carried out in COPD patients, similar behavior could probably be expected (21).

Another point is the relative proportion of type I fibers found in the present study. It was slightly higher than that reported in previous papers (39). However, no relationships were observed between the percentage of type I fibers and lung function. Thus, it is unlikely that these differences were related to the degree of airway obstruction.

Respiratory Muscle Function and Structure of LD

Also of interest are the relationships found between the activity of respiratory muscles and the structure of LD. Patients whose respiratory muscle generated lower pressures (i.e., lower MIP) and whose diaphragm showed a decreased functional reserve during the supplementary ventilatory effort (i.e., higher increase in TT_{di} when breathing 8% CO_2; Table 2) were the individuals with more hypertrophic fibers in their LD (Fig. 3). This would be related with the above-discussed potential recruitment of LD during ventilatory overloads (8, 32), mainly in subjects whose diaphragm has a decreased functional reserve (21).

One possible criticism of the findings of this study could be the potential influence of the nutritional status or the concomitant thoracic malignancy on the muscle structure. However, it is unlikely that these factors were relevant; although all patients had an underlying small lung neoplasm, it was clinically limited to the thorax, there was no clinical evidence of paraneoplastic syndromes, and nutritional parameters were between the normal range. It could be argued that slight correlations were found between some of the nutritional markers and the size of the fibers. However, these correlations would suggest only that both airway obstruction and an adequate nutritional substrate would be necessary to hypertrophy the fibers of LD.

In conclusion, chronic airway obstruction seems to be related to changes in the size of the fibers of the LD. Thus, it would not appear to be the most appropriate control for the structural studies of respiratory muscles. The changes observed in LD could be explained by the eventual recruitment of this muscle under ventilatory overloads (8, 21, 32). A typical position would be when a severe COPD patient leans forward with the arms fixed on the thighs.

APPENDIX

Evaluation of Atrophy, Hypertrophy, and Heterogeneity of the Fiber Distributions

Several comments can be made with reference to the methodology used in this study for evaluating the atrophy, hypertrophy, and overall heterogeneity of fiber distributions. Classically, the morphometric evaluation of a muscle is expressed by three variables: the mean value of the diameter of its fibers, the atrophy factor, and the hypertrophy factor (4–6, 15). The latter two are based on a score that qualifies the fibers with diameters below or above the extreme limits (i.e., 40 and 80 μm, respectively), which has been suggested by Brooke and Engels (4). Thus, the continuous distribution of such fibers is transformed in a semicategorical model. In addition, only the two tails of the distribution curve (atrophy and hypertrophy) are actually evaluated. Furthermore, they are evaluated separately. This method can be useful in some cases, but it appears to be too simple for research purposes. Part of the information is lost and, paradoxically, a particular muscle could show a normal mean diameter with increased atrophy and/or hypertrophy factors. The visual and numerical analyses of the smoothed histograms can be used as a complimentary method for evaluating the overall heterogeneity of a muscle (29). This is an attempt to best characterize the actual size of the fibers by using a mathematical model with a minimal number of compartments. The morphology of this curve would make it possible to identify additional populations of "dystrophic" fibers (either atrophic or hypertrophic). Recent reports have proposed nonparametric methods as alternatives to the histograms in the analysis of fiber distributions (29). In addition, the numeric variables obtained from the curve (particularly the mean but also the SD) could be useful in describing the overall behavior of the fibers and the heterogeneity of the distribution in a specific subject. The shifts of the curve, expressed by changes in the mean, have been generally used to assess the general behavior of the fibers (shifts to the right would represent a hypertrophic tendency, whereas shifts to the left would express an atrophic trend). The additional use of the SD would indicate the dispersion of the distribution.

We acknowledge Angela Ojeda, Montserrat Trenchs, and Nuria Soler for excellent technical assistance; Drs. Jaume Marrugat and Joan Vila from the Municipal d'Investigació Mèdica (IMIM) for statistical advice; and Joseph A. Salazar for editing aid.

This work was supported by Fondo de Investigació Sanitaria Grant 92/0314, Comissió Interdepartamental de Recerca i Innovació Tecnològica Grant AR 91–367, and IMIM Grant 1642380.

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Received 3 December 1993; accepted in final form 17 November 1994.

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