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Gender and skeletal muscle characteristics in subjects with chronic obstructive pulmonary disease

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Summary
Background: The influence of gender in the clinical expression of COPD has received important attention. Limited information exists regarding gender differences in the skeletal muscle characteristics in COPD subjects. The present study was aimed to determine the differences in the skeletal muscle characteristics in men and women with and without COPD.
Methods: For comparison we studied 24 female (61 ± 9 years) and 30 male (65 ± 8 years) COPD patients with similar disease severity. In addition healthy subjects, 17 women (58 ± 8 years), and 9 men (57 ± 8 years) were studied. Pulmonary function, health status, six minute walk distance test (6MWD) and vastus lateralis muscle biopsy were assessed. Fiber type proportion, fiber type cross sectional area (CSA), capillary counts, and activity of citrate synthase (CS), 3-hydroxyacyl-CoA-dehydrogenase (HAD) and lactate-dehydrogenase (LDH) were determined.
Results: Pulmonary function, health status and 6MWD were similar in male and female COPD patients. Fiber type distribution was similar between women (I = 42 ± 9%, IIA = 39 ± 13%, IIX = 19 ± 7%) and men (I = 39 ± 13%, IIA = 38 ± 9%, IIX = 29 ± 10%) with COPD, as well as CSA, capillarity and enzymes (CS 8.59 ± 1.6 vs.9.74 ± 2.6, HAD 9.03 ± 1.9 vs. 9.84 ± 2.5, LDH 124 ± 48 vs. 151 ± 68 μmol min^{-1} g^{-1}). In normal subjects a decrease in type IIX fibers CSA was found in women compared with men (3703 ± 1478 vs. 5426 ± 1386 μm^2, respectively).

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Conclusions: Female and male with COPD have similar skeletal muscle characteristics; it is possible that the disease blurs the gender differences. On the other hand, there seems to be fewer differences in muscle characteristics between older men and women, perhaps due to lower male testosterone levels and physical inactivity.

Introduction

The influence of gender in the clinical expression of COPD has received important attention in the past decade. In general women with COPD report worse symptoms (in particular dyspnea), have lower exercise capacity, worse health related quality of life (HRQoL), and more anxiety and depression, but apparently lower all-cause and respiratory mortality rates.[1–3]

On the other hand, skeletal muscle dysfunction is commonly found in patients with COPD, and is associated with exercise intolerance, daily activities limitation, impaired HRQoL, health care resources utilization and increased mortality.[4–7] It is possible that gender differences in the skeletal muscle function and structure could explain in part some of the differences described between men and women. However, muscle characteristics have not been assessed in many women affected by COPD,[8] and most studies have pooled the female results with those of men assuming no gender differences.[9,10]

In healthy subjects there are some gender differences in the skeletal muscle features. Although an extensive study reported a lower proportion of type I fibers in the female quadriceps muscles,[11] other studies have not found gender differences in the proportion of major skeletal muscle fiber types.[12–14] In young subjects, the cross sectional area (CSA) of the three major fiber types was larger in men compared to women[12–14] and the area occupied by each specific fiber type was IIA > I > IIB for men and I > IIA > IIB for women.[13] Difference in the CSA has also been reported in subjects 50 years and over,[14] whereas others have reported only decreased CSA of the type IIA fibers in older women.[15]

To our knowledge there is limited information available regarding gender differences in the skeletal muscle histochemical and metabolic characteristics in subjects with COPD, therefore the aims of this study were a) to evaluate the gender differences of the skeletal muscle characteristics in COPD patients b) to explore the gender differences of the muscle characteristics in healthy subjects and c) to explore the differences by gender and COPD status in the skeletal muscle characteristics.

Patients and methods

The study group consisted of 24 women and 30 men with COPD recruited from the pulmonary clinic of the Hospital Universitario de Caracas. The control group was formed by healthy subjects of similar age, 17 women and 9 men The study was approved by the human-research review board of the site and all patients and control subjects signed the informed consent.

We used the definition and severity stratification of COPD proposed by the Global Initiative for Chronic Lung Disease (GOLD): a ratio of the post-bronchodilator forced expiratory volume in one second over forced vital capacity (FEV_1/FVC) below 0.70[16] and a history of smoking >20 pack-yrs.

Patients were in a clinically stable condition, defined as no acute exacerbation of COPD for six weeks prior to entry into the study, and were receiving optimal medical therapy without regular use of systemic corticosteroids. Patients were excluded if they had previous diagnosis of asthma, history of atopy or any other chronic inflammatory illness, history of malignancy, congestive heart failure, and metabolic diseases, as well as those involved in regular exercise training. The subjects in the control group had a sedentary life style and were excluded if they performed regular exercise.

Pulmonary function test, health status and exercise capacity

The FEV_1, FVC and FEV_1/FVC were calculated according to the recommendations of the ATS.[17] Normal values for pulmonary measurements were taken from a standard reference source.[18] The HRQoL was assessed with the St. George's Respiratory Questionnaire (SGRQ), Spanish version.[19,20] Functional capacity was assessed with the six-minute walking distance (6MWD) and the test was performed following ATS guidelines.[21]

Skeletal muscle study

All patients and control subjects underwent muscle biopsies. Samples were taken from the vastus lateralis part of the quadriceps femoris muscle, with the Bergström needle.[22] The muscle sample was divided in two parts, one of them was embedded with "optimal cutting temperature" or OCT compound (Tissue Tek II, Sakura Finetek USA Inc. Torrance CA) and frozen in isopentane cooled in liquid nitrogen for histochemical analysis, other part was frozen directly in liquid nitrogen for enzymes determination.

Transverse 10 μm serial sections were cut in a cryostat at −20 °C and mounted on cover slips for staining for adenosine triphosphatase (ATPase) after alkaline (pH: 10.3) and acid (pH: 4.37 and 4.6) preincubation.[23] In some patients, sections were also stained for reduced nicotinamide adenine dinucleotide diaphorase (NADH-d)[24] and α-glycerophosphate dehydrogenase (α-GPD).[25] The fibers were classified as high, medium, or low oxidative activity with NADH-d, and high, medium and low glycolytic capacity according to the intensity of the α-GPD staining, evaluated blindly by two different observers. Capillaries were visualized by the α-amylase-PAS reaction.[26] Photomicrographs at a final magnification of ×200 were taken from these sections and the fibers were identified by comparison with the ATPase sections. An area of the photograph was

delimited, measured with a planimeter, and fibers and capillaries were counted to calculate the mean area of the fibers, capillaries/mm^2, and capillaries/fiber ratio. Also, capillaries around each fiber type were counted and the mean was expressed as capillary contacts. All the fibers of one type were drawn together, and the area was measured by planimetry to calculate the mean cross sectional area (CSA) of each fiber type. Capillaries per area were calculated dividing mean capillary contact for a fiber type $\times$ 1000 by mean CSA (μm^2).

After weighing, the second part of the sample was homogenized in ice-cooled potassium phosphate buffer. The activity of citrate synthase (CS), β-hydroxy-acyl-CoA-dehydrogenase (HAD) and lactate-dehydrogenase (LDH) was assayed using fluorometric techniques.[27] Results are expressed in μmol min^{-1} g^{-1} wet weight.

Statistical analysis

Data are presented as mean ± SD. The differences in the skeletal muscle characteristics and enzymes activity between genders in COPD and control subjects were determined using Student *t* test. Pearson's correlation (*r*) was used to assess the relationship between skeletal muscle characteristics with functional and anthropometric variables. The program used was "Statistica" (Statsoft, Inc. OK, USA). Acceptable level of statistical significance for the test was a probability value equal or less than 0.05.

Results

The clinical, spirometric, and skeletal muscle data of the COPD subjects by gender are shown in Table 1. Weight and height were lower in female COPD patients compared to men. There were no differences in age, body mass index (BMI), spirometric values (% predicted), 6MWD, and SGRQ total score between woman and men with COPD. The fiber type proportion, mean area of the fibers, CSA of each fiber type, percentage of area occupied by each specific fiber type, and capillarity (expressed as capillary density and capillaries per fiber ratio) did not show differences between the genders in COPD patients. The levels of oxidative (CS and HAD) and glycolytic (LDH) enzymes were also similar between men and women with COPD.

The Table 2 shows the anthropometric, pulmonary function and skeletal muscle characteristics of the control subjects by gender. Although, the height and weight were lower in women compared with men, the BMI was similar in both genders, as well as the spirometric values. Control

Table 1 Clinical, spirometric, and skeletal muscle histochemical and metabolic characteristics in COPD patients by gender.

Variables	Women (n = 24)	Men (n = 30)	p-level
Age, years	61 ± 9	65 ± 8	NS
Height, cm	153 ± 7	166 ± 6	<0.00001
Weight, kg	49.8 ± 12.0	65.4 ± 16.1	<0.001
BMI, kg/m^2	21.0 ± 4.1	23.4 ± 5.3	NS
FVC, % pred.	74 ± 12	73 ± 17	NS
FEV_1, % pred.	49 ± 17	46 ± 19	NS
FEV_1/FVC, %	49 ± 8	45 ± 12	NS
SGRQ. Total score	44 ± 17	58 ± 9	NS
6MWD, meter	470 ± 83	448 ± 97	NS
Type I, (%)	42 ± 9	39 ± 13	NS
Type IIA, (%)	38 ± 10	38 ± 9	NS
Type IIX, (%)	19 ± 7	24 ± 10	NS
Mean CSA, μm^2	4355 ± 1348	5042 ± 1783	NS
CSA I fibers, μm^2	5299 ± 1940	5987 ± 2032	NS
CSA IIA fibers, μm^2	4065 ± 1240	4883 ± 2002	NS
CSA IIX fibers, μm^2	3488 ± 1229	3754 ± 1846	NS
% area type I fibers	49 ± 8	45 ± 12	NS
% area type IIA fibers	35 ± 8	37 ± 11	NS
% area type IIX fibers	16 ± 7	18 ± 10	NS
Capillaries/mm^2	353 ± 119	340 ± 195	NS
Capillaries/fiber Ratio	1.43 ± 0.4	1.45 ± 0.3	NS
CS, μmol min^{-1} g^{-1}	8.59 ± 1.62	9.74 ± 2.61	NS
HAD, μmol min^{-1} g^{-1}	9.03 ± 1.85	9.84 ± 2.54	NS
LDH, μmol min^{-1} g^{-1}	124 ± 48	151 ± 68	NS

Abbreviations: BMI: Body mass index; FVC: Forced vital capacity; FEV_1: Forced expiratory volume in one minute; SGRQ: Saint George Respiratory Questionnaire; 6MWD: six-minute walking distance. CSA: Cross sectional area. CS: Citrate synthase. HAD: β-hydroxy-Acyl-CoA- dehydrogenase. LDH: Lactate dehydrogenase.

Table 2 Anthropometric, spirometric, and skeletal muscle histochemical and metabolic characteristics in control subjects by gender.

Variables	Women (n = 17)	Men (n = 9)	p-level
Age, yr	58 ± 8	57 ± 8	NS
Height, cm	153 ± 6	167 ± 14.4	<0.001
Weight, kg	63.1 ± 7.6	73.5 ± 8	<0.05
BMI, kg/m^2	26.8 ± 3.5	26.6 ± 4.3	NS
FVC, % predicted	98 ± 10	102 ± 19	NS
FEV_1, % predicted	99 ± 10	102 ± 15	NS
FEV_1/FVC, %	82 ± 3	81 ± 4	NS
Type I, (%)	54 ± 10	50 ± 14	NS
Type IIA, (%)	36 ± 9	39 ± 14	NS
Type IIX, %	10 ± 5	13 ± 4	NS
Mean CSA,	4893 ± 1628	5967 ± 772	NS
CSA I fibers, μm^2	5726 ± 2080	6814 ± 992	NS
CSA IIA fibers, μm^2	4689 ± 1660	5903 ± 929	0.08
CSA IIX fibers, μm^2	3703 ± 1478	5426 ± 1386	<0.05
% area type I fibers	48 ± 8	46 ± 13	NS
% area type IIA fibers	37 ± 8	40 ± 14	NS
% area type IIX fibers	15 ± 7	14 ± 7	NS
Capillaries/mm^2	322 ± 112	288 ± 63	NS
Capillaries/fiber ratio	1.48 ± 0.18	1.69 ± 0.28	0.06
CS, μmol min^{-1} g^{-1}	10.5 ± 1.7	11.4 ± 2.2	NS
HAD, μmol min^{-1} g^{-1}	10.9 ± 1.8	8.3 ± 3.7	NS
LDH, μmol min^{-1} g^{-1}	180 ± 50	197 ± 49	NS

Abbreviations: FVC: Forced vital capacity. FEV_1: Forced expiratory volume in one minute. CSA: Cross sectional area. CS: Citrate synthase. HAD: β-hydroxy-Acyl-CoA- dehydrogenase. LDH: Lactate dehydrogenase.

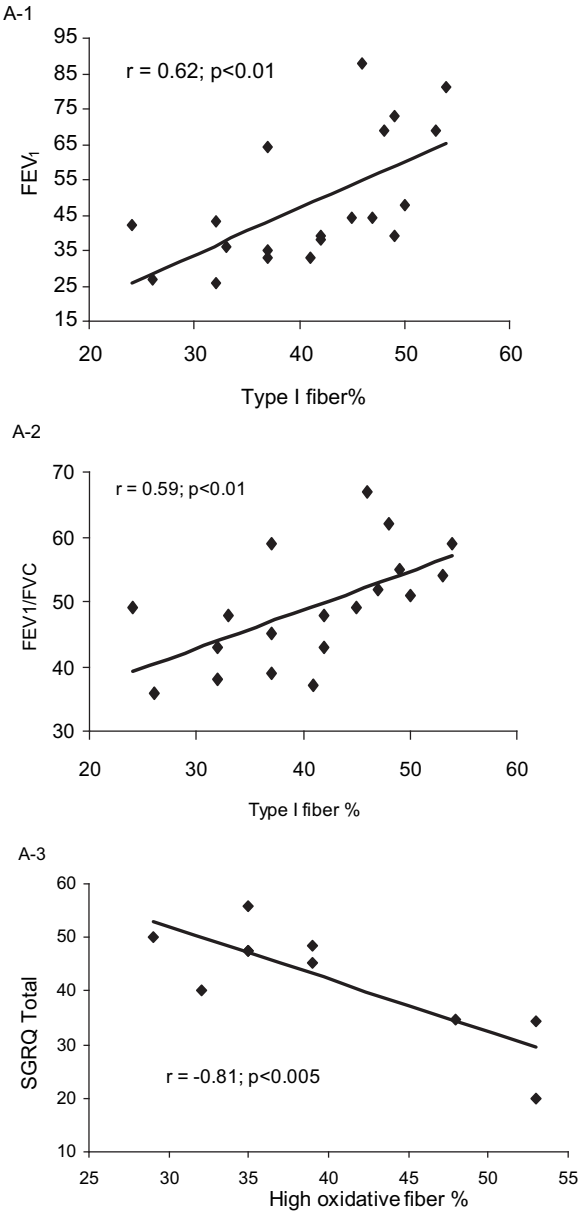

Figure 1 Significant correlations between skeletal muscle characteristics and anthropometric, spirometric and health related quality of life parameters in women. FVC: Forced vital capacity; FEV_1: Forced expiratory volume in one minute; SGRQ: Saint George Respiratory Questionnaire.

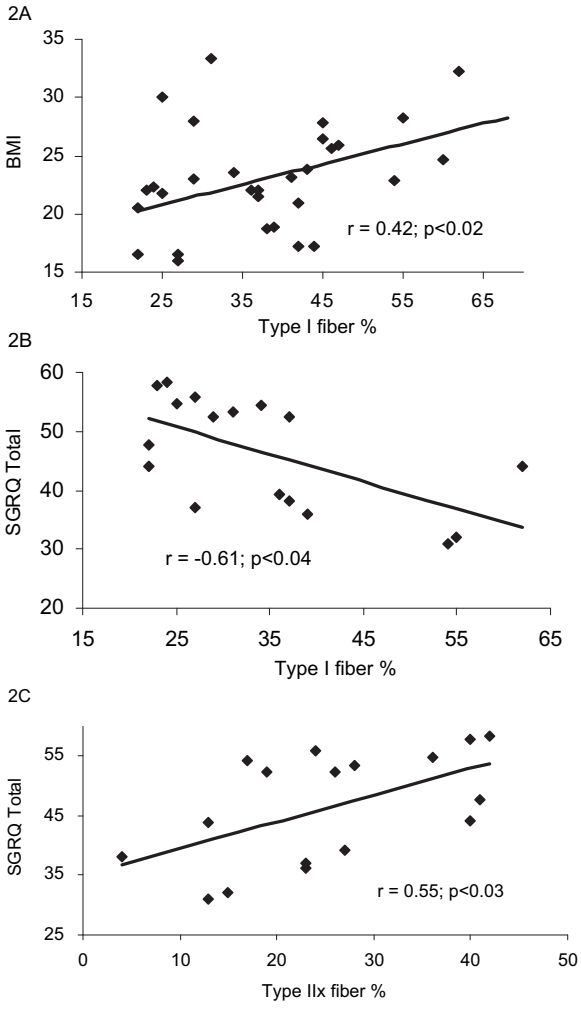

Figure 2 Significant correlations between skeletal muscle characteristics and anthropometric, spirometric and health related quality of life parameters in men. BMI: Body mass index. SGRQ: Saint George Respiratory Questionnaire.

women showed significantly lower type IIX fibers CSA, compared to control men. The mean CSA, type IIA fibers CSA and capillaries/fiber ratio tended to be smaller in women compared to men. The other muscle characteristics were similar in both genders.

Significant correlations between skeletal muscle characteristics with anthropometric and functional parameters are shown in Figs. 1 and Fig. 2. In COPD women, FEV_1 (% of predicted) and FEV_1/FVC directly correlated with type I fiber proportion (Fig. 1A and B, respectively). In addition, SGRQ total score inversely correlated with the percentage of oxidative fibers (Fig. 1C). No other relationships were observed between skeletal muscle characteristic with anthropometric and functional variables in women with COPD. There was a direct correlation between the BMI and type I fibers proportion in men with COPD (Fig. 2A). SGRQ total score inversely correlated with the percentage of type I fibers (Fig. 2B), and directly with the percentage of type IIX fiber (Fig. 2C). No other relationships were observed in this group.

Skeletal muscle characteristics by gender and COPD status is shown in Table 3. COPD females compared to control females had a lower proportion of type I fibers, CS, HAD and LDH levels. A trend to have a higher proportion of type IIX fibers was also observed ($p = 0.10$). Similar values were observed in the other muscle characteristics. Men with COPD had higher proportion of type IIX fibers and lower CSA of type IIX fibers, compared to control males. No other differences were observed between men with and without COPD.

Comparison of skeletal muscle characteristics between COPD patients and control subjects as a group is shown in Table 4. COPD patients had lower type I fiber proportion, as well as percentage of area occupied by type I fibers

Table 3 Skeletal muscle histochemical and metabolic characteristics by gender and COPD condition.

Variables	Female		Male	
	COPD ($n = 24$)	Control ($n = 17$)	COPD ($n = 30$)	Control ($n = 9$)
Type I, (%)	42 ± 9	48 ± 8*	39 ± 13	50 ± 14
Type IIA, (%)	38 ± 10	37 ± 8	38 ± 9	40 ± 15
Type IIX, (%)	19 ± 7	15 ± 7	24 ± 10	14 ± 3†
Mean CSA, μm^2	4355 ± 1348	4893 ± 1628	5042 ± 1783	5967 ± 772
CSA I fibers, μm^2	5299 ± 1940	5726 ± 2080	5987 ± 2032	6814 ± 992
CSA IIA fibers, μm^2	4065 ± 1240	4689 ± 1660	4883 ± 2002	5903 ± 929
CSA IIX fibers, μm^2	3488 ± 1229	3703 ± 1478	3754 ± 1846	5426 ± 1,386†
% area type I fibers	49 ± 8	54 ± 10	45 ± 12	48 ± 14
% area type IIA fibers	35 ± 8	36 ± 9	37 ± 11	39 ± 14
% area type IIX fibers	16 ± 7	10 ± 5	18 ± 10	13 ± 4
Capillaries/mm^2	353 ± 119	322 ± 112	340 ± 195	288 ± 63
Capillaries/fiber ratio	1.43 ± 0.4	1.48 ± 0.18	1.45 ± 0.3	1.69 ± 0.28
CS, $\mu mol\ min^{-1}\ g^{-1}$	8.59 ± 1.62	10.51 ± 1.7*	9.74 ± 2.61	11.4 ± 2.2
HAD, $\mu mol\ min^{-1}\ g^{-1}$	9.03 ± 1.85	10.86 ± 1.84*	9.84 ± 2.54	8.3 ± 3.7
LDH, $\mu mol\ min^{-1}\ g^{-1}$	124 ± 48	180 ± 50*	151 ± 68	197 ± 49

*$p < 0.05$ (female COPD vs. female control).
†$p < 0.05$ (male COPD vs. male control).
Abbreviations: CSA: Cross sectional area. CS: Citrate synthase. HAD: β-hydroxy-Acyl-CoA- dehydrogenase. LDH: Lactate dehydrogenase.

Table 4 Muscle characteristics in COPD patients and control subjects as a group.

Variables	COPD ($n = 54$)	Control ($n = 26$)	p-level
Type I, %	40 ± 11	47 ± 10	< 0.05
Type IIA, %	38 ± 11	38 ± 10	NS
Type IIX, %	22 ± 9	15 ± 6	<0.001
Mean CSA, μm^2	4779 ± 1628	5332 ± 1475	NS
CSA I fibers, μm^2	5684 ± 2001	6175 ± 1838	NS
CSA IIA fibers, μm^2	4523 ± 1743	5178 ± 1552	NS
CSA IIX fibers, μm^2	3634 ± 1589	4331 ± 1687	NS
% area type I fibers	48 ± 10	54 ± 10	<0.05
% area type IIA fibers	36 ± 9	36 ± 9	NS
% area type IIX fibers	17 ± 9	10 ± 5	<0.01
N° of capillary contacts			
Type I	4.43 ± 0.86	4.54 ± 0.67	NS
Type IIA	3.59 ± 0.75	3.88 ± 0.83	NS
Type IIX	3.05 ± 0.82	3.41 ± 0.99	NS
Capillary contact/ fiber CSA			
Type I	0.76 ± 0.27	0.79 ± 0.25	NS
Type IIA	0.86 ± 0.38	0.81 ± 0.37	NS
Type IIX	0.90 ± 0.51	0.82 ± 0.29	NS
Capillaries/mm^2	346 ± 165	314 ± 96	NS
Capillaries/fiber ratio	1.44 ± 0.3	1.58 ± 0.2	NS
CS, $\mu mol\ min^{-1}\ g^{-1}$	9.07 ± 1.9	10.82 ± 2.0	<0.05
HAD, $\mu mol\ min^{-1}\ g^{-1}$	9.54 ± 2.3	9.82 ± 2.0	NS
LDH, $\mu mol\ min^{-1}\ g^{-1}$	140 ± 61	186 ± 50	<0.05

Abbreviations: BMI: Body mass index; CSA: Cross sectional area. CS: Citrate synthase. HAD: β-hydroxy-Acyl-CoA- dehydrogenase. LDH: Lactate dehydrogenase.

compared to controls. COPD patients also had higher proportion of type IIX fibers and percentage of area occupied by this fiber type. CS and LDH activities were lower in COPD patients compared to control group. No differences were observed in HAD activity, fiber CSA and capillarity between COPD patients and control subjects.

Discussion

The skeletal muscles are formed by different proportions of type I, IIA and IIX fibers. Type I fibers are fatigue resistant, show slow contraction speed, high oxidative enzymes activity and high capillary supply; type IIX fibers have low fatigue resistance, show strong and fast contractions, have high glycolytic and low oxidative capacity and lower capillarity; IIA fibers have intermediate properties between I and IIX fibers. Patients with COPD have a progressive redistribution of the muscle fibers from type I to type IIX and reduced oxidative capacity in the vastus lateralis.[9,10]

The results of the present study indicate that there were no significant gender differences in the muscle fiber type distribution, muscle fiber CSA, capillary supply, oxidative and glycolytic capacity, CS, HAD and LDH enzyme activities in the quadriceps muscle of patients with COPD. Although other authors have described gender differences in the quality of well being and functional capacity in patients with COPD,[2] in the present study COPD patients of both genders showed similar 6MWD and HRQoL. It is to note that they were chosen with similar smoking history and severity of the disease, and the results showed no differences in the skeletal muscle characteristics. This suggests (but does not discard) that the clinical differences reported between women and men are more related to other factors, such as severity of the disease or exposure to cigarette smoke, rather than to gender difference in reaction to the disease.

Limited information exists regarding muscle characteristic in older normal subjects. The results of previous

studies indicate that fiber type proportions are similar in both genders, but fibers CSA are larger in men.[12–14] The findings of the present study are in line with those that reported no gender differences of fiber type proportion in healthy subjects[12–14]; however, partially contrast with those that found reduction of the CSA of all fibers types in women, since in our study women only had a significant reduction in type IIX fiber CSA and a trend in the IIA fiber. In addition, no gender difference was found in the percentage of area occupied by type I and IIA fibers. This contrasts with the findings reported by Marquis et al. in young subjects.[6] It is possible that fiber CSA differences between genders reduce with aging, probably due to the presence of hypogonadism in men, since testosterone increases fiber size in healthy young men.[28] Hypogonadism has been reported in about one third of the control male subjects of similar age to COPD patients.[29]

A previous report showed that in control subjects, men have a trend of having higher capillary/fiber ratio compared to women, and this appears to be related with fiber size, because disappears when capillaries are expressed per area of fiber.[30] Our results are in agreement with this finding; after calculating of capillaries expressed per area of fiber (results not shown) there were not differences between control men and women.

The lack of gender differences of the skeletal muscle characteristics in COPD patients could be due to the shift of fiber types from type I to IIX,[10] the decrease of the oxidative capacity of muscle fibers produced by the disease,[9] and the hypogonadism in older men that affects 50% of the COPD patients.[29]

Previous studies in COPD patients that include mainly men showed a reduction in the proportion of type I fibers[9,10,30–32] and, an increase in percentage of IIX fibers[9,30,31] compared with control subjects. Our results are in agreement with this distribution in COPD patients, independent of gender. In these patients, reduction of CSA has been also found in types fibers I, IIa and IIab,[30] as well as in IIX and IIA/IIX fibers compared to normal subjects,[33] however, other authors have not found CSA reduction in the three major fiber types.[32]

In the present study, lower IIX fiber CSA was found in male with COPD compared to control men, whereas no differences were found in females (COPD vs. control) (Table 3). In addition, control women showed lower CSA of this type of fiber compared to control men (Table 2). The discrepancy observed among the studies could probably be explained by the differences of the disease severity, patient's activity and the percentage of fat free mass of the subjects.

The results of capillary density in COPD patients are contradictory.[30,31] Whittom et al.[30] described reduction of capillary contacts in types I, IIA and IIAB, whereas others did not find any difference in capillary contacts between COPD patients and normal subjects.[31] The results of the present study are in agreement with the last report, since no differences were observed in capillary indexes. These discrepancies could be due to modification in the size of the fibers, because they disappeared when capillarity was expressed as capillaries per area of fiber.[30]

Reduction of CS and HAD has been found in a group of COPD patients, mainly composed of men.[9] In the present work this reduction was found in the females but not in males (COPD vs. control) (Table 3). Although all patients had a sedentary way of life, it is possible that differences in activity could produce changes in the level of the oxidative enzymes in the muscle. LDH has been reported to be similar in COPD patients compared to control subjects,[9,34] however, in the present work, it decreased slightly, but significantly, in the female COPD group compared to control female (Table 3); this is an unexpected result, because in a COPD group studied in the same laboratory, LDH levels were similar between COPD patients and control subjects.[34]

In a recent meta-analysis Gosker et al. have assessed whether vastus lateralis muscle fiber type proportions were associated with the disease severity and, have provided reference values for the proportion of fiber types in the vastus lateralis in COPD.[10] Their results indicated that FEV_1, FEV_1/FVC ratio and, BMI were directly associated with the proportion of type I fibers. In the present study, FEV_1 (% pred.) and FEV_1/FVC ratio directly correlated with type I fiber proportion in women with COPD, and in men with COPD there was a direct relationship between BMI and type I fiber proportion (Figs. 1 and 2, respectively). The results suggest that lower airflow obstruction is associated with a higher proportion of type I fibers which are fundamentally oxidative. The reason for the gender differences are not clear and are difficult to explain with the results of the present study, but could be related with the number of subjects studied.

In a previous report we have shown that SGRQ (total score) inversely correlated with type I fiber proportion.[5] In the present study this was confirmed in the male group; moreover SGRQ (total score) was directly related with type IIX fiber proportion. Although in female COPD patients, the SGRQ total score did not correlate with fiber types, this score was inversely related with the proportion of fiber with high oxidative capacity (data not shown), indicating that in general a better HRQoL is associated with the oxidative capacity of muscle fibers.

Finally there is a limitation in the present study that needs to be discussed. Due to the invasive nature of procedure used to obtain the skeletal muscle samples, a relatively small number of subjects were studied, in particular male control subjects. It is difficult to find normal men of comparable age to COPD patients that adjust to our strict inclusion criteria. However, this comparison between men and women with COPD and healthy subjects, appears to be one of the largest number ever reported of skeletal muscle characteristics.

In conclusion, the vastus lateralis muscle in patients with COPD has similar characteristics in female and male subjects; so it seems valid to combine the results of studies in the vastus lateralis of COPD patients of both genders. It is possible that the disease blurs the gender differences. On the other hand, there seems to be fewer differences in muscle fiber size between older men and women, perhaps due to the decrease of testosterone in men. Studies in this direction should be carried out in the future.

Conflict of interest

None of the authors has conflict of interest.

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