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Thigh muscle strength and endurance in patients with COPD compared with healthy controls

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Summary The aim of this study was to evaluate thigh muscle strength and endurance in patients with COPD compared with healthy controls. Forty-two patients (26 women; 16 men) with moderate to severe COPD and 53 (29 women; 24 men) age-matched healthy controls participated in the study. The subjects were tested for maximum voluntary contractions (MVC), endurance and fatigue of the thigh muscles on an isokinetic dynamometer (KinCom®). Endurance was expressed as the number of attained repetitions of knee extension and muscle fatigue as a fatigue index (FI).

MVC in knee extension was 17% lower in female patients ($P = 0.017$) but no difference was found in male patients ($P = 0.56$) compared to controls. MVC in knee flexion was lower both in female (51%) ($P < 0.001$) and male patients (40%) ($P < 0.001$) compared to controls. Both female and male patients had significantly lower muscle endurance compared to controls. Female patients had a higher FI (22.5%) than female controls (10%) ($P = 0.001$) while no difference was found regarding FI between male patients (15%) and male controls (10%) ($P = 0.103$). The level of self-reported everyday physical activity did not differ between groups.

The results showed impaired skeletal muscle function in COPD, except for MVC in knee extension in male patients. Female patients seemed to be more prone to decrease in thigh muscle function. More focus on improving muscle strength and muscle endurance should be considered when designing pulmonary rehabilitation programs. Patients with preserved level of physical activity can be included in exercise programs and gender-related differences should be taken into account.

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Introduction

Exercise intolerance in patients with chronic obstructive pulmonary disease (COPD) contributes to a poor quality of life in these patients and an increased need for medical assistance.[1–3] This exercise limitation has traditionally been explained by the impairment of ventilatory function.[4] However, studies have suggested that many patients with COPD may stop exercising because of leg muscle fatigue prior to ventilatory limitation.[5,6] Furthermore, skeletal muscle dysfunction is common in patients with COPD and might be explained by muscle atrophy, reduced oxidative metabolism, reduced muscle capillarization and change in muscle fiber type, i.e., reduced proportion of type I fibers and increased proportion of type IIb.[7,8]

Inactivity is often assumed to be one of the main reasons for these peripheral muscle abnormalities in patients with COPD.[9] Exercise training has been shown to improve muscle function in patients with COPD, suggesting that deconditioning is an important contributor to the skeletal muscle dysfunction.[10–13] Coronell et al.[14] showed that despite relatively preserved level of physical activity, patients with COPD have reduced muscle function compared to healthy age-matched controls, suggesting that other factors than inactivity may contribute to the alterations in peripheral muscle function. These factors, related to the disease, are suggested to be malnutrition, exposure to systemic corticosteroids, tissue hypoxia, coexisting heart disease, systemic inflammation, skeletal muscle apoptosis, oxidative stress, tobacco use, individual susceptibility and hormone alterations.[4,8] In addition, some authors have found elevated levels of inflammatory cytokines indicating presence of systemic myopathy.[15]

The majority of the studies on lower-extremity muscle function in COPD are focused on muscle strength rather than muscle endurance. Furthermore, it is still unclear which modality of physical training is the best to increase muscle function in these patients. Defining whether patients with COPD have reduced muscle strength and/or muscle endurance compared to healthy controls is necessary in order to be able to find the best exercise modality for these patients. The level of everyday physical activity is important to assess when comparing skeletal muscle dysfunction in patients with COPD with healthy controls. To our knowledge, there are not many studies that have taken this issue into consideration. Moreover, to the authors' knowledge, only Van't Hul et al.[16] have investigated gender-related differences regarding muscle strength and endurance of lower extremities in patients with COPD.

Our hypothesis is that peripheral muscle abnormalities found in patients with COPD might lead to decrease in muscle strength and endurance which consequently results in increased muscle fatigability. The aim of this study was thus (i) to determine whether patients with COPD have impaired strength and endurance in the thigh muscles compared to age-matched healthy controls, (ii) to investigate if the level of self-reported everyday physical activity was decreased in patients with COPD and (iii) whether gender-related differences in muscle performance exist compared to a control group.

Material and methods

Study population

Forty-two patients (26 women and 16 men) aged 53–74 years with moderate to severe, stable COPD and 53 (29 women and 24 men) age-matched healthy controls were included in the study. The patients were clinically diagnosed with COPD according to GOLD criteria[17] and recruited from outpatients on treatment at two Hospitals in Northern Sweden. The inclusion criteria used to select the patients were $FEV_1/VC < 0.7$, $FEV_1 < 80\%$ of predicted, stable medication and no infection during the last month before participating in the study, and absence of cardiac, orthopaedic, neurological or psychological disorders. All patients performed an exercise electrocardiogram test on a cycle ergometer (Rodby TM, RE 829, Enhörna, Sweden) and a spirometry test (Spirolab, Medical International Research, Roma, Italy) before entering the study. The patients were ex-smokers and none of them were treated with long-term oxygen therapy. Thirty-three patients were using inhaled corticosteroids and one used daily oral corticosteroids. None of them was engaged in any organized physical activity before the study. The patients were referred to the clinic to participate in a pulmonary rehabilitation program and were tested, in addition to other tests, for muscle strength and endurance. The healthy control group was recruited from pensioner's associations in Umeå, Sweden. The controls had to meet the following criteria: age between 53 and 74 and no presence of pulmonary, cardiac, orthopaedic, neurological or psychological disorders. The controls should not have smoked in the last 10 years and should not be participants in any organized physical activity. All subjects gave their informed consent before the study. The Research Ethics Committee of

Umeå University, Sweden approved the study (Um dnr 99-067).

One patient was not included in the analyses because he did not understand the instructions and could not complete the protocol. One subject in the control group dropped out because she admitted she had pain in the hips during the tests. Two other control subjects were excluded from the analyses of the endurance test because of technical problems. Anthropometric data for patients with COPD and controls are presented in Table 1.

Isokinetic tests

The tests were performed using an isokinetic dynamometer (KinCom®, Chattanoga, IL) and the dominant leg was evaluated. The test consisted of two different parts: maximal contractions of the thigh muscles and an endurance test. Standardized verbal encouragement and instructions were strictly applied for both groups. During the measurements, the subjects were seated according to the recommendation by the manufacturer. Before the experiment the subjects performed a 5 min warm up on a cycle ergometer (Monark 818E, ergomedic, Sweden) with a light load. In order to become familiar with the test procedure the subjects performed four knee extensions at an angular velocity of 60°/s on KinCom®. The subjects rested at least 2 min before starting the test.

The isokinetic dynamometers are a valid and reliable method for assessing strength and endurance of the thigh muscles.[18–20] The protocol used for the tests has been found to be reliable and has previously been used to evaluate muscle performance in healthy young and elderly persons and patients with ischemic stroke.[21–23]

Maximal voluntary contractions (MVC)

The subjects performed four repetitions of maximal knee extension at 90°/s. They were instructed to extend the leg four times in a row with maximal effort and to rest on the way back (flexion phase). They rested at least 2 min before performing the maximal dynamic flexion.

Four repetitions of maximal knee flexion were performed at 90°/s with a passive extension phase. The subjects were instructed to flex the leg four times in a row with maximal effort and to rest on the way back (extension phase). The subjects rested at least 5 min before the endurance test.

The highest mean force value (Newton) of the four repetitions obtained in the isokinetic device for maximal contractions in extension and flexion was chosen as the outcome measure.

Endurance test

The endurance test consisted of maximally 100 maximal knee extensions at 90°/s. The subjects were instructed to extend the leg as many times as possible and the maximal effort in the extension phase was required. They were supposed to continue until the test leader asked them to stop (when 100 repetitions were attained) or, if less than 100, until exhaustion. No rest was allowed between the passive flexion phase and the active extension phase. The 0–10 category ratio scale by Borg (CR10) [24] was used to rate perceived exertion of the thigh muscles throughout the 100 maximal contractions. The subjects rated their perceived exertion at every fifth contraction until the 60th and, thereafter, at every tenth contraction until exhaustion or at 100th repetition.

Table 1 Characteristics of the study population.

	COPD patients ($n = 41$)		Controls ($n = 52$)	
	Men ($n = 15$)	Women ($n = 26$)	Men ($n = 24$)	Women ($n = 28$)
Age (yr)	66 ± 6	64 ± 5	67 ± 5	64 ± 6
BMI (kg/m^2)	26 ± 3	28 ± 5^a	25 ± 3	25 ± 2
PA score	3.47 ± 0.8	3.30 ± 0.7	3.63 ± 1	3.36 ± 0.7
FEV_1(l)	1.5 ± 0.40	1.2 ± 0.24		
FEV_1% pred.	50 ± 11.5	56 ± 11		
VC (l)	3.7 ± 0.9	2.6 ± 0.6		
VC% pred.	92 ± 15^b	100 ± 21		
FEV_1/VC%	40 ± 12	45 ± 9.5		

Data are presented as mean ± SD. BMI = body mass index; PA score = physical activity score
[a]Significantly different from female controls ($P = 0.004$).
[b]Significantly different from female COPD patients ($P = 0.029$).

Muscle endurance was expressed as the number of attained repetitions of knee extension. Muscle fatigue was expressed as a fatigue index (FI) and was analysed using the first 30 contractions of the endurance test.

Level of self-reported physical activity

A questionnaire, validated to evaluate level of self-reported physical activity in healthy elderly people, was applied.[25] It has also been used for patients with COPD in a previous study.[13] This questionnaire concerns household activities, leisure-time and sports activities during the previous 4 weeks. The level of self-reported physical activity (PA score) was ranging from 1 to 6. Scores 1–2 were classified as low level of physical activity, scores 3–4 were classified as medium level of physical activity and scores 5–6 as high level of physical activity.

Data acquisition and statistics

Based on previous studies, the mean force during the endurance test shows a pattern with a steep decrease during the first 30–50 contractions (fatigue phase) and, after that, a stable level (endurance level).[22] The reason we decided to evaluate fatigue only during the first 30 contractions was because all patients with COPD succeeded to attain at least this number of contractions. For evaluation of fatigue we formed a FI. This index was a slight modification of the dimensionless index suggested by Merletti.[26] To form the FI, the intercept (m) from the regression analysis of the initial 30 contractions of the endurance test was calculated for each subject. The intercept represents the intial value of the endurance test. From m and the force values of each individual, the FI was calculated as

$$\mathrm{FI} = \frac{1}{mN}\sum_{i=1}^{N}(m - X_i),$$

where X is mean force value, i is the contraction number, and N is the number of contractions. Higher values for FI indicate increased muscle fatigue. FI represents the relative loss in mean force throughout the 30 first contractions and is presented in percentage (%).

For statistical analysis the SPSS version 11.5 for Windows was used. Tests of normality (Kolmogorov–Smirnov and Shapiro–Wik) were used to check whether the data were normally distributed or not. In case of normal distribution, independent parametric sample t-test was used to compare the two groups. When data were not normally distributed, as for FI, or data on ordinal level, as CR-10, the non-parametric Mann–Whitney U-test was used to compare differences between groups. Power was calculated when non-significant differences were found. The results are presented as mean and standard deviation (SD) and median, minimum and maximum values for parametric and non-parametric tests, respectively.

Results

Patients with COPD and healthy controls were well matched for age and level of self-reported physical activity. However, a significant difference was found regarding body mass index (BMI) between female patients with COPD and female controls.

MVC in knee extension was 17% lower ($P = 0.017$) in female patients but no difference was found in male patients ($P = 0.56$) compared with controls (Table 2). The statistical power of this variable in males was 9%. MVC in flexion was 51% lower in female ($P < 0.001$) and 40% lower in male ($P < 0.001$) patients compared with controls.

Muscle endurance was lower in patients with COPD. All controls performed 100 repetitions in the endurance test while only 27% of the female patients and 53% of the male patients were able to attain this number (Fig. 1). FI was found to be higher in female patients with COPD (22.5%) compared to female controls (10%) ($P = 0.001$) (Fig. 2b and Table 2). No significant difference was found regarding FI between male patients (15%) and male controls (10%) ($P = 0.103$) (Fig. 2a and Table 2). Both female patients and female controls started the endurance test with approximately 80% of what they performed in the test of maximal contractions in extension. Male controls started the endurance test at their maximum force in extension while male patients began the test at approximately 80% of their maximal force in extension ($P = 0.058$). Female patients rated higher perceived exertion at the 30th contraction compared to female controls ($P = 0.000$) while male patients and male controls rated approximately the same perceived exertion at the 30th contraction (Table 2).

Discussion

The major finding of this study was that thigh muscle function is impaired in patients with COPD both in muscle strength (except for extension in

Table 2 Maximal strength of the thigh muscles and fatigue during the 30 first contractions of the endurance test.

	Men		Women	
	COPD	Controls	COPD	Controls
Maximal strength in extension (Newton)	274±83	289±70	225±61[a]	272±77
Maximal strength in flexion (Newton)	121±51[b]	203±46	87±34[c]	179±47
Intercept (Newton)	243 (51–349)	271 (177–446)	198 (89–337)	230 (96–380)
Fatigue index (FI%)	15 (−222–27)	10 (−90–25)	22.5 (−39–33)[c]	10 (−54–25)
Borg ratings at 30th contraction	4 (2–10)	4 (0–9)	6 (2–10)[c]	3 (0–10)

Data are presented as mean±SD for maximal strength and as median (minimum-maximum) for intercept, FI and Borg.
[a]Significantly different from female controls ($P<0.05$).
[b]Significantly different from male controls ($P<0.001$).
[c]Significantly different from female controls ($P<0.001$).

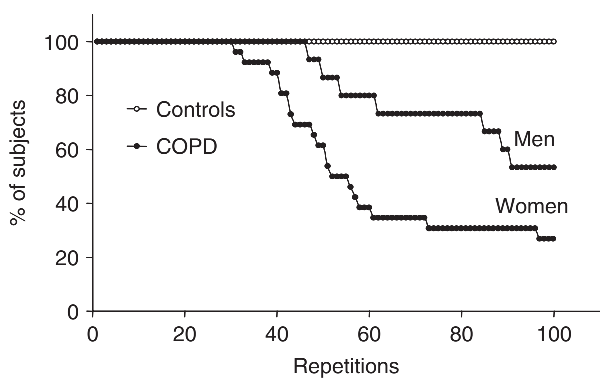

Figure 1 Percentage (%) of subjects succeeding different numbers of repetitions in the endurance test for controls and COPD (men and women).

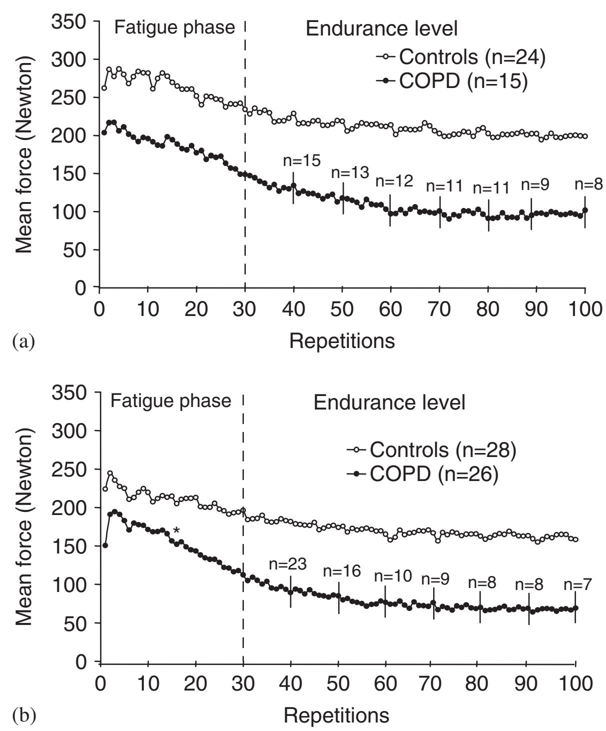

Figure 2 Pattern of force loss during the endurance test for men (a) and women (b) in controls and patients with COPD. All controls performed 100 repetitions and all patients performed 30 repetitions. Some patients dropped out successively during the test. The remaining number of patients is illustrated at every 10th contraction. The dashed line shows the area for calculation of the fatigue index (FI). *Significantly higher FI for women with COPD ($P = 0.01$).

male patients) and muscle endurance compared to age-matched healthy controls. However, the level of self-reported everyday physical activity did not differ between groups. We also found gender-related differences in patients with COPD regarding skeletal muscle dysfunction where women seem to be more prone to decrease in thigh muscle function. There was a significant difference in BMI between female patients and female controls, but this difference (25–28) is probably not of clinical relevance that it could explain the results.

Maximal strength of the thigh muscles was found to be impaired in our group of patients with COPD which agrees with results of previous studies.[14,16,27,28] This muscle weakness may be related to the reduced muscle cross-sectional area (muscle atrophy) previously reported in patients with COPD.[8,29] Interestingly, we did not find any weakness of the thigh muscles in extension in male patients compared to male controls. The reason for this relatively preserved maximal strength in extension of male patients compared to controls is not clear. The small sample of men with COPD might have contributed to this finding. Because of the statistical power for this variable (strength in extension in males) was 9%, we cannot affirm that this non-significant result really exists.

We found that muscle endurance was impaired both in female and male patients compared to controls. This finding is in accordance with results of previous studies.[9,14,16,30,31]. Also, female patients were found to have greater degree of fatigue (FI) during the first 30 contractions of the endurance test compared to female controls, but this was not the case in male patients. Our results differ from findings by Zattara-Hartman et al.[32] who did not find any reduction in endurance of vastus lateralis in patients with COPD compared to controls. Staron et al.[33] studied muscle fiber-type composition of the vastus lateralis in healthy young men and women and showed that the percentage area of the fast oxidative type IIa fibers were the largest for men, whereas the percentage area of the slow oxidative type I fibers were the largest for women. This may explain why we did not find any difference in degree of fatigue (FI) during the first 30 contractions in male patients compared to male controls. Male subjects might preferentially use a greater proportion of type IIa fibers and may, therefore, not be affected to a great extent by a reduced proportion of type I fibers that is present in chronic obstructive pulmonary disease. Another reason might be that the subjects worked at different intensities of their maximal force in extension during the endurance test, a difference that possibly could have accounted for the observed difference. Male controls started the endurance test at their maximal force in extension whereas male patients began the test at approximately 80% of their maximal force in extension. Although this difference was not significant ($P = 0.058$), it might have contributed to a greater fatigue of the control subjects during the 30 first contractions. However, despite the fact that we did not find any difference in FI between male patients and male controls, the patients did not manage to attain 100 repetitions which indicates impaired endurance of the thigh muscles.

In our study, the questionnaire used to evaluate PA score between the two groups has been shown to be a good instrument because it was developed for elderly people and the alternatives were not only about sport and leisure-time activities but also about household activities.[25] Although some subjects in our study cannot be considered elderly, the average age of the groups was approximately 65 years old. In the present study, the questionnaire showed that the patients and the controls had the same score of level of self-reported physical activity and thus no indication of a more sedentary lifestyle was found. In the patient group our results showed impaired strength and endurance of the thigh muscles despite their relatively preserved level of physical activity. Coronell et al.,[14] using another questionnaire, also indicated that dysfunction in strength and endurance of quadriceps can be found in patients with relatively normal level of physical activity. This finding suggests that other factors than inactivity may contribute to the alterations in peripheral muscle function in patients with COPD. However, the PA questionnaire might be sensitive to determine differences regarding what the patients perform, e.g. type, frequency and duration of physical activity but not regarding how they perform the activity, e.g. which intensity. A recent study[34] has showed that patients with COPD walk with lower movement intensity compared to healthy controls. Despite the preserved level of self-reported physical activity, we believe that these patients might experience the exercise as more demanding than healthy controls. Furthermore, female patients had greater degree of fatigue and rated higher perceived exertion at the 30th contraction than female controls. Besides, the main reported reason for the patients with COPD to stop the endurance test before completing 100 repetitions was perceived fatigue and discomfort in the leg and not dyspnoea.

In this study, peripheral muscle dysfunction was found in patients with COPD. Female patients seemed to be more prone to decrease in thigh muscle function. These findings are of clinical importance since muscle weakness is associated with exercise intolerance, poor quality of life and an increased need for medical assistance[1–3]. Based on our findings, pulmonary rehabilitation should be more focused on improving skeletal muscle function. Both muscle strength and muscle endurance training should be included in the exercise training programs. In accordance with our results, two recent reviews[10,35] showed that muscle strength training should be part of the pulmonary rehabilitation. Endurance training has also been shown to be of benefit for patients with COPD.[35] Currently, endurance training programs used for patients with COPD consist mainly of walking and cycling exercises that improve the cardio-respiratory system. However, to improve muscular endurance, specific muscle endurance trainings with many repetitions and low loads are required. Not only sedentary patients with COPD but also non-sedentary patients should be considered for physical training. Moreover, since we found gender-related differences of muscle performance, this issue also needs to be considered when designing rehabilitation programs for these patients.

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