Deficits in muscle strength, mass, quality, and mobility in people with chronic obstructive pulmonary disease

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Abstract

Purpose—Mid-thigh intramuscular fat (IF), a feature of reduced muscle quality, is an important predictor of self-reported mobility loss in the elderly. This study compared measures of muscle strength, mass, IF, and mobility in people with COPD and healthy subjects. Associations between measures of muscle strength, mass, IF and mobility were explored.

Methods—Knee extensors muscle strength was assessed with an isokinetic dynamometer. Cross-sectional area (CSA) and IF of the thigh muscles were measured with computerized tomography. Mobility was assessed with the Repetitive Sit-To-Stand (RSTS), Self-Selected Gait Speed (SSGS) and Six-Minute Walk Distance (6MWT) tests.

Results—Twenty-one people of mean $\pm$ SD age 71.3 ± 8.1 years with COPD and a percentage predicted force expiratory volume in one second (FEV₁) of 47.2 ± 12.9 and 21 healthy subjects matched for age (67.4 ± 8.6), gender and body mass participated in the study. People with COPD showed reduced average knee extensors strength (29%; $p=0.016$) CSA of the thigh muscles (17%; $p=0.007$) and mobility measures ($\sim 23\%$; $p=0.001$). Knee extensors and flexors IF was twofold greater in people with COPD ($p=0.005$). Measures of knee extensors muscle strength, mass and IF were not associated with mobility measures.

Conclusions—Compared with healthy controls, people with moderate to severe COPD show marked deficits in muscle strength, mass, quality as well as mobility. More studies with larger sample size are required to elucidate whether any of these muscle deficits can explain mobility impairments in COPD.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) has many non-respiratory manifestations, including skeletal muscle dysfunction. Deficits in muscle strength and mass in COPD patients are well reported in the literature.^{1,2} However, little attention has been directed at

investigating muscle quality in COPD. Intramuscular fat (IF), a feature of muscle quality, has only been recently investigated in COPD. In a previous study, we reported that COPD patients had ~35% more IF in the thigh muscles than a group of healthy subjects matched for age, gender and body mass (BMI).¹

Intramuscular fat (IF) is associated with muscle weakness³ and self-reported mobility loss⁴ in older adults. Measurements of muscle strength and mass are commonly used in clinical settings as well as research to monitor training adaptations and health status in people with COPD. However, recent studies suggest that deficits in muscle mass do not entirely explain the reduction of muscle strength observed in COPD patients.⁵ Thus, it is possible that muscle quality could partially explain strength deficits in COPD.

The relationship between muscle strength, mass and IF with specific measures of mobility has not been investigated in COPD. Mid-thigh muscle strength and mass are associated with mobility in older adults, however, it is unclear if these associations remain valid for people with COPD. Similarly, it is also unknown if an increased IF is associated with deficits in mobility in these individuals.

The main purpose of this study was to compare measures of muscle strength, cross-sectional area (CSA) and IF of the thigh muscles, as well as mobility in people with COPD and a healthy group. The secondary purpose was to explore associations between muscle and mobility measures. It was hypothesized that people with COPD would show deficits in both muscle and mobility measures and that deficits in muscle measures would be associated with mobility impairments.

METHODS

Participants

Inclusion criteria for people with COPD were: moderate to severe disease based on the Global Initiative for Obstructive Lung Disease (GOLD).⁶ Exclusion criteria were: (1) an acute exacerbation within the 3 months prior to the study; (2) regular participation in an exercise program during the 1-year period prior to the study; (3) currently smoking; (4) co-morbid cardiovascular or neurological disease and lower extremity musculoskeletal problems that could cause risk during the study tests; (5) use of portable supplemental oxygen on a continuous basis; (6) α -1 antitrypsin deficiency without a smoking history.

Inclusion criteria for healthy people were: sedentary healthy people. Exclusion criteria were: (1) regular participation in an exercise program during the 1-year period prior to the study; (2) currently smoking; (3) respiratory, cardiovascular, neurological disease or lower extremity musculoskeletal problems that could cause risk during the study tests. The university clinical research ethics board approved the study and all subjects gave written informed consent prior to participation.

Measurements

Spirometry—To confirm the stage of COPD or to rule out pulmonary disease, people with COPD and healthy subjects, respectively, underwent spirometry using a portable spirometer

(CPFS/D spirometer, Medi Graphics Corp., MN, USA). Spirometry was performed according to international guidelines.⁷

Physical Activity—Physical activity (PA) was assessed with the Physical Activity Scale for the Elderly (PASE),⁸ which has been validated via comparison with PA values assessed using portable accelerometers.⁹

Knee Extensors Muscle Strength—Concentric average peak torque of the knee extensors of the dominant leg was assessed on the KinCom® dynamometer (Chattanooga Group Inc., TN, USA) using a protocol previously described.^{1,2}

Mobility—Mobility was assessed with the Repetitive Sit-To-Stand (RSTS), Self-Selected Gait Speed (SSGS) and Six-Minute Walk (6MWT) tests.¹⁰ In the RSTS the time required to complete five repeated sit-to-stand and stand-to-sit maneuvers was measured. Measuring the self-selected gait speed to complete 5 meters on an 8-meter walkway assessed the SSGS. The 6MWT was performed according to the guidelines of the American Thoracic Society. With the exception of the 6MWT, participants performed two trials for all tests. The same tester (MR) timed the tests manually and the best of the two trials was saved for further analysis.

Thigh Muscles CSA and Intramuscular Fat (IF)—A computerized tomography (CT) scan of the thigh was performed at 50% distance from the tibial plateau to the anterior inferior iliac spine using a Siemens “Sensation 16” multislice CT scanner (Siemens Medical Solutions, Erlangen, Germany). Images were acquired at 120 kVp and 100–250 mA, 0.5-sec gantry rotation time (100 mA) 15mm table speed per rotation. Nine millimeters slices were reconstructed using high (“b50s”) spatial frequency algorithms. Analysis of all CT images was quantified by the same tester (MR) in a blinded fashion using NIH ImageJ, version 1.42 (available at www.rsb.info.nih.gov/ij/Java 1.3.1_03).

The numerical value of each pixel illustrates different attenuation coefficients measured as Hounsfield units (HU) and corresponds to the gray level of the image. Adipose tissue is represented by “dark” pixels (negative attenuation values) while muscle tissue and bone are shown lighter (positive attenuation values). Intramuscular fat (IF) was estimated only for knee extensors and flexors and calculated from the number of pixels within the range of HU for adipose tissue (–190 to –30).¹¹ A larger number of pixels within this range indicates greater fat infiltration.¹¹

Statistical Analyses

Differences between groups in PA were compared with the Mann-Whitney-U test. Pearson or Spearman correlation coefficients were used to explore associations and multicollinearity among dependent variables and potential covariates. A regression model with age as a covariate was used to determine differences between groups in measures of muscle torque and mobility. For differences in IF and CSA, the regression model was adjusted for age and BMI. Bivariate correlations were used to explore associations between measures of muscle strength, CSA and IF with measures of mobility (RSTS, SSGS, 6MWT). Data are presented as medians with percentiles (P₂₅, P₇₅) or means $\pm$ standard deviation (SD) with 95%

confidence intervals (CI). Analyses were performed with the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) using two-tailed probability tests with significance level set at $p < 0.05$.

RESULTS

Participants

Twenty-one non-oxygen dependent, clinically stable people (11 males and 10 females) with moderate to severe COPD and 21 healthy controls matched for age, sex and BMI participated in the study (Table 1). The group with COPD showed moderate to severe levels of airflow limitation. People with COPD tended to show a lower median score (P_{25} , P_{75}) of 103.3 (53.8 to 156.3) in the PASE, compared to values shown by the healthy controls, with a median score (P_{25} , P_{75}) of 141.4 (78.3 to 204.5) ($p = 0.087$).

Knee Extensors Muscle Strength and Mobility

Results for knee extensors muscle strength and measures of mobility are shown in Table 2. Knee extensors concentric torque was 29% lower in people with COPD. The group with COPD also showed lower performance in all mobility tests. In short, COPD patients required 21% more time to complete the RSTS and gait velocity in the SSGS was 20% lower compared with healthy subjects. The distance walked in the 6MWT was 28% lower in the COPD group.

Thigh Muscles CSA and Intramuscular Fat (IF)

Results for CSA and IF of the thigh muscles are shown in Table 2. People with COPD showed, on average, a 17% smaller CSA of the thigh muscles. More specifically, the COPD group had a lower muscle CSA for knee extensors (17%) and knee flexors (16%). However, differences between groups for knee flexors were not significant ($p = 0.076$). Compared with healthy subjects, people with COPD showed greater levels of IF in knee extensors (~89%) and flexors (~113%).

Relationship Between Measures of Muscle and Mobility

In people with COPD, knee extensors IF showed non-significant trends suggestive of a moderate association between increased IF and lower performance in the SSGS ($r = -0.41$; $p = 0.07$) and RSTS tests ($r = 0.43$; $p = 0.06$). In contrast, the association of knee extensors IF and mobility in the healthy group was not apparent. Neither knee extensors CSA nor concentric torque showed significant associations with the mobility tests in any group.

DISCUSSION

The main finding of this study is that, compared with healthy subjects, muscle quality of knee extensors and flexors, assessed as the level of IF, is reduced in people with COPD. In addition, COPD patients show lower levels of knee extensors muscle strength and reduced CSA of the thigh muscles. Furthermore, the group with COPD shows deficits in all measures of mobility. Intramuscular fat of knee extensors showed a non-significant trend suggestive of a moderate association with the SSGS and the RSTS. Interestingly, associations between

muscle strength and CSA with functional performance were not apparent in any of the groups.

This study confirms that people with COPD have reduced muscle quality. The group with COPD showed, on average, ~100% more IF in knee extensors and flexors than the healthy group. In a previous study, in which we used MRI, we found ~35% more IF in the thigh muscles of the COPD.¹ The greater IF in the present study is possibly due to the fact that we adjusted between groups comparisons for age and BMI. Before adjustment, differences in IF between groups were very similar (~45%) to those reported in our previous study.¹ In addition, in this study the group with COPD was slightly older and we used CT rather than MRI. While CT scanning entails the risk of X-ray radiation, it also provides more absolute thresholds to quantify adipose tissue.¹¹

It could be argued that the greater accumulation of IF in people with COPD was caused by reduced PA.¹² However, sedentary controls were purposely recruited to minimize potential confounding arising from differences in PA. Since differences in PA were not significant, the greater IF in the COPD group cannot be solely explained by differences in PA. Moreover, although both groups were matched for age, gender and BMI, covariates associated with IF accumulation (i.e., age and BMI) were factorized into the analysis to reduce potential confounding. The mechanisms for the increase in IF are likely complex and remain largely unknown, however, it is possible that the reduced oxidative capacity and the predominance of glycolytic metabolism observed in the muscles of people with COPD might compromise the ability to utilize intramuscular triacylglycerols and the concomitant increase in IF.¹³

Mobility was measured with the RSTS, SSGS and 6MWT. These tests were chosen because they are associated with different indicators of mobility such as postural control, muscle strength as well as overall function in older adults.¹⁰ Only a few studies have systematically characterized the functional limitations encountered by people with COPD.¹⁴ Our results confirm that people with COPD have deficits in mobility.

We hypothesized that deficits in muscle strength, mass and IF, in particular, would be associated with mobility impairments. We only showed non-significant trends for associations between knee extensors IF and mobility tests in the COPD group. Although recent studies underline the importance of assessing muscle quality as an important factor associated with self-reported mobility loss in the elderly,⁴ associations between IF and mobility impairment were not significant. It is important to note, however, that IF was the muscle measure most strongly associated with mobility.

Neither CSA nor muscle strength of the knee extensors were associated with mobility in people with COPD. Interestingly, these associations were not significant in the healthy control group, although there is some evidence in the literature that lower-extremity strength and CSA are associated with mobility in the elderly. One possible explanation for this lack of association could be the existence of a strength threshold beyond which further increases do not translate into specific functional performance tests. Indeed, non-linear relationships between knee extensors strength and functional performance have been described in older populations.¹⁵

Another explanation for the lack of association concerns the selection of our sample size. Our sample size calculation was appropriate to detect differences between groups in measures of muscle and functional performance. Perhaps this sample size was insufficient to detect associations between measures of muscle and mobility.

This study shows that COPD patients have deficits in muscle strength, CSA, quality (IF) and mobility. However, measures of muscle strength, CSA or IF were not associated with mobility. While our results suggest that other aspects mediate the mobility impairments observed in COPD, further studies with larger sample sizes are required to investigate potential mechanisms for mobility impairments and its potential association with IF in COPD patients.

Acknowledgments

FUNDING

This study is funded by The Lung Association. Marc Roig received support through a Strategic Training Fellowship in Rehabilitation Research from the Canadian Institutes of Health Research (CIHR) Musculoskeletal and Arthritis Institute, a Fellowship in Respiratory Rehabilitation from the BC Lung Association, and a Graduate Fellowship from the University of British Columbia. Janice J Eng received a career scientist award from CIHR (MSH-63617).

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Table 1

Characteristics of the participants of the study. Data are presented as means $\pm$ SD.

Characteristics	Healthy (n=21)		COPD (n=21)	
	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range
Age (y)	67.4 $\pm$ 8.6	50–85	71.2 $\pm$ 8.1	50–85
Height (m)	1.7 $\pm$ 0.1	1.4–1.8	1.6 $\pm$ 0.1	1.5–1.8
Weight (kg)	70.8 $\pm$ 14.6	47–104	70.5 $\pm$ 14.2	48.3–103.4
BMI (kg/m ²)	25.3 $\pm$ 4	20–36	25.7 $\pm$ 4.2	20.1–38.4
FEV ₁ (% predicted)	98.1 $\pm$ 11.9	76–114	47.2 $\pm$ 12.9 *	32–72
FVC (% predicted)	108 $\pm$ 20.6	67–141	80.4 $\pm$ 15.9 *	42–102
FEV ₁ /FVC (% predicted)	69.5 $\pm$ 7.7	57–85	52.4 $\pm$ 17.2 *	27–71

BMI: body mass index; FEV₁: forced expiratory volume in one second; FVC: forced vital capacity

* Indicates significant difference between groups at $p < 0.05$

Table 2

Regression model to assess differences in knee extensors concentric strength, mass (CSA), IF and mobility between groups. Data are presented as means $\pm$ SD and 95% CI for the mean difference.

Measures	Healthy	COPD	Mean difference (95% CI)	p-value
<i>Torque (Nm)</i>				
Knee extensors	80.5 $\pm$ 31.8	56.8 $\pm$ 23.9	23.7 (4.7 to 42.7)	0.016
<i>CSA (cm²)</i>				
Thigh	82.3 $\pm$ 18.9	67.9 $\pm$ 16.6	14.4 (4.2 to 24.6)	0.007
Knee extensors	36.6 $\pm$ 9.4	30.2 $\pm$ 6.9	6.4 (1.7 to 11)	0.008
Knee flexors	15.2 $\pm$ 5.1	12.7 $\pm$ 3.7	2.5 (– 0.3 to 5.2)	0.076
<i>Fat infiltration[#]</i>				
Knee extensors	101.5 $\pm$ 39	190 $\pm$ 120.8	–88.4 (–144.8 to –32.1)	0.003
Knee flexors	56 $\pm$ 39.1	119.1 $\pm$ 116.7	–63 (–106.3 to –19.8)	0.005
<i>Functional performance</i>				
RSTS (s)	9.3 $\pm$ 1.3	11.8 $\pm$ 2.3	–2.5 (–3.6 to 1.4)	<0.001
SSGS (m/s)	1.5 $\pm$ 0.2	1.2 $\pm$ 0.2	0.3 (0.2 to 0.4)	<0.001
6MWT (m)	554.9 $\pm$ 65	397.5 $\pm$ 63.9	157.3 (114.8 to 199.9)	<0.001

RSTS: Repetitive Sit-To-Stand; SSGS: Self-Selected Gait Speed; 6MWT: Six-Minute Walk.

[#] Number of “dark” pixels within the –190 to –30 Hounsfield units (HU), which is the range of attenuation corresponding to adipose tissue.