

ORIGINAL ARTICLE

Muscular performance decreases with increasing complexity of resistance exercises in subjects with chronic obstructive pulmonary disease

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Abstract

Chronic obstructive lung disease (COPD) is associated with impaired muscle functions in addition to the impaired cardiopulmonary capacity inherent to the disease. The purpose of this study was to compare muscular performance between COPD subjects (COPD, $n = 11$, GOLD grade II/III; $FEV_1 = 53 \pm 14\%$ predicted; 61 ± 7 years) and healthy controls (HC, $n = 12$, 66 ± 8 years) in three resistance exercises with different complexity: (a) one-legged knee extension (1KE), and (b) one- and (c) two-legged leg press (1LP and 2LP, respectively). For each exercise, muscular performance was defined as repetitions to exhaustion at 60% of one-repetition maximum or overall exercise volume, calculated as the sum of three exercise sets. In HC, muscular performance increased progressively with increasing physiological complexity: $1KE < 1LP < 2LP$. Using 1KE as reference value, muscular performance increased by 1.9 (repetitions) or 4.6-fold (volume) in 1LP and 3.1 or 7.1-fold in 2LP. In COPD, similar increases occurred going from 1KE to 1LP (1.9 or 4.4-fold change), but not from 1LP to 2LP, where no further increase occurred. In conclusion, in COPD, performance is impaired in exercises involving larger amounts of muscle mass ($>1LP$), advocating utilization of one-legged resistance protocols for rehabilitation purposes.

KEY WORDS

cardiorespiratory capacity, chronic obstructive lung disease, muscular performance, resistance training, strength training, unilateral training

1 | INTRODUCTION

For individuals suffering from chronic obstructive lung disease (COPD), physical exercise is a prerequisite for adequate treatment and rehabilitation. It counteracts the muscle pathophysiology inherent to the disease and improves health-related

quality of life and activities of daily living.¹⁻³ Unfortunately, exercise training is a demanding task for such patients. The accompanying increase in oxygen consumption in working muscles rapidly exceeds the oxygen-delivery capacity of the cardiopulmonary system,⁴ leaving muscles in a state of oxygen deficiency. This occurs already at low intensities and

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upon activation of small bulks of muscle (>4 kg), resulting in dyspnea, discomfort, and impaired exercise performance.⁵ Accordingly, it is difficult to achieve necessary exercise intensities to provoke muscle cell adaptations,^{6,7} which hinders efficient rehabilitative training.^{8,9} Despite this, whole-body endurance exercise training, such as cycling or walking, is the most commonly applied exercise modality in pulmonary rehabilitation.¹⁰

Fortunately, there are ways to solve this issue and to facilitate ergogenic adaptations to exercise training in COPD patients. A readily available solution would be to make use of exercise protocols with lower physiological demands such as resistance exercises, activating smaller amounts of muscle mass.⁴ This strategy should ensure maximal muscle activation regardless of blood oxygenation levels, enabling activation of key cellular signaling pathways, and inducing muscle adaptations. In line with this, resistance training has gained momentum in COPD rehabilitation during the last decade, counteracting the muscle dysfunctions accompanying the disease, improving muscle strength and endurance, and increasing muscle mass.¹¹⁻¹³ However, the magnitude of these effects remains equivocal, with available studies displaying a large span of variation in training adaptations, ranging from negligible or trivial^{14,15} to substantial and highly relevant.^{16,17} Indeed, many patients do not respond to training at all.^{8,9} To date, this heterogeneity has been ascribed pathophysiologicals accompanying the disease, such as a low-grade systemic inflammation,^{18,19} though this is unlikely to explain the between-studies variation. Rather, the heterogeneous response patterns may result from differences in study design, including differences in resistance training protocols. Indeed, the cardiopulmonary limitations of COPD patients may call for specific modifications to resistance training exercises in order to further reduce the physiological demand.²⁰ At present, we know little about this perspective, with only a handful of studies investigating the efficacy of different resistance exercise modalities.²¹⁻²³

Conventional resistance training of the legs typically involves two-legged exercises. In moderate to severe COPD, this is likely to involve too much muscle mass to allow for optimal activation (and arguably adaptation).^{20,24} Intuitively, this is readily solvable by using one-legged resistance exercises, which naturally reduces the amount of active muscle mass. In a recent study, unilateral resistance exercises resulted in superior exercise workloads using elastic bands compared to bilateral exercises in severe to very severe COPD (GOLD grade III/IV), but not in healthy subjects,^{22,23} though analysis of interaction effect for difference in exercise workload^{leg} from single- to two-limb exercises and group (COPD vs healthy) was not performed. This complicates to examine if COPD patients show progressively lowered muscular performance in resistance exercises with increasing complexity compared to healthy subjects. It also remains unknown if this

applies to COPD of less severity (GOLD grade II/III), and if it is applicable to isolated resistance exercises performed in apparatus, perhaps exacerbated by increasing physiological complexities of exercises. For endurance exercises, such unilateral training seems to translate into superior training adaptations for COPD subjects.^{25,26}

The purpose of this study was to compare muscular performance in three resistance exercises of the legs involving different degrees of active muscle mass in COPD and healthy control subjects (one-legged knee extension, and one- and two-legged leg press). We hypothesized that muscular performance in COPD patients would be increasingly impaired with increasing amount of active muscle mass compared to healthy subjects. Muscular performance was defined as repetitions to exhaustion at 60% of 1RM or overall exercise volume, both calculated as the sum of three sets for each exercise.

2 | METHODS

The study was approved by the Regional Ethics Committee of the Norwegian Research Council for Science and the Humanities as a part of “The Granheim COPD Study” (reference nr: 2013/1094) and was preregistered at clinicaltrials.gov (NCT02598830). All subjects signed informed consent. The study was conducted according to the Declaration of Helsinki.

2.1 | Subjects

Twelve subjects with COPD and 11 healthy control subjects participated in the study. For background variables, see Table 1. COPD subjects were recruited from a pulmonary rehabilitation center (Granheim Lung Hospital), while healthy controls were recruited through acquaintances. All subjects were >55 years of age. COPD subjects had GOLD stage II-III (FEV₁ predicted <80 to >30% and FEV₁/FVC <70%) and did not smoke at the time of inclusion and throughout the test period. Healthy controls had normal lung function (FEV₁ predicted >80% and FEV₁/FVC >70%). Exclusion criteria were unstable cardiac disorders and comorbidities that could impair the ability to perform lifts with the lower limbs. COPD subjects received medication as prescribed by their medical doctor (Table 1). None of the subjects utilized supplemental oxygen regularly. Subject characteristics unrelated to muscle strength and performance were similar between groups, except for lung function, oxygen saturation of hemoglobin (SpO₂), and medication use (Table 1).

2.2 | Experimental design

All subjects attended 7 days of performance testing, distributed over a period of 4 weeks. Test days were separated by

TABLE 1 Subject characteristics

	COPD sub- jects (n = 11)	HC subjects (n = 12)	P
Sex (♂/♀)	5/6	5/7	.86
Age	65.5 ± 8.1	61.8 ± 6.7	.24
Height (cm)	165 ± 12	173 ± 10	.11
Weight (kg)	70.1 ± 14.5	76.4 ± 11.5	.26
BMI	25.6 ± 5.1	25.5 ± 2.6	.93
SpO ₂ at rest	94 ± 4%	98 ± 1%	.01
Lung function			
FVC (L)	2.7 ± 1.1	4.1 ± 0.8	.00
FEV ₁ /FVC (%)	49 ± 13	72 ± 6	.00
FEV ₁ (% predicted)	53 ± 14	117 ± 12	.00
PEF (L/s)	4.7 ± 1.9	8.1 ± 1.7	.00
GOLD II/III	7/4	—	—
Medication			
B ₂ -agonists	10	—	—
Muscarinic antagonists	1	—	—
Corticosteroids	1	—	—
4-min step-test (steps)	92 ± 25	137 ± 25	.00

Note: Values are numbers or mean ± standard deviations.

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in one second; FVC, forced vital capacity; HC, healthy control; PEF, peak expiratory flow; SpO₂, oxygen saturation of hemoglobin.

at least 48 hours. On day 1, subjects performed spirometry testing, anthropometric measurements, 4-minute step-test, and familiarization to one-repetition maximum (1RM) tests in one-legged knee extension (1KE), one-legged leg press (1LP), and two-legged leg press (2LP). On days 2-3, subjects performed 1RM tests. These data were subsequently utilized to calculate relative workload for tests of muscular performance (60% of 1RM), which were performed on days 4-7 (two test days for the one-legged exercises and two test days for the two-legged exercise). All tests were supervised by the same physical training instructor, except for spirometry tests, which were conducted by the same nurse specialist. Apparatus settings were adjusted to the needs and were utilized for all tests.

2.3 | Test protocols

2.3.1 | Spirometry and anthropometry

Spirometry testing (Jaeger MasterScreen PFT; Carefusion) was conducted before the other physical tests. The protocol followed guidelines from the American Thoracic Society and the European Respiratory Society.²⁷ COPD patients were tested before and after inhalation of two

bronchodilators (salbutamol, 0.2 mg and ipratropiumbromid, 20 µg). See Table 1 for values on lung function after optimal bronchodilation.

2.3.2 | Fitness test

Subjects performed a 4-minute step-test to evaluate the subjects' general fitness level. A 20-cm high step box with a non-slip rubber surface (Reebok Step; Reebok) was used. Subjects were asked to perform as many steps as possible within four minutes, placing both legs on the box with the hip fully extended during each step up. Moderate verbal motivation was given throughout the test. Data are presented in Table 1.

2.3.3 | Muscular strength

Muscular strength was measured as 1RM in one-legged knee extension (Technogym, Technogym SpA), one- and two-legged leg press (Gym80 Sygnum Legpress, Gym80 mbH). Warm-up consisted of 5 minutes of low-intensity bicycling on a bicycle ergometer, followed by three sets of 12, 8, and 6 repetitions with low, increasing workloads. Subsequently, a maximum of five 1RM attempts were conducted for each exercise. All three exercises were tested in two separate sessions, and the best result was used for further analysis. One-legged muscle strength was tested on both legs, with one leg performing 1RM in one-legged knee extension and the other leg performing 1RM in one-legged leg press, allocated to the two legs in a randomized manner. On the two test days, subjects alternated between starting with one-legged exercises (1KE and 1LP) and two-legged exercise (2LP), giving each subject an attempt for each exercise modality with fully rested lower limbs. In one-legged knee extension, the 1RM attempt was approved if the knee angle exceeded 170°. In one- and two-legged leg press, the 1RM attempt was approved if the knee angle reached 90° in the eccentric phase, with subsequent full extension of the knee joint in the concentric phase.

2.3.4 | Muscular performance

Muscular performance was assessed in one-legged knee extension, one- and two-legged leg press, and was defined as the number of repetitions achieved at 60% of 1RM. Repetitions were quantified as the total number of repetitions achieved over the course of three sets, with 2 minutes of rest in-between. Each of the three exercise performance tests was conducted twice during the test period, on separate days. One-legged muscular performance tests (1LP and 1KE) were conducted within the same session, with one leg performing one-legged knee extension and the other leg performing one-legged leg press, allocated to the two legs in accordance with 1RM testing. The relative order

of one-legged and two-legged test days was randomized between subjects; half the subjects started with one-legged testing and half the subjects started with two-legged testing. The session following one-legged testing was always two-legged testing and vice versa. For each of the three muscular performance tests, the best result was used for further analyses.

Exercises were performed as previously described. Warm-up consisted of 5 minutes of low-intensity cycling on a cycle ergometer, followed by two sets of 12 and 8 repetitions at loads corresponding to 15% and 30% of 1RM, respectively. During muscular performance tests, subjects were instructed to lift at a composed and controlled pace, with no rest longer than 1 second in the lower or upper position. Moderate verbal motivation was given to all subjects. Blood lactate concentration (Lactate Pro, ARKRAY Inc) and SpO₂ (CMS 50F Oximeter, Innovo Medical) were measured at rest and after tests. Rating of dyspnea (Borg CR10)²⁸ was registered immediately after the test.

2.4 | Statistical analysis

Differences between groups (COPD vs healthy control subjects) were assessed using unpaired Student's *t*-tests for numeric data and Pearson's chi-squared test for nominal data (sex). Differences between independent groups with repeated measures were assessed using mixed-design ANOVAs with groups (ie, COPD and healthy control subjects) as between-factor and type of exercise (1KE, 1LP, and 2LP) as within-group factors. When a significant *F* value occurred, a Sidak post hoc test was used to determine differences between and within groups. The relationship between percent difference in muscular performance between one-legged knee extension and two-legged leg press and lung function was tested by Pearson's correlation. Statistical significance was set at $P < .05$, and data are expressed as means \pm standard deviation in text and means \pm 95% confidence intervals in figures. Statistical analyses were performed using IBM SPSS Statistics package (version 24) and figures made using Prism Software (GraphPad 8).

3 | RESULTS

3.1 | Maximal strength

In general, COPD showed lower 1RM strength than healthy controls ($F_{1,21} = 5.7$, $P = .027$; Figure 1). In one-legged knee extension, COPD and healthy controls achieved 33 ± 12 and 42 ± 9 kg, respectively ($P = .052$). In one- and two-legged leg press, corresponding values were 75 ± 22 and 98 ± 18 kg ($P = .012$), and 78 ± 21 and 93 ± 17 kg ($P = .091$, measured as $1RM^{-leg}$), respectively. Within each of the groups, no difference was seen between 1RM-1LP

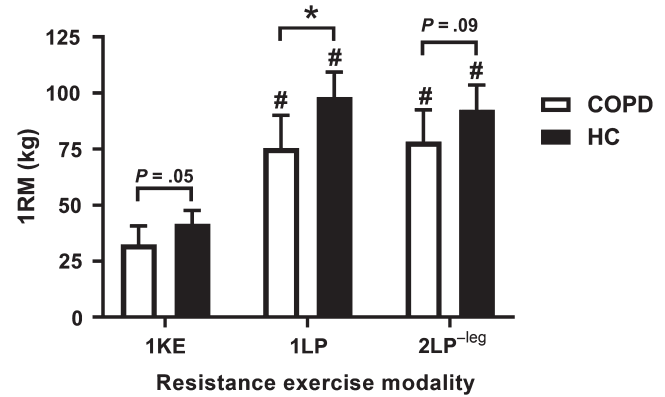


FIGURE 1 Maximal strength per leg for healthy control and COPD subjects. Data are means with 95% confidence levels. 1KE, one-legged knee extension; 1LP, one-legged leg press; 2LP^{leg}, two-legged leg press divided by two; COPD, chronic obstructive pulmonary disease; HC, healthy control. *Significant difference between groups ($P < .05$); #significant different from 1KE ($P < .05$)

and $1RM^{-leg}$ -2LP performance (COPD, $P = .656$; healthy controls, $P = .137$).

3.2 | Muscular performance in resistance exercises

There was an interaction effect for groups and exercises on muscular performance, measured as both total number of repetitions achieved during three sets of resistance exercises at 60% of 1RM ($F_{2,42} = 7.3$, $P = .002$; Figure 2A) and as exercise volume ($F_{2,42} = 8.3$, $P = .001$; Figure 2C). In all three exercises, healthy controls generally managed to conduct more repetitions and higher exercise volumes than COPD, except for in one-legged leg press, where there was no difference in repetition to exhaustion between groups ($P = .10$). For healthy controls, muscular performance increased progressively with increasing complexity and physiological demand of the exercise: 1KE < 1LP < 2LP ($P < .05$; Figure 2A,C). For COPD, a similar increase was seen going from one-legged knee extension to one-legged leg press ($P = .004$, repetitions to exhaustion; $P < .001$, exercise volume), but not from one- to two-legged leg press, where no increase occurred ($P = .932$, repetitions to exhaustion; $P = .852$, exercise volume; Figure 2A,C). This progressive increase was highlighted in a subset of analysis where we calculated one- and two-legged leg press performance as relative performance to one-legged knee extension (Figure 2B,D). In this subanalysis, there was a significant interaction effect for groups and exercises for both repetitions to exhaustion ($F_{1,21} = 9.2$, $P = .006$) and exercise volume ($F_{1,21} = 5.5$, $P = .029$), highlighting that muscular performance was impaired during two-legged leg press in COPD compared to healthy controls. In healthy controls, muscular performance in one-legged leg press was 1.9 ± 0.7 fold (repetitions; Figure 2B) and 4.6 ± 1.8 (volume;

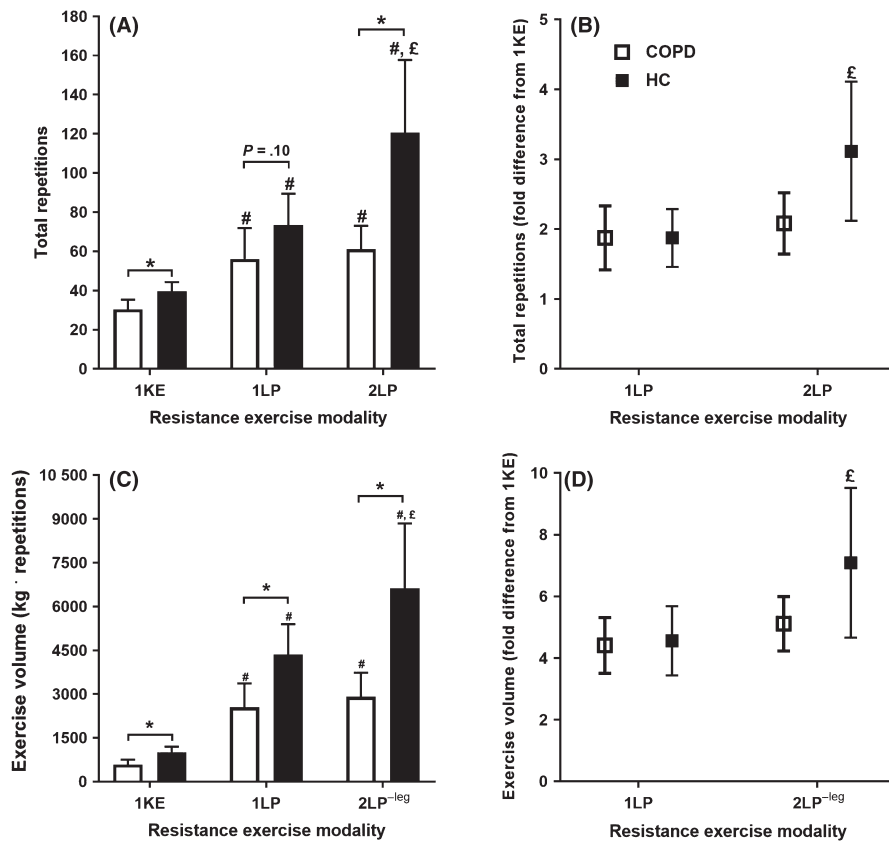


FIGURE 2 Exercise performance in resistance exercises for healthy control and COPD subjects performed as three sets to exhaustion at 60% of 1RM. Exercise performance was measured as A, total number of repetitions to exhaustion, B, number of repetitions to exhaustion in 1LP and 2LP relative to 1KE, C, total exercise volume (kg · repetitions) per leg and D, total exercise volume for 1LP and 2LP^{-leg} relative to 1KE. Data are means with 95% confidence levels. 1KE, one-legged knee extension; 1LP, one-legged leg press; 2LP, two-legged leg press; 2LP^{-leg}, two-legged leg press divided by two; COPD, chronic obstructive pulmonary disease; HC, healthy control. *Significant difference between groups ($P < .05$); #significant different from 1KE ($P < .05$); £significant different from 1LP ($P < .05$)

Figure 2D) fold higher than in one-legged knee extension ($P < .001$). A further increase was seen going from one- to two-legged leg press, which was 3.1 ± 1.6 fold (repetitions; Figure 2B) and 7.1 ± 3.8 fold (volume; Figure 2D) higher than in one-legged knee extension ($P < .001$). In COPD, muscular performance increased in a similar manner going from one-legged knee extension to one-legged leg press (1.9 ± 0.7 fold, repetitions; 4.4 ± 1.3 fold, volume; $P < .005$) (Figure 2B,D), with no differences between COPD and healthy controls ($P = .992$, repetitions; $P = .823$, volume). However, in COPD, no further increase was seen going from one-legged to two-legged leg press (2.1 ± 0.7 fold higher than 1KE, repetitions; 5.1 ± 1.3 fold higher than 1KE, volume; $P = .403$ and 0.226 , respectively) (Figure 2B,D). This resulted in tendencies to higher performance in two-legged leg press relative to one-legged knee extension in healthy controls compared to COPD subjects (3.1 vs 2.1 fold and 7.1 vs 5.1 fold, $P = .055$ and 0.118 , respectively; Figure 2B,D).

Chronic obstructive lung disease and healthy control subjects displayed similar within-session occurrences of muscular fatigue, measured as differences in muscular performance between set 3 and 1 in each exercise (1KE, healthy controls = -18% , COPD = -23% , $P = .874$; 1LP, healthy controls = -15% , COPD = -23% , $P = .720$; 2LP, healthy controls = -23% , COPD = -27% , $P = .144$). In a merged data set encompassing data from both groups, there was a significant correlation between differences in muscular performance of one-legged knee extension and two-legged leg

press and predicted FEV₁ (Pearson $r = .49$, $P = .018$). This suggests that impaired lung function was associated with impaired muscular performance during two-legged leg press.

During muscular performance tests, COPD generally displayed greater falls in oxygen saturation ($F_{1,21} = 9.9$, $P = .005$) and higher degrees of dyspnea ($F_{1,21} = 9.5$, $P = .006$) within each of the three different resistance exercises compared to healthy controls (Table 2). In both COPD and healthy control subjects, there was a significant increase in dyspnea with increasing complexity and physiological demands of the exercises ($1KE < 1LP < 2LP$; $P < .001$). This increase was not evident for oxygen saturation. Healthy controls displayed greater increases in blood lactate concentration from before to after exercises ($F_{1,21} = 5.9$, $P < .05$; Table 2).

4 | DISCUSSION

The primary finding of this study is that patients with moderate to severe COPD (GOLD grade II or III) display lower muscular performance in the legs compared to healthy controls. This difference increases with the complexity of the exercise, that is, the amount of active muscle mass and associated increases in physiological demands. In particular, in COPD, muscular performance was clearly impaired going from one-legged exercises to two-legged leg press, compared to healthy controls. Whereas the overall reduction in muscular performance seen in COPD compared to healthy controls

TABLE 2 Physiological responses to muscular performance tests

	One-legged knee extension			One-legged leg press			Two-legged leg press		
	COPD	Healthy	b/w groups	COPD	Healthy	b/w groups	COPD	Healthy	b/w groups
SpO ₂ (% change)	-3.0 ± 2.1	-2.0 ± 1.0	<i>P</i> = .16	-3.1 ± 2.0	-1.3 ± 1.0	<i>P</i> = .01	-3.6 ± 2.9	-1.4 ± 1.2	<i>P</i> = .03
[BLa ⁻] (% change)	236 ± 101	365 ± 225	<i>P</i> = .10	240 ± 108	352 ± 162	<i>P</i> = .07	355 ± 83 ^{***}	539 ± 278	<i>P</i> = .05
Degree of dyspnea (0-10)	4.5 ± 2.1	2.9 ± 0.8	<i>P</i> = .02	5.6 ± 1.6 [*]	3.9 ± 1.2	<i>P</i> = .01	6.3 ± 1.6 [*]	4.4 ± 1.6 [*]	<i>P</i> = .01

Note: SpO₂ and [BLa⁻] values are presented as percentage change from rest. All values presented as means ± standard deviations.

[BLa⁻], blood lactate concentration; degree of dyspnea (1-10); b/w, between; SpO₂, oxygen saturation of hemoglobin.

*Significant different from one-legged knee extension (*P* < .05).

**Significant different from one-legged leg press (*P* < .05).

is likely due to suboptimal muscle functionality,¹⁹ the exaggerated reductions seen in COPD in two-legged leg press is likely due to the cardiopulmonary limitations inherent to the disease.²⁹ This agrees with previous data on endurance-⁵ and resistance-like exercises.^{22,23} Overall, these data underline the suitability of one-legged resistance exercises in subjects with COPD, advocating their use in rehabilitation programs.

Overall, COPD subjects displayed lower muscular performance in all exercises compared to healthy controls (total repetitions to exhaustion, -23%, -24%, and -49% for 1KE, 1LP, and 2LP, respectively; overall exercise volume, -41%, -42%, and -56% for 1KE, 1LP, and 2LP, respectively). The reduced performance in one-legged knee extension corroborates with previous observations of ~30% reductions in one-legged knee extension performance in subjects with moderate COPD compared to healthy controls.^{30,31} For one-legged exercises, the attenuation in muscular performance is likely due to the muscle pathophysiology inherent to the disease, including reduced proportions of type I muscle fibers, increased proportions of type II (specially IIX) fibers, and reduced oxidative capacity.^{19,32,33} Furthermore, the previous studies have shown that subjects with moderate to severe COPD (such as the participants in this study) are not limited by ventilatory capacity during one-legged knee extension exercises.^{5,34} Our data supports this perspective, with COPD and healthy control subjects showing similar increases in muscular performance going from one-legged knee extension to one-legged leg press. This increase occurred without concomitant increase in lactate concentration, suggesting that oxygen supply was sufficient to fuel the increase in working muscle mass in one-legged leg press.

Chronic obstructive lung disease subjects were unable to increase muscular performance going from one-legged leg press to two-legged leg press. This contrasts data from healthy controls, who displayed 65% and 52% increases in performance (repetitions and volume, respectively), and agrees with data from previous studies.³⁵⁻³⁸ In effect, this led to an exaggerated difference between COPD and healthy control subjects in muscular performance in two-legged leg

press, which cannot be attributed muscular dysfunctions. Instead, the causative explanation likely resides in the cardiopulmonary limitations inherent to the COPD disease. Unfortunately, we do not have cardiorespiratory measurements to support this view. However, it is logical that the increase in working muscle mass accompanying going from one-legged leg press to two-legged leg press led to oxygen requirements that surpassed the oxygen-delivery capacity of the cardiopulmonary system, hence impairing muscle function and performance. This is supported by data from Nyberg *et al*,²³ who found evidence for ventilatory limitation in COPD patients at workloads corresponding to two-legged knee extension exercise. There, a decrease in muscular performance^{-leg} for COPD subjects was present going from one- to two-limb exercises, but whether this decrease was different from what the healthy subjects experienced was not evaluated. Nyberg *et al*²³ performed their study on COPD patients with more severe pulmonary obstruction (38% vs 53% of predicted FEV₁), which may explain the absence of impaired muscular performance in one-legged leg press in the present data. In our study, the crossing point between exercising with sufficient amounts of oxygen and exercising with insufficient amounts of oxygen occurred around or slightly after activation of muscle mass corresponding to one-legged leg press.

In the present data set, a comparison of 1RM data from healthy subjects and COPD provides an unexpected observation. In healthy controls, 1RM^{-leg} in two-legged leg press was 6% lower than 1RM in one-legged leg press (though without reaching statistical significance). This phenomenon is frequently described in the literature and is coined the bilateral deficit.³⁹ In contrast, in COPD, 1RM^{-leg} in two-legged leg press was 5% higher (non-significant) than 1RM in one-legged leg press, suggesting that the bilateral deficit was absent in these patients. This is not common, but has been previously observed in populations such as well-trained individuals.^{40,41} This absence of a bilateral deficit in COPD is likely due to underperformance in one-legged leg press 1RM tests (and not overperformance in two-legged leg

press), perhaps related to poor technical performance caused by instability of the exercising limb or psychological factors. Regardless of causation, this phenomenon may have affected muscular performance during one-legged leg press testing, arguably lowering loads corresponding to 60% of 1RM and increasing estimates of muscular performance measured as repetitions to exhaustion,³⁸ potentially disguising impairing effects of cardiopulmonary limitations. Accordingly, for this exercise, there was no difference between COPD and healthy subjects in repetitions to exhaustion at 60% of 1RM ($P = .10$). This indirectly supports the notion that 1RM estimates for one-legged leg press were too low, as each of the two other exercises revealed clear reductions in muscular performance in COPD compared to healthy controls. Indeed, after taking into account workload (ie, exercise volume), one-legged leg press was also associated with marked reductions in muscular performance in COPD. Importantly, this potential issue does not change the take-home message in our data: muscular performance in COPD subjects is impaired in two-legged leg press, advocating the use of resistance exercises with lower amounts of active muscle mass.

4.1 | Perspectives

We have shown that COPD subjects display impaired muscular performance in resistance exercises compared to healthy controls. This impairment was exacerbated in exercises involving larger amounts of muscle mass (>one-legged leg press), suggesting that performance in such exercises was negatively influenced by the cardiopulmonary limitations inherent to the disease. A similar observation has previously been made in COPD patients with more severe diagnoses,^{22,23} but not in the present patient population and not in connection with isolated resistance exercises performed in apparatus. This is also the first study to explicitly show that COPD patients show progressively lowered muscular performance in resistance exercises compared to healthy controls. Our data advocate implementation of resistance exercises targeting smaller amounts of muscle mass into rehabilitation programs for COPD subjects, including one-legged exercises.

Importantly, in healthy adults, one-legged resistance training leads to similar improvements of muscle functions as two-legged training, measured as strength and hypertrophy.⁴²⁻⁴⁴ For COPD patients, there seems to be “a threshold” of muscle mass that can be exercised before muscular performance is limited by the cardiopulmonary capacity. In our study, this threshold seemed to occur around the muscle mass needed to perform one-legged leg press, though this remains circumstantial, as it was beyond the scope of the project to set such a threshold. Adding to this, the threshold is probably of individual character, determined by the subjects' cardiorespiratory capacity and the severity of the disease. Based on our data, we cannot conclude that

one-legged resistance training will bring higher efficacy to COPD rehabilitation, which may resolve the seemingly lowered responses to training observed in this population. However, such training may enable COPD patients to perform resistance training on equal terms as healthy individuals, freeing them from the obstructions of cardiopulmonary limitations. Future studies should aim to target this perspective.

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