Targeting Limb Muscle Dysfunction in COPD

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Abstract

Chronic obstructive pulmonary disease (COPD), is today one of the world's most common chronic diseases, estimated by the World Health Organization to be the third leading cause of death worldwide by the year 2030. An often neglected aspect of COPD is that the course of the disease is linked to extrapulmonary manifestations that are currently not dealt with optimally, but that has a direct and substantial impact on the condition. Limb muscle dysfunction, at the functional level defined as the reduction of either strength or endurance (or both) properties of the muscle, is highly prevalent in COPD, closely linked to critical clinical and prognostic outcomes including functional status, quality of life, and even mortality. If the goal is to improve limb muscle function among people with COPD is exercise training recommended before other treatment modalities, highly prioritized in international guidelines. In this chapter, why and how to assess and manage limb muscle dysfunction among people with COPD will be targeted, highlighting the vital role of physical therapy and the physiotherapist.

Keywords: chronic obstructive pulmonary disease, limb muscle dysfunction, muscle strength, muscle endurance, dynamic measurements, static measurements, exercise training, resistance training

1. Introduction

Chronic obstructive pulmonary disease (COPD) is one of our most common chronic diseases and accounted for 2.6% of the entire global burden of disease 2015 with 63.9 million disability-adjusted life years. From 1990 to 2015, the prevalence of COPD increased by 44.2% and is now estimated to 174.5 million people worldwide [1]. COPD is by the World Health Organization anticipated to be the third leading cause of death worldwide by the year 2030.

Although COPD is primarily a disease of the respiratory system, with structural and functional impairments of the lungs [2], the disease is often accompanied by manifestations outside the lungs. One of the most common extrapulmonary manifestations in COPD is limb muscle dysfunction, defined as a pathological change of muscle proprieties with a variety of structural and morphological abnormalities that compromise the muscle function. The latter evidenced by a reduction in the strength and/or endurance capacity of the limb muscles [3], with or without a loss of muscle mass [4]. Limb muscle dysfunction is evident in up to a third of all people with COPD and closely linked to the prognosis of the disease. For example, individual factors such as reduced mid-thigh cross-sectional area [5], fat-free mass [6], lower quadriceps strength [7], and vastus lateralis fiber type shift [8] are all predictors of mortality in COPD. Additionally, limb muscle dysfunction is also associated with other important clinical outcomes including reduced quality of life [9], reduced exercise tolerance [10–12], and higher healthcare use [13].

Thus, the clinical and prognostic importance of limb muscle dysfunction in COPD stress the importance of assessing the limb muscle and develop therapies aiming at stopping or slowing down the progression of limb muscle dysfunction, for which the physiotherapist has a crucial role. In this chapter, the etiology and pathophysiology of limb muscle dysfunction in people with COPD will be briefly overviewed; the main objective is to highlight why and how to assess and manage limb muscle dysfunction in people with COPD within the clinical context.

2. Features and importance of limb muscle dysfunction in COPD

Limb muscle dysfunction includes a variety of structural and morphological abnormalities within the muscle resulting in muscle atrophy, weakness, and reduced endurance [4, 14]. Most studied is the quadriceps muscle, this since the quadriceps muscle is an essential muscle for everyday activities such as standing up and walking.

Aspects of limb muscle dysfunction in COPD include larger amounts of intramuscular fat [15] effectively reducing the contractile mass within the muscle; mitochondrial dysfunction including a reduced absolute and relative number of mitochondria but also a changed oxidative capacity of the mitochondria [16]; and a shift from muscle fiber type I toward fiber type IIx which is inconsistent with healthy aging and displays the muscle's poor ability for aerobic work [17].

The structural changes affect functional capacity with impairments such as reduced oxidative capacity and a greater reliance on anaerobic work [18], as well as reduced muscle strength or endurance [3, 19]. It should be noted that the structural changes mentioned here apply to the quadriceps muscle, and other muscle groups, especially upper limb muscle are not affected to the same extent [20]; thus, limb muscle dysfunction is a heterogenic rather than homogenous process. Furthermore, physiological responses to activities can be different across limb muscles and depending on the type of exercise performed [21–27].

2.1. Etiology and pathophysiology of limb muscle dysfunction

People with COPD are inactive [28], and deconditioning due to disuse seems to play a vital role in limb muscle dysfunction. There is, however, evidence to suggest that the limb muscle dysfunction is linked to COPD or at least share the same contributing risk factors. Thus, limb muscle dysfunction is not as simple as a direct consequence of inactivity and disuse (**Figure 1**).

First, when people with COPD are compared to people without COPD but matched with equally low physical activity levels, differences in structure and function remain [29]. Second, quadriceps weakness occurs already in the early stages of COPD [30] when the reduced respiratory capacity should be of minor importance. And third, the training response seems blunted on a structural level for people with COPD [31]. Additional systemic factors, including tobacco smoking, systemic inflammation, exacerbations, nutrition, gas exchange abnormalities, and drugs, can also influence the function of both respiratory and peripheral muscles, by inducing changes in their local microenvironment. Under all these circumstances may, protein metabolism imbalance, oxidative stress, inflammatory events, as well as muscle injury occur, determining the final structure and modulating the function of different muscle groups. For thorough reviews of the pathophysiology, we refer to other sources [4, 32]. Last, the heterogeneity of limb muscle dysfunction in COPD emphasizes a need for specificity, which is equally true for assessment of the limb muscles as well as concerning therapies. We, therefore, present aspects of limb muscle dysfunction separate and do not have a one solution fits all.

2.2. Muscle mass

Muscle mass refers to the amount of muscle available for contractile work and can be reported on a whole-body level, a segmental level, the individual muscles, or on a muscle fiber level depending on the assessment method. Reduction or loss of muscle mass is the leading cause of weight loss within the COPD population [33] and has been demonstrated to be a better predictor of health-related quality of life [9] and survival [5] than, for example, body weight or Body Mass Index (BMI) [34]. Reduced limb muscle mass over time can be defined as muscle wasting and is part of sarcopenia (that is, changes in muscle proprieties due to aging) and cachexia (defined as a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat mass) [35].

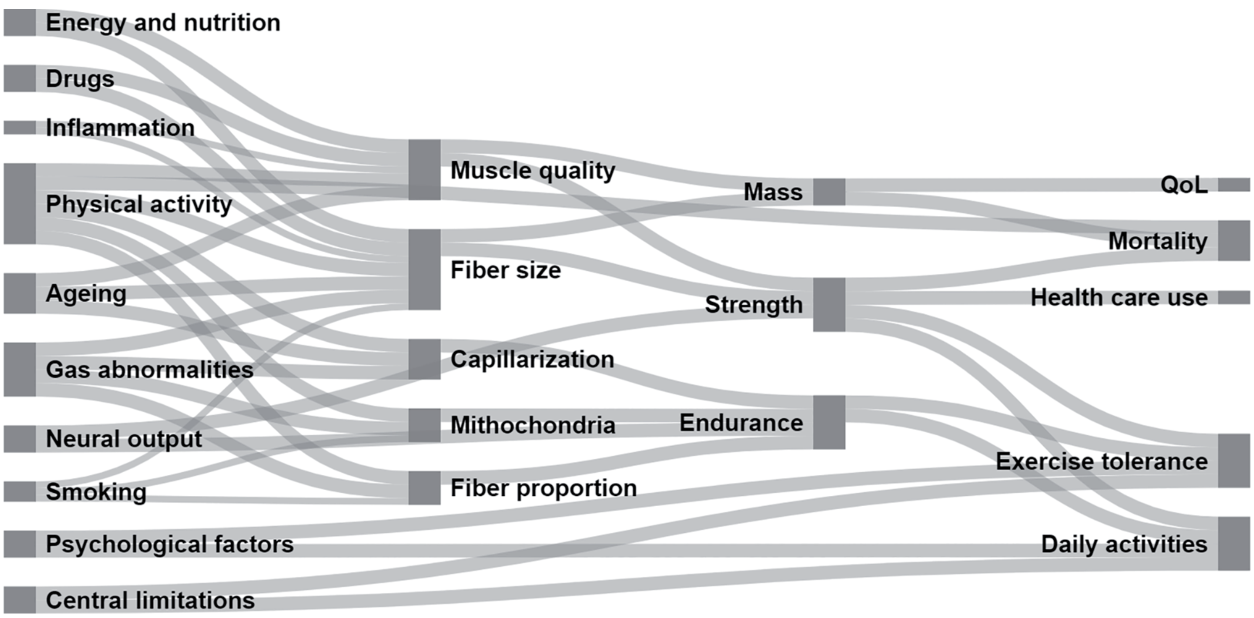

Figure 1. Illustration of the complex interplay of factors and outcomes were limb muscle dysfunction playing a role for people with COPD, some have been thoroughly studied whereas others have not.

Fat-free mass is frequently used as a proxy for muscle mass on a whole-body level and is usually reported as a fat-free mass index by dividing the fat-free mass by the individual's length in meters squared (fat-free mass/m^2). Several criteria have been suggested to define low muscle mass, but irrespective of the criteria used, low muscle mass is common in COPD [4]. Moreover, a low-fat free mass index has been reported in 26% of patients with COPD with a normal BMI [36]. Irrespective of BMI, a low-fat free mass index is a strong predictor of mortality [6], and mid-thigh cross-sectional area is a better predictor of mortality than body mass index [5]. A fat-free mass index <16 kg/m^2 (male) or <15 kg/m^2 (female) is linked with approximately a twofold increase in mortality among people with COPD [6, 37, 38]. A low-fat free mass is also associated to reduced quality of life [9]. Another important notion is that the lower limb muscles are particularly vulnerable to the muscle wasting process in COPD [39, 40], and the loss of thigh muscle mass is relatively more significant than that of whole-body weight, indicating a preferential loss of muscle mass in the legs of people with COPD [41].

2.3. Muscle strength

Reduced muscle strength or muscle weakness, defined as the force generated by a specific muscle or group of muscles in a single contraction [42], has been found in one-third of people with COPD attending hospital respiratory outpatient services [43]. However, when quadriceps strength is normalized by thigh muscle cross-sectional area or by muscle mass, the difference may no longer be significant [41, 44]. Therefore, the reduced quadriceps strength could mostly be a reflection of the loss in muscle mass [40]. This finding is not universal, and the weakness is sometimes disproportional to the reduction in muscle mass [43]. A disproportional reduction in quadriceps weakness may occur in individuals with a high dose of oral corticosteroids [41]. This may however only apply to individuals treated with a high dose of oral corticosteroids over long periods, as no further decrease in quadriceps strength was reported in short-term corticosteroid-treated people with COPD compared with untreated people with COPD [45]. Reduced limb muscle strength is associated with reduced exercise tolerance [10, 11], mortality [7], and higher healthcare use [13].

2.4. Muscle endurance

Quadriceps muscle strength and quadriceps muscle endurance are both reduced in people with COPD. However, quadriceps muscle endurance, defined as the ability to maintain or repeat a contraction over time [42], might be more reduced than quadriceps strength. For example, quadriceps muscle endurance has been reported to be reduced with up to 82% among men and up to 76% among women compared to matched people without COPD, while quadriceps muscle strength was decreased with 29 and 19% among men and women, respectively [3]. Furthermore, using a non-volitional approach with a magnetic nerve stimulator strapped around the quadriceps muscle, people with COPD had approximately 45% of the muscle endurance capacity of people without COPD [46]. However, the variability between studies is vast, and it is probably due to differences in test procedures since quadriceps muscle endurance has been assessed in numerous ways [19]. Limb muscle endurance is essential for work tolerance over time, and it has been shown that people with COPD rate leg fatigue higher than dyspnea in exercise tests [47]. Quadriceps endurance also seems to be

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closer related to functional tests such as the 6-minute walk test than the quadriceps strength [48–50], implicating importance for performing daily activities. Contradictory to quadriceps strength, quadriceps endurance to muscle mass ratio is lower in people with COPD compared to people without COPD [51], and people with COPD, regardless of fat-free mass, have a higher degree of fatigue during endurance tests compared to people without COPD [52]. Most studies have been conducted in a population of severe COPD, but the reduced quadriceps muscle endurance is also evident in people with mild to moderate COPD [53].

2.5. In summary

Limb muscle dysfunction encompasses several manifestations including, muscle atrophy and weakness, reduced endurance, and susceptibility to muscle fatigue, which reflects both structural and morphological muscle adaptations that are seen in limb muscles among people with COPD.

Limb muscle dysfunction is evident in up to a third of all individuals with COPD and has a direct and substantial impact on the condition. For example, limb muscle dysfunction is intimately linked to relevant clinical outcomes, including physical activity, exercise tolerance, quality of life, healthcare use, and even survival.

Thus, limb muscle dysfunction is an essential area for physical therapy and should be prioritized among physiotherapists.

3. How to assess limb muscles in clinical practice

Assessment of limb muscle mass and function should always be a priority within clinical praxis of COPD management, due to its clinical and prognostic relevance [4, 54, 55].

Considering the complexity of limb muscle dysfunction in COPD, no single test could be used to assess and monitor all aspects of the limb muscles within the COPD population, resulting in a wide range of available tests and measurement techniques [14, 54–56].

When deciding on how to assess limb muscles in clinical practice, several factors should be considered and will influence the choice of technique and strategy used. **Table 1** highlights some factors that physiotherapists need to take into account when making this decision [55].

For example, among people with COPD, assessment of limb muscle mass and function should always include the quadriceps muscle due to its clinical and prognostic value [4, 7]; however, as all assessments are muscle group-specific, other limb muscles may also be assessed to provide valuable information [4].

Furthermore, the availability of measurement equipment will likely vary between clinical settings and contexts, thus impacting the choice of the assessment strategy. The physiotherapist needs to acknowledge that measurement equipment and assessment strategies are not interchangeable and may provide different information even if the goal of the assessment would be the same [55, 57].

Different assessment strategies might also vary concerning important quality aspects, including but not limited to validity, reliability, and responsiveness. For example, test–retest reliability is of importance to consider when performing assessments before and after exercise

• What is the aim of the measurement?	
For example, diagnostic purposes? Evaluation purposes?	
• Which muscle(s) should we target?	
For example, upper extremity/lower extremity, unilateral/bilateral, one/several muscle(s).	
• Which aspect(s)?	
For example, muscle mass, strength, endurance, fatigue, power, etc.	
• Which type(s) of muscle contraction?	
For example, static/dynamic concentric/eccentric, volitional/non-volitional.	
• Which equipment?	
For example, weight-machines/free-weights, elastic/functional, availability.	
• Measurements quality.	
For example, validity, reliability, accessibility, feasibility, responsiveness.	

Table 1. Factors to consider when deciding on how to assess limb muscles [53].

interventions to interpret findings [57–61], while validity, for example, could be an issue when using simple field tests to provide information on aspects of limb muscle function [62–65].

Irrespective of the goal of the measurement technique used, standardization plays a crucial role to increase the measurement quality when assessing limb muscles in COPD, including standardization of preparation guidelines (e.g., guidelines for medications, caffeine, activities, etc. before an assessment), equipment (e.g., free weight/weight-machines/dynamometers), instructions (e.g., written/oral/visual), familiarization (to minimize learning effect), warm-up (e.g., general vs. specific warm-up of targeted muscles), positioning, the range-of-motion (e.g., start and end positions), velocity (e.g., seconds in concentric/eccentric phase of movement), and rest (between contractions/sets, etc.). For further details on what to consider to standardize assessments, we refer to previously published work [42, 54, 55].

Nevertheless, irrespective of all factors to consider when deciding on how to assess limb muscles in clinical practice, the take-home message is that the limb muscles should be evaluated. Despite the prognostic and clinical relevance of limb muscle dysfunction in people with COPD, and even though assessment of limb muscles is recommended in international guidelines [4], it remains to be an integrated part of the routine evaluation and management of COPD.

3.1. Muscle mass

Assessing only BMI is inadequate to quantify the impact of COPD on different muscle compartments or to provide valid information on muscle mass [36] since BMI does not give any information on body composition or fat distribution [54]. Instead, fat-free mass could be targeted and is frequently used as a proxy for muscle mass on a whole-body level among people with COPD [4].

The gold standard and reference method in COPD for assessing fat-free mass is through determining total body water by deuterium dilution [66]; however, this technique is invasive, and use of the method is likely limited to research centers [56]. Fat-free mass could also be assessed using simple techniques such as skinfold anthropometry. However, this technique generally overestimates the fat-free mass when compared to other techniques, especially if measured on more obese individuals [67, 68].

Two techniques that are realistic to be used in the clinical environment to monitor and provide accurate assessments of fat-free mass in COPD are bioelectrical impedance (BIA) and dual-energy X-ray absorption (DEXA). Both techniques are noninvasive and have shown to provide valid and reliable information on the distribution of fat-free mass among people with COPD [7, 67, 69–71]. BIA has the advantage of being less expensive and often more easily accessible than DEXA in clinical settings [69]. When estimating fat-free mass from BIA, it is vital to use equations that have been validated within the COPD population and to be cautious with built-in equations provided by manufacturers [72, 73]. Also of importance is that since BIA is influenced by total body water, fluid balance and time of day need to be controlled, primarily when a longitudinal assessment is performed. For example, if used as an outcome measure after an exercise training period [54]. About the latter, it should be noted that even though BIA (and DEXA) assessments could provide information for body compartments (e.g., left/right arm, trunk, left/right leg), these techniques might be less sensitive to change than if direct assessments of regional muscle mass using more advanced techniques such as computed tomography, magnetic resonance, or ultrasound imaging are performed [27, 74]. Furthermore, the correlation between local and whole-body muscle mass is weak in COPD, thus suggesting that direct assessment of regional muscle mass indeed has additional value [74]. Nevertheless, as availability of different measurement equipment likely varies between clinical settings, it is important to note that, except BMI measurements, all techniques listed above theoretically could be used to assess muscle mass in people with COPD. However, the physiotherapist needs to acknowledge and take into account the advantages and disadvantages of each technique when performing the assessment.

3.2. Muscle strength

Assessment of limb muscle strength could be done in numerous ways using both volitional (effort dependent) and non-volitional (independent from the patient's motivation and effort) techniques. Both techniques provide valid and reliable results independent of disease severity [58, 59, 65, 75]. Even though non-volitional assessments of muscle strength could be performed through electrical or magnetic stimulation of the muscle or its motor nerve [76], these non-volitional techniques are in a similar way as assessing total body water by deuterium dilution (to determine muscle mass), mainly limited to research centers and clinical research [14]. Non-volitional assessments are also rarely used within COPD research to assess the effect of exercise interventions over time [26]. Thus, voluntary, effort dependent maneuvers, is the most clinically feasible way of measuring limb muscle strength in people with COPD [77].

Limb muscle strength measurements could be performed using various devices and techniques, including strain gauges, handheld or fixed portable dynamometers, weight machines, or manual muscle testing techniques as well as more complex systems such as computerized dynamometers [78, 79]. Furthermore, such assessments could be performed using static (isometric), or by using dynamic (isotonic [fixed external loading] or isokinetic [fixed speed of movement]) techniques (**Table 2**).

To date, static measurements of quadriceps muscle strength have been put forward and recommended, as they provide essential prognostic information [7]. Static measurements of grip strength have also been used among people with COPD; however, current research is contradictory, and grip strength does not appear to be associated with disease severity or to be decreased more than among the general older population [80], even though this is not a universal finding [81]. Even though static measurements of quadriceps muscle strength is recommended, recent literature suggests that dynamic measures of limb muscle strength should not be neglected as the dynamic capacity of the muscle seems to be more closely related to factors associated with functional tasks, such as walking or standing up from a chair, than isometric (static) measurements [49, 79].

Thus, the decision on how to assess muscle strength should be dependent on the clinical question we would like to answer.

3.3. Muscle endurance and fatigue

Assessment of limb muscle endurance could in a similar way as limb muscle strength measurements were performed using both volitional and non-volitional techniques, with the former being the most clinically feasible. In COPD, direct measures of limb muscle endurance have primarily targeted the quadriceps muscle using sustained (isometric) or repeated (isokinetic/isotonic) contractions [19], providing reliable results [57].

However, as the endurance capacity of the limb muscles reflect the ability to perform tasks requiring a low number of contractions such as climbing a set of stairs as well as tasks requiring a high number of contractions such as bicycling or walking over a long distance, it is apparent that the same method cannot be used to evaluate muscle performance in both situations and that no single test can evaluate all aspects of limb muscle endurance [19].

	Isometric*	**Isokinetic†**	**Isotonic†**
Strength	Performing 3–5 MVC held for ~5 s, spaced with 30–60s rest periods at a fixed position.	Performing a minimum of 3–5 maximal contractions at an angular velocity of 60°–90°s	Performing a 1 RM test following ACMS guidelines with the addition of standardized range-of-motion and speed of contraction
Endurance	Sustained contraction at an intensity equal to 20–60% of isometric MVC until failure using visual feedback	Total work obtained from (typically 30) maximal contractions at an angular velocity of 60°–90°s	A maximum number of repetitions performed using external loads corresponding to 10% up to 50% of the individual 1 RM until failure.

MVC, maximal voluntary contraction; ACSM, American college of sports medicine; RM, repetition maximum.

*Normally 60°–90° flexion.

†Normally 90° flexion to full extension.

Table 2. Commonly used procedures for assessment of quadriceps muscle strength and endurance among people with COPD [19, 55, 58, 61, 79, 82].

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Thus, to date, there is no specific recommendation on how to assess limb muscle endurance among people with COPD, and a vast variation of techniques and strategies have been used, including both static and dynamic measurements [19]. Similarly, as for limb muscle strength assessments, dynamic measurements of quadriceps endurance seem to be more closely related functional tasks than isometric measurements [49].

Furthermore, in comparison to limb muscle strength, the endurance capacity of the limb muscles does also seem to be more closely associated with both upper and lower limb functional capacity among people with COPD [50], highlighting one reason for why the endurance capacity of should not be neglected when assessing the limb muscles. For an example of commonly used procedures for quadriceps muscle testing see **Table 2**.

3.4. Functional testing

In the assessment of limb muscles in people with COPD, the use of functional tests is quickly becoming more and more popular. One key advantage of using functional tests is that they are often cheap, time-efficient, and require minimal equipment and usually a limited amount of space. Furthermore, as there is more to limb muscle function in COPD other than strictly the ability to exert a specific torque over a particular period of time [55], functional tests may provide valuable information that cannot be obtained from direct measurements of limb muscle function or mass.

Several different functional tests have been used in people with COPD, with field walking tests and different versions of the sit to stand test, being the most common in recent years [62, 83].

Similarly, as for direct measurements of limb muscle mass and function, different functional tests provide various information depending on which test is used, and the physiotherapist is required to use different tests depending on the objective of the assessment.

Furthermore, the physiotherapist should keep in mind that functional tests and limb muscle function assessments evaluate different constructs (as evident by low to moderate associations between limb muscle function assessments and functional tests), and thus cannot replace another [49, 79, 84]. Therefore, when deciding on how to assess the limb muscles in COPD, the objective should always be the driving factor.

3.5. In summary

Assessment of limb muscle mass and function should be part of the routine management of people with COPD. One aspect that sometimes is overlooked is the complexity, a wide variety of assessment methods could be used for this purpose.

Examples from this chapter include muscle mass assessed on whole-body level [6] or by a thin slice of the thigh [5], quadriceps strength, and endurance that could be measured static [43] or dynamic [40], resulting in somewhat different conclusions dependent on the type of assessment performed. As such, several factors need to be taken into account by the physiotherapist when deciding on how to assess limb muscle mass and function in COPD (see **Table 1** for further details).

Nevertheless, standardization of testing procedures is of utmost importance to provide accurate and reliable assessments, irrespective of measurement technique used.

4. How to improve limb muscles among people with COPD?

Strategies aiming at stopping or slowing down the progression of limb muscle dysfunction are highly warranted, and interventions focusing on exercise training, nutritional supplementation, and medication alone, or in combination, have all been shown to improve various aspects of limb muscle function and mass in people with COPD [4]. The focus in this section will be on the use of exercise training, this since exercise training is recommended before all other available modalities or combination of modalities [4].

4.1. Exercise training

In one sense, exercise training interventions for people with COPD are no different than for other populations; the same general exercise principles (specificity, progression, reversibility, periodization, etc.) and acute program variables (choice of exercise, order of exercise order, intensity [duration], number of sets, rest period lengths, type of muscle action, speed of movement, volume, frequency, etc.) apply [85–87]. However, for people with COPD, some of these variables might need to be altered to maximize benefits [88].

Considering the complexity of limb muscle dysfunction in COPD, no single exercise regimen could be used to target all aspects of the decreased function and altered structure of limb muscles [4, 26]. In a recent review, the effects of different modalities including aerobic or resistance training, high-intensity interval training, electric or magnetic muscle stimulation, whole-body vibration, and water-based exercise modalities to improve limb muscle function and mass among people with COPD were summarized. Overall, limb muscle strength was increased in 78%, limb muscle endurance in 92%, and muscle mass in 88% of the cases where that specific aspect of the limb muscle was measured [26] using these different modalities. On average, this corresponded to a mean increase in limb muscle strength of 15–34%, limb muscle endurance of 8.7–96.6%, and limb muscle mass of 4.2–12.1% and was highly dependent on which type of assessment strategy used. For limb muscle strength and endurance, isotonic assessment strategies seemed to be most responsive while for muscle mass, direct measurements using ultrasound demonstrated the most substantial adaptations, independent of exercise modality used [26]. However, there is considerable heterogeneity in the type of exercise modalities used, and it is currently unknown which type of exercise modality that is most effective in different subgroups of people with COPD. To date, several different exercise modalities are available for people with COPD including but not limited to resistance training (strength or endurance targeted), aerobic training (continuous or interval), whole body vibration training, neuromuscular electrical stimulation, active mind body therapies (e.g., Tai Chi, Qigong, etc.), as well as using different strategies to structure (e.g., nonlinear periodization) or to perform (e.g., single limb) exercises [21–25, 89]. Nevertheless, the most commonly used approaches are aerobic and resistance exercises, and in the design of both modalities for people with COPD, the American College of Sports Medicine frameworks [85, 86] has been recommended [88]. However, even though both continuous and interval training have shown positive effects of limb muscle function and mass in people with COPD, if the aim is to increase these aspects of the limb muscles in COPD, resistance training may be a more effective modality than aerobic exercises [90–93].

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More significant effects on muscle strength have been observed after resistance training in comparison to aerobic training alone or when resistance training is added to an aerobic training protocol [88, 91, 93]. This fits with the specificity principle of exercise, that is, that exercise adaptation is specific to the type of activity and the volume and intensity of the activity performed [86, 94]. However, this also means that different kinds of resistance training protocols are necessary to target various aspects of limb muscle dysfunction. For example, if the goal is to improve limb muscle strength and mass, high-load/low-repetition programs are favorable [92, 95, 96], while if the goal is to enhance limb muscle endurance, low-load/high-repetition programs should be used [86, 96, 97]. In addition to decreased limb muscle mass and function, limb muscle dysfunction in COPD is also characterized by altered intramuscular characteristic, that is, structural and muscle metabolic alterations on the functional level result in the decreased function of limb muscles in COPD [4, 31]. Thus, of importance is that exercise-based training interventions also result in both structural and metabolic changes within the limb muscles [31], including, but not limited to, changes in fiber type proportion, fiber size, capillary to fiber ratio, muscle protein turnover regulation, and mitochondrial enzyme activity, while markers of oxidative and nitrosative stress and inflammation does not seem to be affected [31]. However, in a similar way as for effects on muscle mass and function, exercise responses are heterogeneous, dependent on the type and intensity of the activity performed. Alterations in fiber proportion, fiber size, and capillary to fiber ratio tend to increase more after combined aerobic and resistance training, but predominantly with excellent results after higher intensity interval training [31]. Thus suggesting that the intensity of the activity performed is of importance to achieve intramuscular adaptations, even though this needs to be confirmed in future studies.

4.2. In summary

Exercise training, and resistance training in particular, is the most efficacious approach to ameliorate limb muscle dysfunction among people with COPD, with the latter resulting in the most substantial improvements in limb muscle mass and function. However, COPD limb muscle is characterized by a large heterogeneity of muscle phenotypes and muscle dysfunction, stressing the importance of identifying those specific factors that should be considered in the development of individualized resistance training programs among people with COPD. Thus, no single intervention is sufficient to target all aspects of limb muscle dysfunction in the disease. To achieve intramuscular adaptations, exercise intensity seems to be an important factor, and high intensity interval training seems to be the most promising approach. Lastly, irrespective of exercise training modality, general exercise principles and acute program variables should always be incorporated when designing the exercise program.

5. Conclusions

Limb muscle dysfunction is a highly prevalent and clinically relevant manifestation of COPD, closely linked to important clinical outcomes, including exercise tolerance, quality of life, and survival. Limb muscle dysfunction seems to be heterogeneous, with the lower limbs, and the quadriceps muscle in particular, mostly affected.

Assessment of limb muscle mass and function should be routinely performed in clinical practice, and simple valid and reliable tools are available for the physiotherapist to use.

Independent of measurement strategy, standardization of measurement properties are crucial and several different factors such as type of contraction, choice of exercise or equipment need to be acknowledged by the physiotherapist when deciding on how to assess the limb muscles among people with COPD.

Lastly, to improve limb muscle mass and function, exercise training, and resistance training in particular is recommended before other available modalities, and general exercise principles and acute program variables should always be incorporated into the design of the exercise program.

Conflict of interest

The authors report no conflict of interest.

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