

Measuring and monitoring skeletal muscle function in COPD: current perspectives

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Abstract: Skeletal muscle dysfunction is an important systemic consequence of chronic obstructive pulmonary disease (COPD) that worsens the natural cause of the disease. Up to a third of all people with COPD express some form of impairment which encompasses reductions in strength and endurance, as well as an increased fatigability. Considering this complexity, no single test could be used to measure and monitor all aspects of the impaired skeletal muscle function within the COPD population, resulting in a wide range of available tests and measurement techniques. The aim of the current review is to highlight current and new perspectives relevant to skeletal muscle function measurements within the COPD population in order to provide guidance for researchers as well as for clinicians. First of all, standardized and clinically feasible measurement protocols, as well as normative values and predictive equations across the spectrum of impaired function in COPD, are needed before assessment of skeletal muscle function can become a reality in clinical praxis. This should minimally target the quadriceps muscle; however, depending on the objective of measurements, eg, to determine upper limb muscle function or walking capacity, other muscles could also be tested. Furthermore, even though muscle strength measurements are important, current evidence suggests that other aspects, such as the endurance and power capacity of the muscle, should also be considered. Moreover, although static (isometric) measurements have been favored, dynamic measurements of skeletal muscle function should not be neglected as they, in a larger extent than static measurements, are related to tasks of daily living. Lastly, the often modest relationships between functional tests and skeletal muscle function measurements indicate that they evaluate different constructs and thus cannot replace one another. Therefore, for accurate measurements of skeletal muscle function in people with COPD, specific and formal measurements should still be prioritized.

Keywords: chronic obstructive pulmonary disease, measurement properties, muscle strength, muscle endurance, muscle power

Introduction

In people with chronic obstructive pulmonary disease (COPD), skeletal muscle dysfunction is a common extrapulmonary manifestation.¹ Although both respiratory and limb muscles are altered, the latter are usually more severely affected.² Furthermore, respiratory muscle dysfunction is mainly seen in advanced disease,² and even though the extent of impaired function of the limb muscles is greater in more advanced disease, it may also occur in earlier stages of the disease. Quadriceps muscle weakness' prevalence rate, for example, approximates up to 20% even in people with mild COPD.³ Thus, due to space constraints, the focus of the current perspective will be on measuring and monitoring the function of the limb muscles, henceforth denoted as skeletal muscle function.

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Several morphological and structural deviances within the muscle comprise the impaired skeletal muscle function in COPD, most of which have been reported in the quadriceps.¹ Importantly, impaired skeletal muscle function is intimately linked to key clinical and prognostic outcomes such as health care utilization,⁴ exercise intolerance^{5,6} and even life expectancy.⁷ For example, isometric quadriceps strength is more closely related to mortality than age, body mass index and forced expiratory volume in 1 s.⁷ Thus, impaired skeletal muscle function is an important extrapulmonary manifestation in COPD, whose potential identification should be included in the routine assessment of these patients in the clinic.^{1,2}

Various objectives could be pursued when measuring the function of skeletal muscles, including diagnostic purposes in order to characterize the nature of dysfunction, or as a mechanism for monitoring progress when measured before and during pulmonary rehabilitation. The latter would also facilitate the prescription of targeted training programs. Whatever the objective of measurement, choice of measurement strategy should always be specific to the clinical question it should answer, considering both advantages and limitations of available techniques, equipment and clinical realities.^{2,8}

In this paper, we aim to provide a brief overview on the features and mechanisms of muscle dysfunction of the limb muscles in COPD and summarize what we currently know

on the topic of measuring and monitoring skeletal muscle function in COPD. More specifically, we will highlight important aspects and properties related to measurement strategies used to monitor and measure skeletal muscle function in COPD. In addition, we also aim to highlight some new perspectives relevant to skeletal muscle function measurements among people with COPD in research as well as within the clinical realm.

Features and mechanisms of skeletal muscle dysfunction

Although the clinical significance of skeletal muscle dysfunction is well established in COPD, the underlying mechanisms of this problem are not fully understood. An overview of etiological factors, morphological and structural abnormalities, as well as impaired aspects of skeletal muscle function in COPD, is summarized in [Figure 1](#). In short, the etiology of skeletal muscle dysfunction is likely multifactorial with possible contribution from cigarette smoke, genetic and epigenetic alterations, metabolic, drugs (corticosteroids), comorbidities, exacerbations, systemic inflammation, malnutrition as well as chronic physical inactivity.^{1,2} Since the latter leads to deconditioning, a process that initiates intramuscular and functional alterations, this is arguably one of the most important

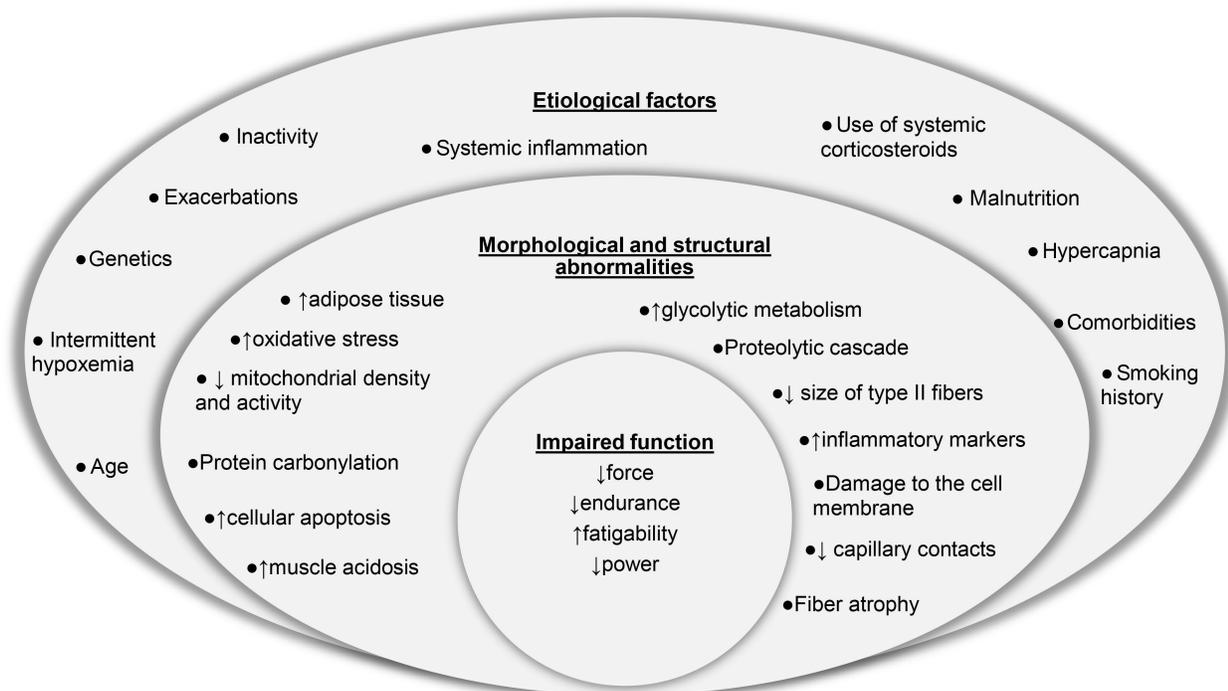


Figure 1 Overview of etiological factors, morphological and structural abnormalities and impaired skeletal muscle function in chronic obstructive pulmonary disease.

contributing factors to skeletal muscle dysfunction in COPD.⁹ However, the discovered range of skeletal muscle abnormalities seems to need a broader explanation than the level of physical activity alone. This since muscle impairment in COPD is vaguely related to the degree of activity,^{10,11} and as differences in skeletal muscle structure and function persevere between people with COPD and healthy controls even when controlling for physical activity.¹¹

Features of skeletal muscle dysfunction include atrophy, a shift in fiber-type distribution from type I to type IIx fibers, reduced oxidative capacity, mitochondrial function and capillarization,¹ most of which have been reported in the quadriceps muscle,¹ even in mild disease.¹² The fiber-type shift is seen in about one-third of people with COPD, fiber atrophy in 20%.¹⁰ In a similar way, mid-thigh cross-sectional area has been reportedly reduced by 15–20% in people with moderate COPD.¹³ Furthermore, the shift in skeletal muscle fiber-type proportion opposes what is typically seen with aging,¹⁴ contributes to the muscles' susceptibility to fatigue¹⁵ and has been associated with premature mortality.¹⁶ Consistent with this shift, the reduced oxidative capacity and impaired mitochondrial function of the quadriceps muscle¹⁷ contribute to impaired performance during endurance-based activities.¹⁸ However, intrinsic muscle alterations alone cannot fully explain the decreased skeletal muscle function observed in people with COPD. In fact, aspects of skeletal muscle dysfunction such as increased susceptibility to muscle fatigue also seem to be related to the central nervous system. For example, mechanical and metabolic changes caused by exercise and activities have shown to stimulate metaboreceptive group III and IV muscle afferent fibers. These signals lead to the

inhibition of the central motor drive, which thus prevent subsequent locomotor recruitment and the development of potentially dangerous and irreversible fatigue.^{19,20} At the functional level, these lead to decreased exercise capacity as well as increased limb muscle fatigue.²¹ Estimations of impaired skeletal muscle function in COPD vary according to disease severity and the criteria used to define dysfunction. Nevertheless, up to a third of all people with COPD expresses some form of impaired skeletal muscle function and encompasses reductions in strength, endurance, and power as well as an increased fatigability.^{1,22,23}

Measuring and monitoring skeletal muscle function in COPD

The 2014 American Thoracic Society and European Respiratory Society statement on Limb Muscle Dysfunction in COPD recommends that assessment of isometric skeletal muscle function, at least quadriceps muscle function, should be an integrative part of the routine assessment of people with COPD.¹ In addition, measurements of different aspects of skeletal muscle function (eg, strength or endurance) during exercise training would provide a mechanism for monitoring progress.²⁴ However, several factors influence the choice of strategy when measuring and monitoring skeletal muscle function in people with COPD (Figure 2).

First of all, all measurements of skeletal muscle function are muscle group-specific as well as heavily dependent on the type of contraction, velocity of movement and equipment used. In COPD, measurements of quadriceps muscle function should always be considered due to its clinical and prognostic

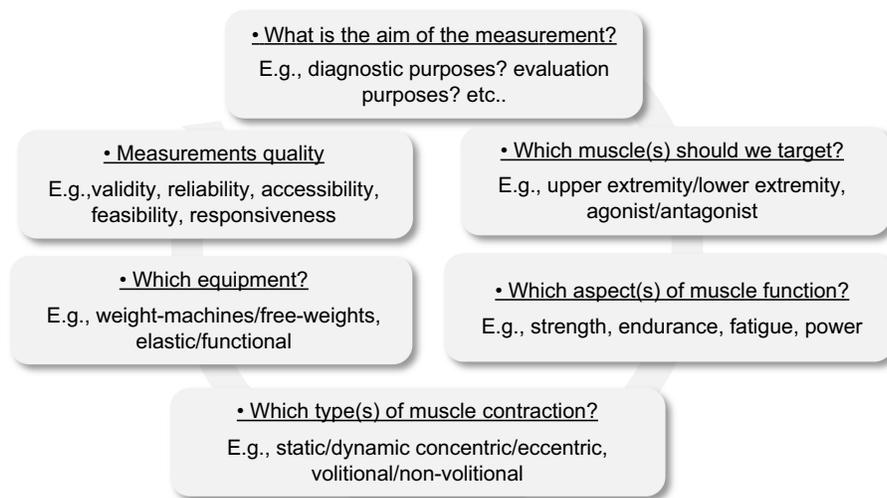


Figure 2 Factors that influence the choice of the measurement technique.

value, but other lower and upper limb muscles may be evaluated to provide valuable information.^{1,8} Furthermore, the availability of measurement equipment will evidently impact on the selection of measurement technique; however, it is important to acknowledge that different measurement techniques are not interchangeable and may provide different information since they measure different aspects of skeletal muscle function. Thus, in a similar way to exercise training adaptations that are specific to the stimulus applied,²⁵ the choice of skeletal muscle measurement strategy should also be specific to the clinical question it aims to answer.^{8,26} For example, during static testing (isometric), the tested limb is fixed and there is no change in muscle length throughout the contraction. This would suggest that this parameter may be less informative about the ability to perform functional activities as a part of daily living which often include dynamic components (except for isometric grip strength, more associated to carrying groceries in daily life for example). Thus, specific dynamic measurements in which information is provided on skeletal muscle function throughout the full range of motion might more accurately reflect functional activities.^{27,28} Dynamic contractions could be isotonic, that is when there is no noticeable change in the load applied to the muscle or isokinetic where the speed of the movement is constant.⁸ Even though isokinetic dynamometer measurements of skeletal muscle function often are considered the gold standards of skeletal muscle strength measurements, the availability of isokinetic dynamometers is limited, mostly because of the cost of equipment and need of trained personnel,⁸ reducing the clinical applicability. Furthermore, as skeletal muscle dysfunction is evident by a decrease in various aspects of skeletal muscle function (eg, reduced strength or endurance),^{1,8} this implies that no single test could be used to measure and monitor skeletal muscle function among people with COPD.⁸

All measurement techniques mentioned, so far, consist of voluntary contraction measurements. However, since skeletal muscle function may be affected by external factors such as motivation and cooperation of the patient,¹ nonvolitional measurements of skeletal muscle function using electrical or magnetic twitch stimulation of peripheral nerves have been developed. The latter technique activates the neuromuscular system without stimulating skin nociceptors, resulting in less discomfort and pain.²⁹ Such measurements can be performed in a rested muscle (unpotentiated twitch stimulation) or seconds after a maximum volitional contraction (potentiated twitch stimulation).^{1,30} Nonvolitional muscle function assessment can be especially relevant in investigating the mechanistic and functional aspects of muscle fatigue.³¹

Irrespective of which measurement techniques that are used, important aspects, including but not limited to the feasibility, validity, responsiveness, and reliability of the selected measurement technique, need to be considered when deciding on how to measure and monitor skeletal muscle function in people with COPD.²⁶ For example, the selected measurement technique should be feasible in the intended clinical context, which could relate to the time needed to perform the test or the availability of the measurement equipment. Another example is related to the reliability of skeletal muscle function measurements, for which standardization plays a key role. For example, standardization of measurement instructions, positioning, rhythm and external visual/audio feedback are all important factors that could influence the degree to which the measurement is free from error.^{32,33} Readers are invited to refer to the following section for detailed information about these aspects in relation to what we currently know on skeletal muscle strength, endurance/fatigue and functional measurements in people with COPD. Lastly, standardization of preparation guidelines, including, but not limited to, use of medications or caffeine prior the assessment or avoidance of strenuous physical activities the day(s) before measurements, etc., should also be standardized. An overview of key aspects to consider with regard to standardization of measurement procedures is summarized in [Table 1](#)

What is currently known?

Skeletal muscle strength measurements

The most commonly measured aspect of skeletal muscle function in COPD is skeletal muscle strength, defined as the force-generating capacity of the muscle and often measured as the maximal voluntary contraction (MVC).³⁵ Skeletal muscle strength measurements could be performed using numerous devices including strain gauge, handheld or fixed portable dynamometer, weight machines or manual muscle testing techniques as well as more complex systems such as computerized dynamometers.^{8,35} Even though skeletal muscle strength can also be assessed independently from the patient's motivation and effort with electrical or magnetic stimulations of the muscle or its motor nerve,^{36,37} these techniques are almost solely used in the realm of clinical research. Thus, this section will focus on volitional measurements of quadriceps muscle strength that include static (isometric) as well as dynamic (isokinetic and isotonic) measurement techniques.

Table 1 Standardization of measurement procedure.

<ul style="list-style-type: none"> ● Preparation guidelines: (eg, guidelines for medications, caffeine, activities etc.) ● Equipment: free weight/weight machines/dynamometer/strain-gauge, etc. ● Instructions: written/visual/oral. ● Demonstration: especially when using functional tests. ● Familiarization: mostly when using isokinetic/computerized dynamometers, to avoid learning bias and improve test–retest reliability ● Warm-up: general and/or specific warm-up of targeted muscles/movements ● Position: eg, seated with knee and hip flexed at 90° for isometric strength measurements ● The range of motion: start and end positions of tested muscle(s)/movement(s) ● Velocity of contraction: eg, fast (<1:1), traditional (1:1), moderate (1–2:1–2), slow (5:5) ● Feedback/encouragement: none/visual/oral. ● Rest: between contractions/sets/exercises (if multiple tests are performed). ● Test order: if multiple tests are performed (agonist/antagonist, upper/lower extremity)

Note: Data from Nyberg et al⁸ and Thompson et al.³⁴

Isometric strength measurements

Isometric quadriceps strength measurements have been highly recommended in COPD¹ since they provide important prognostic information.⁷ Recently, these measurements have also been shown to respond to interventions such as exercise training, with a suggested minimal important difference of 7.5 Nm.³⁸ With regard to measurement properties, isometric quadriceps strength measurements have shown very high relative test–retest reliability, intra-class correlation coefficient (ICC) >0.9 and a minimal detectable change of 18–22% for strain-gauge as well as isokinetic dynamometer measurements, respectively.^{37,39}

With regard to measurements of upper limbs, handgrip strength has been commonly assessed in COPD studies.³⁵ However, the clinical purpose of isometric strength measurements is still uncertain in COPD since it does not appear to be associated with disease severity or to be decreased more than in the general older population.⁴⁰

During isometric strength measurements, standardization of limb position, performing ≥ 3 MVC held for 4–5 s, spaced with 30–60-s rest periods, is important to obtain valid and reproducible results.^{8,35,37} When using portable dynamometers, fixation on rigid support is of utmost importance to avoid a possible underestimation of strength measurements and to provide reliable and valid results.^{41,42}

Dynamic strength measurements

Dynamic measurements of skeletal muscle strength are performed using either isokinetic (fixed speed of movement) or isotonic (fixed resistance applied to the muscle during the movement) techniques.

Isokinetic measurements are usually performed at a fixed angular velocity of 60°–90°/s³⁵ while isotonic skeletal muscle strength can be assessed with hydraulic resistance devices, force transducer platforms adapted to weightmachines or

with 1-repetition maximum (1-RM) tests.³⁵ The latter represents the highest load that can be lifted once throughout the whole range of motion, while the former represents the peak torque obtained at any specific joint angle.³⁵ In addition to the standardized procedure from the American College of Sports Medicine,⁴³ the velocity of the movement, positioning, warm-up, rest period as well as familiarization should also be standardized (Table 1), although this is often missing in COPD studies.³⁵

Skeletal muscle endurance and fatigue measurements

Skeletal muscle endurance refers to a muscle's ability to sustain or repeat a specific task over time,⁴³ while fatigue refers to a reversible reduction in force generated by the muscle during a given task.⁴³ Reduced quadriceps endurance is common in COPD,⁴⁴ often reported decreased to a larger magnitude than weakness,²³ and has also shown to have relevance to tasks of daily living.⁴⁴ Importantly, the impairment in skeletal muscle endurance cannot be predicted from muscle strength, highlighting that both aspects of muscle function should be evaluated.⁶

Furthermore, skeletal muscle endurance could be evaluated in various ways, using either sustained or repeated contractions and using a variety of different techniques.⁴⁴ In people with COPD, isometric, isotonic and isokinetic skeletal muscle endurance measurements have recently demonstrated high to very high relative reliability (ICC 0.76–0.94, 0.85–0.94 and 0.78–0.99, respectively). Meanwhile, isokinetic work fatigue index, eg, the ratio of work performed during the last ten repetitions to the work performed during the first ten repetitions, has demonstrated very low to high relative reliability (ICC –0.24 to 0.77).^{32,33} All techniques were also clinically feasible with a mean time consumption

of <7.5 mins.³³ Isokinetic shoulder flexion and knee extension endurance measurements have also found to be moderately to largely responsive to resistance training.⁴⁵

How to perform measurements of skeletal muscle endurance

Static measurements of skeletal muscle endurance are performed by asking the subject to sustain a muscle contraction at an intensity corresponding to a pre-specified intensity of their MVC, normally from 20% to 60% of individual MVC until exhaustion using visual feedback.^{33,44} To get dynamic measurements, the recommendations are that isokinetic endurance and fatigue measurements are recorded/observed at a fixed angular velocity of 90°/s during maximal contraction(s) (normally 30), and throughout the whole joint range of motion.^{32,33} Isotonic endurance protocols are performed with constant external loading and standardization of range of motion, and speed of movement (eg, using a metronome) is recommended in order to minimize variation in testing.³³ In COPD, external loads corresponding to 10% up to 50% of the individual MVC have been used during repeated contractions performed until failure.^{6,33,46} Results are quantified by reporting the time or number of repetitions performed.^{33,44,46} An advantage of isotonic muscle testing over isometric and isokinetic techniques is that it could be performed using simple equipment such as elastic bands,⁴⁶ exercise platforms/benches⁶ or pulley systems.⁴⁷

The role of functional tests

Since there is more to skeletal muscle function than strictly the ability to exert a certain torque over a certain period of time and since muscle impairments do not fully explain impaired daily functional activities,⁴⁸ increased interest has been given in the last few years to examine the relationships between muscle dysfunction and limitations in functional activities of patients with COPD, among others through tools that represent patients' global functioning and that assess activities that are meaningful to them.^{8,49–51} Functional tests assess in a standardized environment patients' ability to perform activities that mirror what they actually do in their daily life. They can help to provide insights on how the physiological, structural and functional changes happening in peripheral muscles impact and contribute to limitations and restrictions of participation in the daily life of patients and ultimately their quality of life.⁵¹

Determinants of performance in functional tests in COPD include sensory integration, balance, age, psychological factors, the severity of airflow limitation, exercise tolerance and often various muscle groups coordinated work.^{50,52} Muscles' contribution differs in functional tests: some seem to require more muscle endurance (such as the unsupported upper limb exercise test), some muscle strength (such as a five-repetition-sit-to-stand test) and others muscle power (such as the stair power climbing test – SCPT). Other functional tests rely more importantly on exercise tolerance and patients' cardiorespiratory limitations, such as the six-minute walk test, incremental and endurance shuttle tests, the Glittre-Activities of Daily Life (ADL) test, the thirty-second, and one-minute sit-to-stand tests, and the step tests. Based on the lesser implication of upper or lower muscle function, these tests were not included in this paper. Recent literature reviews^{49,50} detailed standardized assessments, psychometric properties, and main advantages and limitations of upper- and lower-extremity functional tests commonly used to assess functional performance in COPD. In Table 2, major characteristics of functional tests in COPD that seem to rely more heavily on muscle strength, power or endurance are presented. Interestingly, the SCPT, Short Physical Performance Battery (SPPB), usual gait speed test, and the Timed-Up and Go tests were all recommended to assess physical functional performance by the European Working Group on Sarcopenia in Older People⁵³ in the sarcopenia diagnosis process. Their definition and diagnosis of sarcopenia rely on impaired muscle strength or physical functional performance (or both in severe conditions), combined with impaired muscle mass,⁵³ a clinical syndrome prevalent in people with COPD (14.5% [95% CI 11.8%–17.4%]).⁵⁴

However, one should keep in mind that functional tests and muscle function assessments evaluate different constructs (as shown by the low to moderate strengths of their correlations and often lack studies looking at correlations between the proper required muscle aspect and the functional test) and thus cannot replace one another.^{42,49,50} For example, impaired skeletal muscle strength could indicate a potential difficulty to stand from a chair without using one's arms and could thus hint a professional toward administering a five-repetition-sit-to-stand test to that patient. However, less is known about functional tests' ability to detect muscle dysfunction in patients with COPD and their use in prescribing and individualizing muscle resistance training for these patients.⁵⁰ Further

Table 2 Main characteristics of physical function tests in COPD and their associations with skeletal muscle function

Tests	UULEX	SCPT	SPPB	TUG	4MGS	5STS
Brief description	Seated patient must lift a weighted plastic bar (0.2–2 kg) through 8 levels at a 30-bpm cadence, with 0.5 kg weight increases when the upper level is reached and after every minute of the test	Patient must ascend as fast and safely as possible a 10-step flight of stairs.	Patient must complete three separate tasks: balance for 10 s in three static positions, gait speed over the 4-m track and five-repetition sit-to-stand task	When instructed to start, the patient stands from a chair, walks 3 m, turns around, walks back to the chair and sits down	Patient walk over a 4-m course at his or her usual speed	Arms across the chest, the patient must fully stand from a chair five times
Outcome(s)	Time to exhaustion (s)	Stair climb time in seconds; velocity: distance (total vertical height of stairs)/time (s); power calculates by velocity times force (body mass times acceleration due to gravity) in Watt	Each task is scored from 0 (unable/ unsafe) to 4 (best performance) points, for a total ordinal score out of 12	Fastest time of two trials at the patient's usual speed (s)	Fastest time of two trials at the patient's usual speed (s)	Time to complete five repetitions (s)
Aspect of muscle function	Dynamic upper limb shoulder muscles flexion endurance	Dynamic lower limb muscles power	Dynamic lower limb muscles strength and power	Dynamic lower limb muscles strength and power	Dynamic lower limb muscles strength	Dynamic lower limb muscles strength and power
Correlation with skeletal muscle function*	To isometric shoulder muscle strength: $r=0.56$ To isokinetic shoulder muscle endurance: $r=0.50$	To eccentric quadriceps peak torque: $r=0.53-0.72^{2,73}$ To isometric quadriceps power (RTD): $r=0.727^{73}$ To double leg press power at 40% of 1RM: $r=0.47^{74}$	To isometric quadriceps strength: $r=0.49$, ⁷⁵ $r=0.27$ and isometric quadriceps endurance: $r=0.07^{27}$ To dynamic average quadriceps power: $r=0.46$ isokinetic strength: $r=0.49$, isokinetic endurance: $r=0.48$, and isotonic endurance: $r=0.46^{27}$	To eccentric quadriceps strength: $r=0.90$; To isometric quadriceps power (RTD): $r=-0.69^{73}$	In a multivariable linear regression model: 2.4% of 4MGS variance explained by quadriceps strength ⁵² To isometric quadriceps strength: $r=-0.31^{28}$	To isometric quadriceps strength: $r=-0.33^{76}$ To dynamic average quadriceps power: $r=-0.32$ to -0.38^{28}

(Continued)

Table 2 (Continued).

Tests	UULEX	SCPT	SPPB	TUG	4MGS	5STS
Reliability/ responsiveness in COPD	Test-retest reliability: ICC=0.98 ⁷⁷ Responsive to change after 1) upper limb muscle strength training (SRM 1.8) 2) endurance training (MGD 127 s, effect size 1.46) ⁷⁸	Test-retest reliability: ICC=0.90 ²²	Interobserver reliability ⁷⁹ Total score ICC=0.82 SPPB subscores 1) balance ICC=0.33; 2) gait speed ICC=0.75; 3) STS ICC=0.84	Within-day test-retest reliability: ICC among 3 trials: 0.94 with a possible learning effect between first and second trials ⁸⁰ Intra-/interrater reliability: ICC=0.99 and 0.92 respectively ⁸¹	Test-retest reliability: ICC=0.97 Interobserver reliability: ICC=0.99 ⁸² Responsiveness to PR: 0.08 m/s; effect size 0.4 ⁸³	Test-retest reliability: ICC=0.97 Interobserver reliability: ICC=0.99 ⁷⁶ Responsiveness to PR: ≥-1.7s
Reference values	Unavailable	Unavailable	Available for adults >70 years old ⁸⁴	Available	Available ⁸⁵	Available ⁸⁶

Notes: *Significant correlations for SCPT and TUG with other aspects of muscle function (concentric peak torque, isometric strength, etc.) are also available in Butcher et al.⁷³ Different protocols for muscle strength/power/endurance assessments were used in the cited studies.

Abbreviations: 1RM, one-repetition maximum; 4MGS, 4-meter gait speed; 5STS, five-repetition sit-to-stand; ICC, intraclass correlation coefficient; MGD, mean group difference; PR, pulmonary rehabilitation; RTD, rate of torque development; SCPT, Stair Climb Power Test; SPPB, Short Physical Performance Battery; SRM, standardized response mean; UULEX, Unsupported Upper Limb Exercise Test.

studies investigating these links and muscle training specifically designed according to the impaired skeletal muscle parameter (strength, endurance, fatigability or power) required for specific functional activities are necessary.

New perspectives Measuring and monitoring skeletal muscle power

An aspect of skeletal muscle function that, to date, has received less attention among people with COPD is muscle power, defined as the ability to generate an increase in contractile force over a certain unit of time (product of force and velocity).⁵⁵ Interestingly, this aspect of skeletal muscle function declines faster with aging than muscle strength does.⁵⁶ The decline in skeletal muscle power may be linked to various age-related neuromuscular changes, including but not limited to loss of size of fast-twitch muscle fibers, a reduction in the number of spinal motor neurons and excitable motor units, as well as a decrease in muscle fiber contraction time.⁵⁷ In COPD, leg muscle power has been found to be reduced with approximately 28% compared to healthy age, sex and body mass matched adults when estimated using the functional SCPT.²² However, even though these findings suggest that leg muscle power is possibly impaired in people with COPD, formal assessments of leg muscle power using more mechanistic measures of muscle power are needed to confirm these results. Various protocols could be used, eg, measuring peak velocity during isotonic contractions, the rate of torque development (RTD) from isometric contractions,⁵⁸ or peak/average power during dynamic isokinetic and isotonic contractions.⁵⁹

Even though not yet used to determine the presence of a possibly reduced skeletal muscle power in COPD, these measurement techniques have been found to be more strongly associated with physical capacity and mobility, such as walking distance, gait speed and balance, than muscle strength in people with COPD and older adults.⁵⁹⁻⁶¹ Indeed, Hernandez et al⁶⁰ found that dynamic muscle power at 50% 1RM in COPD was positively correlated with objectively measured light-intensity physical activity, while they found no associations with skeletal muscle strength. Thus, measuring dynamic skeletal muscle power in people with COPD may provide important clinical value. Recently, data from our laboratory (unpublished) indicate high to very high relative reliability (ICC 0.78-0.99) for dynamic power measurements in people with COPD

while static RTD measurements demonstrated moderate to very high relative reliability (ICC 0.63–0.86). Measures of absolute reliability (SEM%) was <10% for dynamic techniques while >30% for RTD. Furthermore, all participants were able to perform the test and no adverse events were reported, thus indicating that the procedure used for assessing muscle power seems to be safe. Even though detailed information regarding muscle power deficits in people with COPD is not yet available, the closer link between dynamic muscle power and physical capacity⁶⁰ and with daily life physical activity than muscle strength⁶⁰ highlights a need to explore this aspect of skeletal muscle function more thoroughly.

Dynamic versus static measurements and specificity of measurement techniques

As highlighted previously, isometric measurements of quadriceps strength using strain gauges are recommended when measuring skeletal muscle function in people with COPD.¹ However, the best measurement strategy is the one that fits the goal of the measurement.²⁶ Thus, even though isometric measurements have shown to provide important prognostic information, this does not denote that isometric measurements should always be favored. For example, if the goal of the measurement is to provide information on factors associated with functional tasks, such as walking or standing up from a chair, recent studies have actually highlighted that dynamic measurements seem to be superior, independent of whether the strength or the endurance capacity of the skeletal muscle is targeted. Indeed, Géphine et al²⁷ found closer relationships between dynamic than isometric measurements of quadriceps muscle strength and endurance and common functional tests such as the 6-min walk test, the one-minute sit-to-stand test, the Glittre-ADL test as well as the SPPB test. With regard to the latter, similar findings were seen by Bui et al²⁸ when exploring the relationship between isometric and dynamic measurements of quadriceps muscle strength and the SPPB. If we considered that activities such as walking or standing from sitting require skeletal muscles to work over a dynamic range of motion at the joint in a similar way as during dynamic measurements, rather than at a specific joint angle (which is the case during isometric measurements⁶²), these findings seem reasonable.

Furthermore, even though isometric, isokinetic, as well as isometric measurements have been reported to be responsive to exercise training,^{38,63,64} the magnitude of effect seems to differ between techniques.⁶³ For example,

in a systematic review by De Brandt et al,⁶³ percentage changes in isokinetic quadriceps endurance following different exercise interventions were on average 16%, while corresponding numbers for isometric and isotonic measurement strategies were 42% and 67%, respectively. One important explanatory factor for these observed differences could be related to the specificity of the exercise technique or equipment used with the exercise(s) performed, a concept that has been referred to as mechanical specificity.⁶⁵ To our knowledge, this was first exemplified in 1990 in a study by Boyer et al⁶⁶ in which participants exercised similar muscle groups with similar exercise setups but with different exercise equipment (either free weights or weight machines). After the intervention period, the free-weight group showed significantly greater strength gains than the weight machine group when tested using free weights (20.8% vs 12.3%). In the opposite way, the weight machine group showed significantly greater strength gains than the free weight group when tested using weight machines (40.7% vs 19.9%). If this is applied in the studies involved in the review by de Brandt et al,⁶³ it could be noted that neither of the studies that evaluated quadriceps muscle endurance using isokinetic measurement techniques performed training exercises using isokinetic equipment while all studies that evaluated quadriceps endurance using an isotonic measurement technique also included isotonic exercises. Similar findings were seen by our research group, in which larger increases in elastic knee extension endurance than isokinetic knee extension endurance (37% vs 11%) were seen after 8 weeks of elastic band resistance training (unpublished data). Even though these findings need further investigation, they suggest that the choice of measurement technique and equipment should mirror what was or will be used during training.

Indirect measurements of muscle function

In addition to direct measurements of skeletal muscle function using dynamic or static measurements, indirect measurements of skeletal muscle function, eg, with the addition of motion sensors or electromyography may provide additional and clinically relevant information. For example, Ehsani et al⁶⁷ found that by adding low-cost wearable motion sensors to a dynamic elbow flexion/extension test, in addition to the number of repetitions, they could also record speed, range of motion, speed reduction and speed variability. From these results, they produced a “frailty score” for the inpatients that was better

than the number of repetitions alone or other measurements such as the COPD assessment test scores to predict both all-cause 30-day readmission and unfavorable discharge disposition following exacerbations. In another study with outpatients, the same test scores were also strongly correlated to clinical measurements such as the six-minute walk test and lung function parameters.⁶⁸ Furthermore, Boccia et al⁶⁹ used multichannel surface electromyography to measure muscle fiber conduction velocity during an isometric knee extension endurance test, providing useful insight into muscle fatigability and muscle abnormalities in COPD. Additionally, multichannel surface electromyography has also shown to be moderately to very strongly correlated to lung function measurements, six-minute walk distance as well as direct measurements of quadriceps endurance (time to exhaustion).⁷⁰ However, to our knowledge, research on the topic of using, for example, motion sensors or electromyography as an “add-on” to direct measurements of muscle function in COPD is relatively sparse and more research is necessary. For example, we need to determine the clinical feasibility, reliability and the responsiveness of the test procedures and further investigate the potential additional benefit of using these measurement techniques on different muscles and muscle groups.

Measurement of skeletal muscle function – how to become a reality in the clinical setting?

Despite the prognostic and clinical relevance of skeletal muscle function in people with COPD,^{4–7} measurements and monitoring of skeletal muscle function remain to be an integrated part of the routine assessment and management of COPD. In order to facilitate the implementation of skeletal muscle function measurements into the clinical arena, we believe that are some key aspects that need to be considered.

Development of clinically feasible and standardized measurement protocols

First of all, clinically feasible and standardized measurement protocols that are valid, reliable and responsive are needed. With regard to the standardization of measurement properties, some key aspects that should be considered when measuring or monitoring skeletal muscle function have been outlined (Table 1). Furthermore, in order to increase clinical feasibility, measurement protocols need to minimize time consumption and include equipment that are widely available across different clinical context. With regard to the latter, the

use of functional tests is intriguing. However, as highlighted previously, the often modest relationships between functional tests and skeletal muscle function measurements indicate that they evaluate different constructs and thus cannot replace one another. Thus, for accurate assessments of skeletal muscle function, specific and formal assessments of muscle function should be prioritized. Furthermore, and of utmost importance, the validity and reliability of measurement techniques need to be established in the targeted population in order to ensure accurate and reproducible measurements. About the latter, the add-on of, for example, motion sensors may be one way to accurately estimate both range of motion and speed of motion during dynamic measurements of skeletal muscle function, which is crucial to maximize the reliability of measurements for the individual patient. Lastly, in order to identify changes in skeletal muscle function following a clinical intervention that is meaningful for the patient, the minimal clinically important difference of different aspects of skeletal muscle function needs to be established.

Predictive equations and normative values

Secondly, equations to predict normative values that are widely applicable have to be developed, and normative values that will be obtained from these predictive equations have to be validated in the population of interest. To date, predictive equations and normative values are available for some aspects of skeletal muscle function, eg, isometric quadriceps strength.^{3,5,71} However, to our knowledge, no equation has been widely accepted within the pulmonary community. This is an issue because if used, large variations are seen between available equations. For example, if utilized on a random sample of isometric knee extension strength data from our laboratory, the percentage of patients with an isometric knee extension strength <70% of predicted would be 10%,⁵ 22%³ and 76%,⁷¹ respectively, using available equations. In addition, the predictive ability of the best equation explained 51% of the variance in actual isometric knee extension strength.³ This can be compared with the best predictive equations for the 6-min walk test that explained 77% of the total variance in walking distance.⁷² Furthermore, to our knowledge, no predictive equations or normal values exist for other aspects of skeletal muscle function, for eg, endurance or power at least not that has been validated among people with COPD.

Conclusion

Considering the complexity of skeletal muscle dysfunction in COPD,¹ no single test could be used to measure and monitor skeletal muscle function within the COPD

population. Nevertheless, due to its clinical and prognostic value, measuring and monitoring skeletal muscle function should be a part of the routine assessment of people with COPD, even though this is yet to become a clinical reality. In order to achieve this goal, standardized and clinically feasible measurement protocols, as well as normative values and predictive equations across the spectrum of impaired function in COPD, are needed. This should minimally target the quadriceps muscle; however, depending on the objective of measurements, other muscles could also be tested in order to aid design and individualization of exercise programs or to evaluate effects of various interventions.⁸ Even though quadriceps muscle strength measurements are of utmost importance, current evidence suggests that other aspects of skeletal muscle function such as the endurance and power capacity of the muscle should also be considered. Moreover, current evidence also suggest that even though isometric measurements have been recommended, dynamic measurements of skeletal muscle function should not be neglected as they, in a larger extent than isometric measurements, are related to functional daily life tasks in patients with COPD.

Disclosure

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