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Abstract

Disability in chronic respiratory diseases (CRD) represents the impact of the disease on the patient's life. Chronic airway diseases, included but not limited to COPD, are leading this burden.

Overall, the mobility-related dyspnea and the resulting decrease in exercise capacity substantially contribute to increased risk of disability, even after taking lung function impairment into account. Therefore, non-pharmacological interventions such as pulmonary rehabilitation (PR) might be particularly beneficial for these symptomatic patients to limit and to counteract the progressive loss of physical function and related problems.

In this chapter we will discuss the most recent evidence related to the assessment of individual's disability in this population, and we will describe the variety of methods used in the clinical process of care called PR.

To date, PR results in substantial effectiveness when applied at the very early onset of disability in individuals suffering from CRD. Programme composition and strategies aimed at behavioural changes in the long-term appear the keys for success in the clinical practice.

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11.1 Disability in Chronic Respiratory Disease

11.1.1 The Vicious Cycle of Dyspnea

Disability in chronic respiratory diseases (CRD) is a significant health burden with relevant implications both for the individual patient and the society: indeed, it represents the real impact of the disease on the patient's life, with an important influence on the society overall work productivity [1]. Chronic obstructive pulmonary disease (COPD), among these, accounts for one of the top five causes of disability all over the world. Although respiratory impairment contributes to and increases the risk of disability, the presence of limitations of the individual's general function and the occurrence of non-respiratory symptoms with the presence of comorbid extra-pulmonary conditions have a great impact on disablement as well. Table 11.1 shows some of the conditions that may cause or aggravate dyspnea in individuals with CRD. The mobility-related dyspnea and the resulting decrease in exercise capacity substantially contribute to increased risk of disability, even after taking lung function impairment into account [2]. Therefore, the assessment and treatment of airway obstruction, as for patients with COPD, are not sufficient to prevent and care for the development of individual's disability.

11.1.2 Peripheral Muscle Weakness as the Hallmark of Disease

Limb muscle dysfunction, defined as the reduction of either strength or endurance (or both) [3], is frequent in patients with CRD [2], and in particular in COPD, with muscle fibre shift, atrophy and changes in capillarization that are commonly seen in their peripheral muscles [4, 5].

Although the extent of muscle atrophy and weakness is greater in advanced disease, it is important to recognize that muscle dysfunction may even occur at an early stage [5, 6]. For instance, symptomatic COPD patients referred to and entering a

Table 11.1 Causes of dyspnea in patients with chronic respiratory disease

Increased resistive work of breathing from airflow limitation
Increased elastic work of breathing and "pseudo-restriction" from static and dynamic hyperinflation
Physical and cardiovascular deconditioning from sedentary
Gas exchange abnormalities: hypoxemia and increased physiologic dead space
Cardiovascular limitations: cardiac or peripheral vascular co-morbidity, leading to early lactate production with exercise
Skeletal muscle abnormalities: decreased mass, fibre-type alterations (reduction in type I, increase in type IIx), capillarization defect, decreased oxidative enzymes, also leading to early lactate production with exercise
Coexisting obesity, increasing workload requirements for a specific task
Anxiety associated with dyspnea-producing activity

rehabilitation programme have already lost about 30% of their muscle mass and strength [7].

The prevalence of peripheral muscle weakness varies (from 20 to 40%) among patients, with a typical interindividual heterogeneity, but increases with the severity of the respiratory condition.

Furthermore, peripheral muscle weakness is not equally distributed among muscle groups: compared to the lower limbs, the strength of the upper limb muscles (although reduced) seems better preserved, especially in COPD [8], probably reflecting the heterogeneous distribution of muscle structural abnormalities. The annual rate decline in quadriceps strength in patients with COPD is 4.3% per year [9], in comparison with 1–2% per year in the elderly people. Although quadriceps muscles represent a typical example of a primary locomotor muscle that is underused in symptomatic patients who become sedentary, upper limb muscle function is also affected, as shown by a reduced handgrip strength during acute care [10].

Thus, muscle strength/weakness represents a clinical hallmark of several CRD and drives both individual's physical activity and functional capacity [11–13]. Weakness, in particular, has been associated with relevant negative outcomes such as dyspnea burden, exercise intolerance [14], morbidity, mortality [15, 16] and poor quality of life [9].

11.2 Assessment of Individual's Disability

11.2.1 Muscle Function

The assessment of muscle function (strength and endurance) is muscle group specific. It also varies depending on the measurement technique (isokinetic, isometric or isotonic) and the device used, which must be chosen based on their advantages and limits as well as on the desired information [16]. Some of the daily life activities rely on of the isometric contraction (e.g. carrying grocery bags, standing up from and sitting down on a chair, pushing and pulling). However, most of the functional activities of daily living may be better assessed by dynamic techniques, i.e. isokinetic (fixed speed of movement) and isotonic (fixed resistance applied to the muscle during the movement), which provide information on limb muscle function throughout the full range of motion at different speeds. Table 11.2 shows an overview of the methods used for assessing muscle function, as valid in COPD.

Muscle atrophy is another common manifestation of CRD and in COPD in particular. Atrophy can be included under the umbrella term of muscle dysfunction since the loss of muscle mass may have important implications on strength [7, 14, 17] and exercise tolerance [18–20]. Muscle atrophy is the main cause of weight loss in COPD patients [18] independently on the degree of airway obstruction [21], and it is a predictor of health status [22] and survival [23].

Several techniques are available to assess the mass of peripheral muscles [4]: anthropometry (mid-arm muscle circumference), bioelectric impedance analysis (BIA), dual-energy X-ray absorptiometry (DXA) as well as more advanced imaging

Table 11.2 Methods used to assess muscle function in patients with COPD

Measuring equipment	1. Strain-gauge or hand-held systems	2. Computerized dynamometers	3. Repetition maximum	4. Handgrip gauges	5. Non-volitional (electrical or magnetic nerve stimulation)
Type of contraction	Isometric	Isometric and isokinetic	Isotonic	Isometric	Isometric
Positioning of tested limbs in COPD studies [85–87]	Knee and hip flexed at 90°, elbow and/or shoulder flexed at 90°	<i>Isometric:</i> Elbow flexed at 90° knee flexed 60°–120°. <i>Isokinetic:</i> Knee flexed at 90° to full knee extension	Not well described in COPD studies	Elbow flexed at 90° with arm unsupported	Knee and hip flexed at 90°
Measurements of muscle strength in COPD studies [85, 88]	Perform 3 MVC, each lasting 3 to 5 s with at least 30-s rest between attempts. Highest value used as measurement of strength	Perform 3–5 MVC (<i>isometric: hold each contraction for 3 s</i>) and 1–2-min rest between attempts. Highest value used as measurement of strength	Not well described in COPD studies. Follow ACSM recommendations + use metronome and control start and stop positions	Perform 3 MVC with each lasting at least 3 s and 30-s rest between attempts. Highest value used as measurement of strength	Three stimulations at 100% stimulator output in a relaxed muscle. Highest value used as measurement of strength
Measurements of muscle endurance in COPD studies [87, 89–91]	Measure the time during which a contraction at 60–80% of MVC can be maintained in one set (only performed using strain gauges in COPD studies)	<i>Isometric:</i> Has not previously been used in COPD. <i>Isokinetic:</i> Measure the total amount of work performed from 1 set of 30 MVC at 60° or 90°/s	Number of repetitions performed. One set of dynamic contractions at 30–40% of MVC until exhaustion. Contraction cycle of 6–12 contractions	Has not previously been done in COPD. Strain-gauge procedure might be feasible	One set of repeated magnetic stimulations using a train of impulses at 20–30% of MVC until a 70–80% reduction in force is seen

<p>Advantages [88, 92–95]</p>	<p>Results are valid, reliable and reproducible. Easy to use, portable, time efficient and inexpensive</p>	<p>Results are valid, reliable and reproducible. Easy to standardize. Different speeds and angles could be tested</p>	<p>Assesses muscle function in the whole range of motion. Can be executed using available equipment</p>	<p>No familiarization, easy to use, easy to standardize</p>	<p>Less affected by external factors. Lower day-to-day variability than assessments of MVC</p>
<p>Limitations [85, 96–98]</p>	<p>Measures only in one angle. Standardization is crucial for validity and reliability</p>	<p>Low availability. Requires expensive equipment. Needs familiarization session</p>	<p>Time-consuming and more difficult to standardize than isometric measurements</p>	<p>Measures only handgrip strength</p>	<p>More in the realm of research. Requires expensive equipment</p>

technologies like computed tomography (CT) and nuclear magnetic resonance (NMR). Two common methods to estimate muscle mass in clinical practice are BIA and DXA. BIA is a valid, non-invasive, inexpensive, quick and easy to perform technique that, like DXA, requires no active collaboration from the patient. Like most body composition methods (included DXA), BIA does not directly measure muscle mass but provides indirect estimates of fat-free mass (as a proxy of muscle mass) from the measurement of resistance of body tissues to an electric current passing through the body. Alternatively, directly measured raw BIA variables, such as phase angle, have been demonstrated to relate to muscle function, disease severity and prognosis in COPD patients better than fat-free mass estimates [24–27]. DXA is another valid, reliable, safe and non-invasive technique for assessment of muscle mass. It is based on the comparison of X-ray attenuations of two different energies measuring body composition with a higher degree of accuracy [28]. It is however more expensive and often less easily accessible than BIA in clinical settings [25].

11.2.2 Symptoms

As part of a comprehensive assessment of individual disability, quantifying symptoms (dyspnea and fatigue) through specific tools is crucial in order to describe the level of chronic disability and to retest changes following interventions (i.e. rehabilitation). Currently, a number of scales are available to classify symptoms, but the most widely used ones are the Modified British Medical Research Council (mMRC) and the Borg scale. The former is a simple measure of breathlessness, as the person perceives it. It ranges from 0 (“I only get breathless with strenuous exercise”) to 4 (“I am too breathless to leave the house, or I am breathless when dressing”), and it is considered adequate for assessment of symptoms since it correlates well with health status [29] and mortality risk [30]. The latter measures the perception of symptoms (dyspnea or fatigue) during physical activity [31].

In addition to these “categorical”, different scales (e.g. visual analogue scale, VAS) where the determination of the severity of dyspnea is of an analogical type can be used [32]. Finally, as part of the individual’s overall health status, symptoms can be measured by generic or disease-specific questionnaires, such as the Chronic Respiratory Questionnaire (CRQ), the St. George Respiratory Questionnaire (SGRQ), the COPD Assessment Test (CAT) and the COPD Control Questionnaire (CCQ).

11.2.3 Exercise Capacity

Assessment of exercise capacity in patients with CRD can be obtained with a number of different methods that essentially can be divided into *field* or *laboratory* tests [33].

Field tests, such as the timed walk tests, are the most popular ones, because they are easy to perform and related to the individual’s daily functional activities. On the

other hand, they are performed at submaximal capacity and are not able to provide physiologic information about those complex mechanisms that may limit exercise on an individual basis.

Laboratory tests to physiologically assess the cardiopulmonary adaptation to exercise include the incremental (iCPET) and constant (cCPET) work rate cardiopulmonary exercise tests [34].

Cardiopulmonary exercise testing (CPET)—CPET represents the gold standard for exercise performance assessment [34]. Indeed, continuous displacement of cardiovascular, respiratory and haematological parameters as well as the individual's perception (symptoms) during exercise provides information about the physiological reserve, systems' interaction and mechanisms of limitation to exercise. In particular, the typical iCPET provides continuous data on the ventilatory adaptation (e.g. tidal volume (VT) and minute ventilation (VE)), respiratory gas exchange (e.g. oxygen saturation (SatO₂), oxygen uptake (VO₂) and carbon dioxide output (VCO₂)), cardiovascular response (e.g. cardiac frequency (HR), blood pressure (BP) and cardiac rhythm) and symptom response (e.g. perceived dyspnea and/or leg fatigue reported by a numeric or visual analogue scale). Given these characteristics, CPET enables accurate determination of the physiologic reserves of the heart and lungs as well as functional capacity [35, 36], and it is a test therefore used both to assess the individual's normality and to look for cardiopulmonary limitations. Notwithstanding, although its use is becoming more widespread, CPET still remains largely underutilized in the general practice due to costs for the appropriate setting and apparatus, as well as for complexity and limited practicability in the more severe diseases. An example of CPET laboratory setting is shown in Fig. 11.1.

Submaximal field tests and physical functioning—Standard submaximal exercise tests to estimate maximal oxygen uptake (as described in the *American College of Sports Medicine's Guidelines for Exercise Testing and Prescription*) [37] are based on the primary assumption that the maximal heart rate of the individual undergoing this test is similar to a predicted maximal heart rate based on a formula such as "220 minus age". Such formulae may be applied with caution to healthy individuals as long as one is aware of the significant interindividual variability (SD = 10–12 beats/min) of his/her maximal heart rate. However, many studies that measured maximal aerobic capacity of persons with a variety of medical conditions such as cardiovascular, metabolic, neurologic or neuromuscular disease found significantly lower maximal heart rates in these patient populations.

Compared with maximal exercise testing, submaximal exercise testing appears to have greater applicability to the "world" of healthcare practitioners (physicians, physical therapists, nurses) in their role as clinical exercise specialists. Therefore, these tests are usually the preferred choice for the majority of individuals suffering from CRD that are likely to be limited by dyspnea and/or fatigue or also present abnormal gait and impaired balance.

There are several submaximal tests validated for the clinical practice as described in Table 11.3.



Fig. 11.1 Example of a cardiopulmonary exercise testing in a laboratory setting

In the clinical practice, however, 6-min walk distance (6 MWD), shuttle walk (SW), timed up and go (TUG) and sit to stand (STS) are those more frequently used in patients suffering from CRD. Therefore, we briefly describe each of these four as follows:

- The *6 MWT* is the easiest test that requires a 100 ft. hallway. It measures the distance that a patient can quickly walk on a flat, hard surface in a period of 6 min (the 6 MWD) [38]. Before the test starts, the patient should sit at rest in a chair, located near the starting position, for at least 10 min. During this time, pulse and blood pressure will be measured, and patient's baseline dyspnea and overall fatigue will be recorded using the Borg scale [39]. Patient will be instructed to walk back and forth in the hallway for 6 min. At the end of the test, post-walk Borg dyspnea and fatigue levels will be recorded again.

Table 11.3 Submaximal exercise capacity assessment tests

Tests	Aims	Administration	Main outcomes	Advantages	Limitations
Constant-rate cardiopulmonary test	Endurance cardiorespiratory exercise capacity	Constant work rate proportional to peak exercise capacity (e.g. 60% of peak work rate), until exhaustion on treadmill or bicycle	Time until exhaustion cardiorespiratory function variables	Greater sensitivity to identify changes after intervention cardiorespiratory function diagnostic cardiovascular risk assessment	Requires a previous maximal test equipment and certified personnel-related costs
6-min walk test	Functional exercise capacity	Walking back and forth on a 30 m course self-paced speed	Total distance walked in 6 min	Reliability and validity low complexity and cost good correlation with activities of daily living	Does not provide cardiopulmonary diagnosis no detailed information on physiological variables ($\dot{V}O_2$, $\dot{V}E$) and exercise limitation mechanisms may require a previous familiarization test
Incremental shuttle walk test	Functional exercise capacity	Walking back and forth on a 10 m course with paced increments of walking speed, until inability to keep the pace	Total distance walked until exhaustion	Fast to prepare and perform good correlation with $\dot{V}O_2$ max in CPET low cost	Higher risk of cardiovascular events less widespread uses subject to patient motivation
Endurance shuttle walk test	Endurance functional exercise capacity	Walking back and forth on a 10 m course with fixed paced of walking speed, until inability to keep the pace	Time until exhaustion	Good correlation with CPET cardiorespiratory responsiveness low complexity and cost	Requires a previous incremental shuttle test same as incremental shuttle test

- The *SW* test is similar to the 6MWT, but it uses a series of audio signals to direct the walking pace [40, 41]. During this test, patients will be asked to walk between two cones spaced 10 m apart. Patients will start by walking at a very slow pace; this pace is set by a *beep*. Patients will walk around the 10 m course and will turn around a cone at the first beep and around the second cone at the next beep. The beeps will gradually get faster, which means patients will start to walk at a quicker pace, getting faster until he/she cannot keep up with the set pace, or until he/she is too tired or too breathless to continue.
- The *TUG* test is performed using a standard chair (height of the seat being 45 cm). Subjects are seated with their back supported against the chair. They are instructed to stand up, walk 3 m to a mark on the floor, cross the mark, turn around, walk back to the chair and sit down. The task needs to be performed at their normal comfortable pace. A stopwatch is started on the word “go” and stopped as the subject sit down; the time recorded in seconds represents the outcome value. Applicability and repeatability of this test in patients with COPD have been recently reported [42].
- The *STS* requires participants to stand up from and to sit down on a slightly padded armless chair as quickly as possible consecutively for five times. Patients fold their arms across their chests and are instructed to stand up completely while making firm contact when sitting. Timing count begins on the command “go” and ceases when the participants sit at the end of the fifth elevation up to the standing position. Subjects are allowed a practice trial of two repetitions before the recorded series of two consecutive trials of five repetitions. The faster of the two trials is then used for evaluation [43].

11.3 Rehabilitation as Process of Care

Pulmonary rehabilitation (PR) is defined as “a comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education, and behaviour change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviours” [44]. The two mainstays of PR are exercise training and education, followed by psychosocial support and nutritional counselling [44]. We briefly summarise in the following subparagraphs the main contents of each component in a structured programme of PR at which patients with CRD are commonly referred. Indeed, although literature developed around the impact of PR in the “COPD model”, other patients suffering from respiratory disorders including asthma, cystic fibrosis and bronchiectasis, interstitial lung diseases and neuromuscular disorders involving the respiratory system are likely to potentially benefit from a rehabilitation course [45].

11.3.1 Exercise Training

Exercise training is the cornerstone of effective PR and may include several activities, such as endurance exercise training, interval exercise training, walking exercise, Nordic walking [46, 47], resistance training, aquatic exercise, classroom callisthenics and Tai Chi [48]. Although it does not change pulmonary function, exercise training improves capacity and reduces dyspnea. In order to achieve clinically relevant results, training should be strictly supervised and performed properly and for appropriate duration and frequency. Table 11.4 shows the main body sites for application of training and modalities on how to deliver exercise targeted at therapy in respiratory patients.

High-intensity exercise is more commonly employed in PR. However, patients may not be able to sustain high intensities for long time. In these cases, adherence with high-intensity training schedules may be difficult. As an alternative, low-intensity training, such as classroom callisthenics, may occasionally be considered. Furthermore, training duration and intensities vary among patients [49, 50] depending on specific deficits and individual requirements. In parallel with exercise training, improved self-efficacy resulting from education, psychosocial support and nutritional counselling (in patients with nutritional abnormalities) may lead to better long-term adherence to the training prescriptions.

Aerobic training—Aerobic training is the key component of exercise training in patients with COPD, in particular [44]. It can be performed on a cycle ergometer and/or a stationary treadmill (most frequently) but also by means of stair climbing, stepping, free walking, Nordic walking and/or swimming. In order to optimize the performance of activities of daily living [51], upper limb aerobic training can also be prescribed. High-intensity endurance-based exercise (exercise tests >10 min) is

Table 11.4 Body sites and modalities on how to deliver exercise training along PR course

Body sites	Type	Intensity	Duration of the training	Length of the programme
Lower limbs	Endurance	70–90% of the max HR or VO ₂	20–45 min	3–5 times/week up to 8 weeks
	Strength	50–80% fraction of max weight lifted	8–10 rep up to 3 series	3 times/week up to 8 weeks
Upper limbs	Endurance	70–90% of the max HR or VO ₂	20–45 min	3–5 times/week up to 8 weeks
	Strength	50–80% fraction of max weight lifted	8–10 rep up to 3 series	3 times/week up to 8 weeks
Respiratory muscles	Strength	15–60% of MIP or MEP	1 h	3–6 times/week up to 3 months

HR heart rate, VO₂ oxygen uptake, MIP maximal inspiratory pressure, MEP maximal expiratory pressure

the main aerobic training method. Specifically, high-intensity interval training appears to be practicable even in patients with a severe respiratory disease, resulting in similar improvements of 6-min walking distance and health-related quality of life compared to traditional endurance training [52–54].

Resistance training—Resistance training is based on repetitive lifting of relatively high loads. Compared to aerobic training, resistance training produces lower cardiorespiratory responses and less dyspnea, which is highly desirable in patients with more severe CRD [55]. One to 3 sets of 812 repetitions should be performed on 2 to 3 days per week in order to reach the best results in terms of muscle strength [56]. The main results of an adequate (60–70% of one-repetition maximum [57]) high-intensity resistance training are the increased muscle mass and muscle strength, paralleled by an increased submaximal exercise tolerance [58].

Combined training and additional means of increasing exercise capacity—If on one hand aerobic training improves skeletal muscle strength and resistance training improves aerobic exercise tolerance, evidences suggest that the best results are reached by combining aerobic and resistance training together [59] and by challenging both the cardiorespiratory fitness and the muscular strength capacity.

Recent research has focused on interventions that can be used as an adjunct to exercise training in PR, especially in patients with more severe CRD and disabling breathlessness. Among these interventions, the use of supplemental oxygen and ventilator support during training was tested in COPD patients and resulted in greater improvement of exercise tolerance [60] and dyspnea [61, 62]. Probably these improvements are related to the reduction in the high inspiratory muscle load secondary to the effects of hyperinflation. Furthermore, a recent paper studied the effects of helium and oxygen (Heliox) mixtures on exercise capacity in severe COPD [63]. The rationale of using Heliox to reduce breathlessness is based on the principle that nitrogen in inspired air is substituted with helium at a lower density, which reduces resistance in the airway, improving ventilation and gas exchange.

11.3.2 Education

Education is another key component of pulmonary rehabilitation. It has gradually evolved from a didactic approach to the promotion of behaviour changes and collaborative self-management [64]. Examples of positive behaviour changes include higher adherence to medication, increased physical activity, better nutritional habits, breathing regulation techniques and applying energy-saving strategies during activities of daily living [65]. These strategies promote the self-efficacy in managing health through increasing the patients' knowledge and stimulating patients to participate with healthcare professionals in better managing their illness [66]. In Table 11.5, the main topics concerning educational component of pulmonary rehabilitation are displayed.

Table 11.5 Educational component of pulmonary rehabilitation: topics

- Normal pulmonary anatomy and physiology.
- Pathophysiology of chronic respiratory disease.
- Communicating with the healthcare provider.
- Interpretation of medical testing.
- Breathing strategies.
- Secretion clearance techniques.
- Role and rationale for medications, including oxygen therapy.
- Effective use of respiratory devices.
- Benefits of exercise and physical activities.
- Energy conservation during activities of daily living.
- Healthy food intake
- Irritant avoidance.
- Early recognition and treatment of exacerbations.
- Leisure activities.
- Coping with chronic lung disease.

11.3.3 Psychological Support

Together with education, psychological support is an integral part of PR programmes. Indeed, the incidence of depression in patients with CRD is more than twice higher compared with the general population [67]. PR programmes including psychological interventions improve the mood disorders more than those consisting of exercise training only [68]. Psychological support may be of benefit to those patients presenting with symptoms of anxiety and depression, helping them to better understand the psychological modifications that may occur in CRD [69, 70] and to encourage active participation in healthcare. Furthermore, psychologists are the best healthcare providers who can also discuss smoking cessation strategies within the course of PR and with the goal to optimise benefits.

Supervised exercise combined with stress management education and psychotherapy in PR may offer management strategies for patients with anxiety and depression [71] and may induce reduction in dyspnea sensation [72], probably due to the social interaction and distraction from negative perceptions that occur during exercise within a group of patients who have the same condition.

11.3.4 Nutritional Counselling

Nutritional counselling has a pivotal role in the PR programme for people with CRD and consists of teaching patients about how to plan and follow a healthy diet. Indeed, weight loss and body composition abnormalities are prevalent in CRD and can indirectly affect disease severity and prognosis (hospitalization and mortality) [73]. Furthermore, being undernourished in COPD is likely to be associated with longer in-patient hospital stays [74], a higher risk of being readmitted [75] and an increase

in healthcare utilisation [76] in comparison with normally nourished individuals. Patients who are overweight will get advice about planning a diet that will help them to lose weight; underweight patients will receive advice about foods that can help them to gain weight. However, more cost-effectiveness studies about nutritional counselling and supplementation are still needed to support decision-making and to tackle with organisational problems, such as dealing with reimbursement for these interventions in CRD.

11.3.5 Tips and Pitfalls

Timing—Although most PR programmes enrol patients with moderate to severe CRD [77], recent studies suggest that patients with less severe degree of airflow limitation also benefit from PR programmes in terms of several outcomes. In fact, low physical activity, problems during the activities of daily living, exertional dyspnea, lower limb muscle weakness, osteoporosis, anxiety and depression may also occur in mild to moderate disease [5, 44]. Furthermore, by improving exercise tolerance and body composition and promoting self-efficacy and behaviour change, PR at an earlier stage of disease has the potential to significantly modify the course of the illness. Hence, irrespective of the degree of lung function impairment, the correct timing of PR should be rather set on the individual's clinical status and disability [44]. Therefore, early intervention and physiotherapy following clinical deterioration and/or at the very early onset of symptoms may provide substantial benefit even in these patients.

Maintenance of benefits—Without any maintenance strategy, benefits of PR tend to diminish over 6–12 months with particular regard to the physical performance. This is probably due to a decrease in adherence to regular exercise [78, 79] as well as a worsening of main disease and the clinical impact of related comorbidities [80]. Studies have examined the effects of maintenance strategies (i.e. weekly or monthly follow-up session) after PR with equivocal results about improvements in exercise tolerance/capacity and health-related quality of life [81, 82]. On the other hand, behaviour change, incorporating self-efficacy and self-management techniques, seems to be the most effective strategy for optimization and long-term maintenance of any achieved health benefit [44].

Adherence to exercise and physical activity—Monthly phone calls accompanied by a formal home programme have been shown to encourage long-term adherence to exercise, not only leading to improved walked distance and perceived health-related quality of life but also reducing lung function decline, in patients with moderate COPD after a 3-week outpatient rehabilitation [82].

Qualitative data provide further opportunities for additional peer support in patients who have completed PR, through group activities with other individuals who have similar needs and experience, including drop-in centres and exercise classes [81]. This “voluntary and mutually supportive, people like us” approach may be a valid and important alternative to regular phone calls from staff and appointments with therapists and physicians.

11.4 Conclusions

Pulmonary rehabilitation is a recognized and effective clinical process providing specific benefits to symptomatic patients with CRD, in particular those suffering from COPD. It appears essential to recognize the most appropriate programme content and setting to be delivered on an individual basis following patient's selection and referral.

To date, it is important to recognize that this therapeutic but non-pharmacological approach results in substantial effectiveness when applied at the very early onset of disability following CRD, such as during acute exacerbation of the disease [83]. Behavioural changes (i.e. improvement in long-lasting physical activity, in particular) remains a true challenge to target in the whole population of patients with CRD with the final scope to prompt interventions and limit their disability which is more and more problematic with the increasing complexity of the underlying diseases.

Notwithstanding, other perspectives are still to come in the field of PR and should be subjected to special attention from both the professionals and the stakeholders involved. Indeed, despite the evidence, there is actual low applicability, access and homogeneity of programmes across different countries [84]. Furthermore, barriers for patients should be better focused and overcome; in this light, e-health and new technologies might be helpful to achieve this goal.

Key Points

- Disability represents the hallmark of the disease important to the patient's life and must be assessed in chronic respiratory diseases (CRD).
- The mobility-related dyspnea and the resulting decrease in exercise capacity substantially contribute to increased risk of disability.

Pulmonary rehabilitation (PR) is beneficial for these symptomatic patients to limit and to counteract the progressive loss of physical function.

References

1. Harber P. Respiratory disability: what is it, how can we measure it, what causes it and is it important? *Thorax*. 2009;64(4):280–2.
2. Eisner MD, Iribarren C, Blanc PD, Yelin EH, Ackerson L, Byl N, et al. Development of disability in chronic obstructive pulmonary disease: beyond lung function. *Thorax*. 2011;66(2):108–14.
3. Barreiro E, Gea J. Respiratory and limb muscle dysfunction in COPD. *COPD*. 2015;12(4):413–26.
4. Maltais F, Decramer M, Casaburi R, Barreiro E, Burelle Y, Debigare R, et al. An official American Thoracic Society/European Respiratory Society statement: update on limb muscle dysfunction in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2014;189(9):e15–62.

5. Seymour JM, Spruit MA, Hopkinson NS, Natanek SA, Man WD, Jackson A, et al. The prevalence of quadriceps weakness in COPD and the relationship with disease severity. *Eur Respir J*. 2010;36(1):81–8.
6. Shrikrishna D, Patel M, Tanner RJ, Seymour JM, Connolly BA, Puthuchery ZA, et al. Quadriceps wasting and physical inactivity in patients with COPD. *Eur Respir J*. 2012;40(5):1115–22.
7. Bernard S, LeBlanc P, Whittom F, Carrier G, Jobin J, Belleau R, et al. Peripheral muscle weakness in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 1998;158(2):629–34.
8. Gosselink R, Troosters T, Decramer M. Distribution of muscle weakness in patients with stable chronic obstructive pulmonary disease. *J Cardiopulm Rehabil*. 2000;20(6):353–60.
9. Hopkinson NS, Tennant RC, Dayer MJ, Swallow EB, Hansel TT, Moxham J, et al. A prospective study of decline in fat free mass and skeletal muscle strength in chronic obstructive pulmonary disease. *Respir Res*. 2007;8(1):25.
10. Spruit MA, Gosselink R, Troosters T, Kasran A, Gayan-Ramirez G, Bogaerts P, et al. Muscle force during an acute exacerbation in hospitalised patients with COPD and its relationship with CXCL8 and IGF-I. *Thorax*. 2003;58(9):752–6.
11. Osthoff AK, Taeymans J, Kool J, Marcar V, van Gestel AJ. Association between peripheral muscle strength and daily physical activity in patients with COPD: a systematic literature review and meta-analysis. *J Cardiopulm Rehabil Prev*. 2013;33(6):351–9.
12. Butcher SJ, Pikaluk BJ, Chura RL, Walkner MJ, Farthing JP, Marciniuk DD. Associations between isokinetic muscle strength, high-level functional performance, and physiological parameters in patients with chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis*. 2012;7:537–42.
13. Patel MS, Mohan D, Andersson YM, Baz M, Samantha Kon SC, Canavan JL, et al. Phenotypic characteristics associated with reduced short physical performance battery score in COPD. *Chest*. 2014;145(5):1016–24.
14. Gosselink R, Troosters T, Decramer M. Peripheral muscle weakness contributes to exercise limitation in COPD. *Am J Respir Crit Care Med*. 1996;153(3):976–80.
15. Swallow EB, Reyes D, Hopkinson NS, Man WD, Porcher R, Cetti EJ, et al. Quadriceps strength predicts mortality in patients with moderate to severe chronic obstructive pulmonary disease. *Thorax*. 2007;62(2):115–20.
16. Nyberg A, Saey D, Maltais F. Why and how limb muscle mass and function should be measured in patients with chronic obstructive pulmonary disease. *Ann Am Thorac Soc*. 2015;12(9):1269–77.
17. Engelen MP, Schols AM, Does JD, Wouters EF. Skeletal muscle weakness is associated with wasting of extremity fat-free mass but not with airflow obstruction in patients with chronic obstructive pulmonary disease. *Am J Clin Nutr*. 2000;71(3):733–8.
18. Schols AM, Soeters PB, Dingemans AM, Mostert R, Frantzen PJ, Wouters EF. Prevalence and characteristics of nutritional depletion in patients with stable COPD eligible for pulmonary rehabilitation. *Am Rev Respir Dis*. 1993;147(5):1151–6.
19. Baarends EM, Schols AM, Mostert R, Wouters EF. Peak exercise response in relation to tissue depletion in patients with chronic obstructive pulmonary disease. *Eur Respir J*. 1997;10(12):2807–13.
20. Kobayashi A, Yoneda T, Yoshikawa M, Ikuno M, Takenaka H, Fukuoka A, et al. The relation of fat-free mass to maximum exercise performance in patients with chronic obstructive pulmonary disease. *Lung*. 2000;178(2):119–27.
21. Schols AM, Mostert R, Soeters PB, Wouters EF. Body composition and exercise performance in patients with chronic obstructive pulmonary disease. *Thorax*. 1991;46(10):695–9.
22. Mostert R, Goris A, Weling-Scheepers C, Wouters EF, Schols AM. Tissue depletion and health related quality of life in patients with chronic obstructive pulmonary disease. *Respir Med*. 2000;94(9):859–67.
23. Marquis K, Debigare R, Lacasse Y, LeBlanc P, Jobin J, Carrier G, et al. Midthigh muscle cross-sectional area is a better predictor of mortality than body mass index in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2002;166(6):809–13.

24. de Blasio F, Santaniello MG, de Blasio F, Mazzarella G, Bianco A, Lionetti L, et al. Raw BIA variables are predictors of muscle strength in patients with chronic obstructive pulmonary disease. *Eur J Clin Nutr.* 2017;71(11):1336–40.
25. Maddocks M, Kon SS, Jones SE, Canavan JL, Nolan CM, Higginson IJ, et al. Bioelectrical impedance phase angle relates to function, disease severity and prognosis in stable chronic obstructive pulmonary disease. *Clin Nutr.* 2015;34(6):1245–50.
26. de Blasio F, Scalfi L, Alicante P, Miracco Berlingieri G, Bellofiore B, de Blasio F. Malnutrition and sarcopenia in chronic obstructive pulmonary disease according to the new ESPEN definition and EWGSOP criteria. *Eur Respir J.* 2017;50(Suppl 61):PA400.
27. de Blasio F, Scalfi L, Di Gregorio A, Miracco Berlingieri G, De Martino M, de Blasio F. Raw bioelectrical impedance variables are predictors of survival in chronic obstructive pulmonary disease. *Eur Respir J.* 2017;50(Suppl 61):PA1094.
28. St-Onge MP, Wang J, Shen W, Wang Z, Allison DB, Heshka S, et al. Dual-energy x-ray absorptiometry-measured lean soft tissue mass: differing relation to body cell mass across the adult life span. *J Gerontol A Biol Sci Med Sci.* 2004;59(8):796–800.
29. Bestall J, Paul E, Garrod R, Garnham R, Jones P, Wedzicha J. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax.* 1999;54(7):581–6.
30. Sundh J, Janson C, Lisspers K, Ställberg B, Montgomery S. Dyspnoea, obstruction, smoking and exacerbation (DOSE) index and mortality in COPD. *Eur Respir J.* 2011;38(Suppl 55):542S.
31. Borg G. Ratings of perceived exertion and heart rates during short-term cycle exercise and their use in a new cycling strength test. *Int J Sports Med.* 1982;3(3):153–8.
32. Aitken RC. Measurement of feelings using visual analogue scales. *Proc R Soc Med.* 1969;62(10):989–93.
33. Goldstein RE. In: Walker HK, Hall WD, Hurst JW, editors. *Clinical methods: The History P, and Laboratory Examinations.* 3rd ed. Boston: Butterworths; 1990. Chapter 8.
34. Palange P, Ward SA, Carlsen KH, Casaburi R, Gallagher CG, Gosselink R, et al. Recommendations on the use of exercise testing in clinical practice. *Eur Respir J.* 2007;29(1):185–209.
35. Weisman IM, Zeballos RJ. An integrated approach to the interpretation of cardiopulmonary exercise testing. *Clin Chest Med.* 1994;15(2):421–45.
36. Sue DY, Wasserman K. Impact of integrative cardiopulmonary exercise testing on clinical decision making. *Chest.* 1991;99(4):981–92.
37. Ferguson B. ACSM's guidelines for exercise testing and prescription 9th Ed. 2014. *J Can Chiropr Assoc.* 2014;58(3):328.
38. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med.* 2002;166(1):111–7.
39. Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc.* 1982;14(5):377–81.
40. Singh SJ, Morgan MD, Scott S, Walters D, Hardman AE. Development of a shuttle walking test of disability in patients with chronic airways obstruction. *Thorax.* 1992;47(12):1019–24.
41. Revill S, Morgan M, Singh S, Williams J, Hardman A. The endurance shuttle walk: a new field test for the assessment of endurance capacity in chronic obstructive pulmonary disease. *Thorax.* 1999;54(3):213–22.
42. Albarra AM, Gale NS, Enright S, Munnery MM, Cockcroft JR, Shale DJ. A simple and rapid test of physical performance in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis.* 2016;11:1785–91.
43. Bohannon RW, Bubela DJ, Magasi SR, Wang YC, Gershon RC. Sit-to-stand test: performance and determinants across the age-span. *Isokinet Exerc Sci.* 2010;18(4):235–40.
44. Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med.* 2013;188(8):e13–64.

45. Holland AE, Wadell K, Spruit MA. How to adapt the pulmonary rehabilitation programme to patients with chronic respiratory disease other than COPD. *Eur Respir Rev.* 2013;22:577–86.
46. Breyer MK, Breyer-Kohansal R, Funk GC, Dornhofer N, Spruit MA, Wouters EF, et al. Nordic walking improves daily physical activities in COPD: a randomised controlled trial. *Respir Res.* 2010;11:112.
47. Dolmage TE, Goldstein RS. Effects of one-legged exercise training of patients with COPD. *Chest.* 2008;133(2):370–6.
48. Andrianopoulos V, Klijn P, Franssen FM, Spruit MA. Exercise training in pulmonary rehabilitation. *Clin Chest Med.* 2014;35(2):313–22.
49. Normandin EA, McCusker C, Connors M, Vale F, Gerardi D, ZuWallack RL. An evaluation of two approaches to exercise conditioning in pulmonary rehabilitation. *Chest.* 2002;121(4):1085–91.
50. Casaburi R, Patessio A, Ioli F, Zanaboni S, Donner CF, Wasserman K. Reductions in exercise lactic acidosis and ventilation as a result of exercise training in patients with obstructive lung disease. *Am Rev Respir Dis.* 1991;143(1):9–18.
51. Janaudis-Ferreira T, Hill K, Goldstein R, Wadell K, Brooks D. Arm exercise training in patients with chronic obstructive pulmonary disease: a systematic review. *J Cardiopulm Rehabil Prev.* 2009;29(5):277–83.
52. Vogiatzis I, Nanas S, Roussos C. Interval training as an alternative modality to continuous exercise in patients with COPD. *Eur Respir J.* 2002;20(1):12–9.
53. Varga J, Porszasz J, Boda K, Casaburi R, Somfay A. Supervised high intensity continuous and interval training vs. self-paced training in COPD. *Respir Med.* 2007;101(11):2297–304.
54. Kortianou EA, Nasis IG, Spetsioti ST, Daskalakis AM, Vogiatzis I. Effectiveness of interval exercise training in patients with COPD. *Cardiopulm Phys Ther J.* 2010;21(3):12–9.
55. Probst VS, Troosters T, Pitta F, Decramer M, Gosselink R. Cardiopulmonary stress during exercise training in patients with COPD. *Eur Respir J.* 2006;27(6):1110–8.
56. Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee IM, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc.* 2011;43(7):1334–59.
57. Gloeckl R, Marinov B, Pitta F. Practical recommendations for exercise training in patients with COPD. *Eur Respir Rev.* 2013;22(128):178–86.
58. O'Shea SD, Taylor NF, Paratz J. Peripheral muscle strength training in COPD: a systematic review. *Chest.* 2004;126(3):903–14.
59. Ortega F, Toral J, Cejudo P, Villagomez R, Sanchez H, Castillo J, et al. Comparison of effects of strength and endurance training in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2002;166(5):669–74.
60. Emtner M, Porszasz J, Burns M, Somfay A, Casaburi R. Benefits of supplemental oxygen in exercise training in nonhypoxemic chronic obstructive pulmonary disease patients. *Am J Respir Crit Care Med.* 2003;168(9):1034–42.
61. Hawkins P, Johnson LC, Nikolettou D, Hamnegard CH, Sherwood R, Polkey MI, et al. Proportional assist ventilation as an aid to exercise training in severe chronic obstructive pulmonary disease. *Thorax.* 2002;57(10):853–9.
62. Garrod R, Mikelsons C, Paul EA, Wedzicha JA. Randomized controlled trial of domiciliary noninvasive positive pressure ventilation and physical training in severe chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2000;162(4 Pt 1):1335–41.
63. Wedzicha JA. Heliox in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2006;173(8):825–6.
64. Mazzuca SA. Does patient education in chronic disease have therapeutic value? *J Chronic Dis.* 1982;35(7):521–9.
65. Velloso M, Jardim JR. Study of energy expenditure during activities of daily living using and not using body position recommended by energy conservation techniques in patients with COPD. *Chest.* 2006;130(1):126–32.
66. Bourbeau J, Nault D, Dang-Tan T. Self-management and behaviour modification in COPD. *Patient Educ Couns.* 2004;52(3):271–7.

67. van Manen JG, Bindels PJ, Dekker FW, IJzermans C, van der Zee JS, Schade E. Risk of depression in patients with chronic obstructive pulmonary disease and its determinants. *Thorax*. 2002;57(5):412–6.
68. de Godoy DV, de Godoy RF. A randomized controlled trial of the effect of psychotherapy on anxiety and depression in chronic obstructive pulmonary disease. *Arch Phys Med Rehabil*. 2003;84(8):1154–7.
69. Casaburi R, ZuWallack R. Pulmonary rehabilitation for management of chronic obstructive pulmonary disease. *N Engl J Med*. 2009;360(13):1329–35.
70. Norwood R. Prevalence and impact of depression in chronic obstructive pulmonary disease patients. *Curr Opin Pulm Med*. 2006;12(2):113–7.
71. Harrison SL, Greening NJ, Williams JE, Morgan MD, Steiner MC, Singh SJ. Have we underestimated the efficacy of pulmonary rehabilitation in improving mood? *Respir Med*. 2012;106(6):838–44.
72. Haas F, Salazar-Schicchi J, Axen K. Desensitization to dyspnea in chronic obstructive pulmonary disease. In: Casaburi R, Petty TL, editors. *Principles and practice of pulmonary rehabilitation*. Philadelphia: W.B. Saunders; 1993. p. 241–51.
73. Vestbo J, Prescott E, Almdal T, Dahl M, Nordestgaard BG, Andersen T, et al. Body mass, fat-free body mass, and prognosis in patients with chronic obstructive pulmonary disease from a random population sample: findings from the Copenhagen City Heart Study. *Am J Respir Crit Care Med*. 2006;173(1):79–83.
74. Gupta B, Kant S, Mishra R, Verma S. Nutritional status of chronic obstructive pulmonary disease patients admitted in hospital with acute exacerbation. *J Clin Med Res*. 2010;2(2):68–74.
75. Hallin R, Koivisto-Hursti UK, Lindberg E, Janson C. Nutritional status, dietary energy intake and the risk of exacerbations in patients with chronic obstructive pulmonary disease (COPD). *Respir Med*. 2006;100(3):561–7.
76. Odenrants S, Ehnfors M, Ehrenberg A. Nutritional status and patient characteristics for hospitalised older patients with chronic obstructive pulmonary disease. *J Clin Nurs*. 2008;17(13):1771–8.
77. Lacasse Y, Goldstein R, Lasserson TJ, Martin S. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2006;4:Cd003793.
78. Griffiths TL, Burr ML, Campbell IA, Lewis-Jenkins V, Mullins J, Shiels K, et al. Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: a randomised controlled trial. *Lancet*. 2000;355(9201):362–8.
79. Spruit MA, Troosters T, Trappenburg JC, Decramer M, Gosselink R. Exercise training during rehabilitation of patients with COPD: a current perspective. *Patient Educ Couns*. 2004;52(3):243–8.
80. Carr SJ, Goldstein RS, Brooks D. Acute exacerbations of COPD in subjects completing pulmonary rehabilitation. *Chest*. 2007;132(1):127–34.
81. Steele BG, Belza B, Cain KC, Coppersmith J, Lakshminarayan S, Howard J, et al. A randomized clinical trial of an activity and exercise adherence intervention in chronic pulmonary disease. *Arch Phys Med Rehabil*. 2008;89(3):404–12.
82. Waterhouse JC, Walters SJ, Oluboyede Y, Lawson RA. A randomised 2 × 2 trial of community versus hospital pulmonary rehabilitation, followed by telephone or conventional follow-up. *Health Technol Assess*. 2010;14(6.):i–v, vii–xi):1–140.
83. Spruit MA, Singh SJ, Rochester CL, Greening NJ, Franssen FME, Pitta F, et al. Pulmonary rehabilitation for patients with COPD during and after an exacerbation-related hospitalisation: back to the future? *Eur Respir J*. 2018;51:1.
84. Vogiatzis I, Rochester CL, Spruit MA, Troosters T, Clini EM. Increasing implementation and delivery of pulmonary rehabilitation: key messages from the new ATS/ERS policy statement. *Eur Respir J*. 2016;47(5):1336–41.
85. Robles PG, Mathur S, Janaudis-Ferreira T, Dolmage TE, Goldstein RS, Brooks D. Measurement of peripheral muscle strength in individuals with chronic obstructive pulmonary disease: a systematic review. *J Cardiopulm Rehabil Prev*. 2011;31(1):11–24.

86. Bachasson D, Wuyam B, Pepin JL, Tamisier R, Levy P, Verges S. Quadriceps and respiratory muscle fatigue following high-intensity cycling in COPD patients. *PLoS One*. 2013;8(12):e83432.
87. Evans RA, Kaplovitch E, Beauchamp MK, Dolmage TE, Goldstein RS, Gillies CL, et al. Is quadriceps endurance reduced in COPD? *Chest*. 2015;147(3):673–84.
88. Vieira L, Bottaro M, Celes R, Viegas CA, Silva C. Isokinetic muscle evaluation of quadriceps in patients with chronic obstructive pulmonary disease. *Rev Port Pneumol*. 2010;16(5):717–36.
89. Thompson WR, Gordon NF, Pescatello LS. ACSM's guidelines for exercise testing and prescription. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins; 2010.
90. Couillard A, Koechlin C, Cristol JP, Varray A, Prefaut C. Evidence of local exercise-induced systemic oxidative stress in chronic obstructive pulmonary disease patients. *Eur Respir J*. 2002;20(5):1123–9.
91. Couillard A, Maltais F, Saey D, Debigaré R, Michaud A, Koechlin C, et al. Exercise-induced quadriceps oxidative stress and peripheral muscle dysfunction in patients with COPD. *Am J Respir Crit Care Med*. 2003;167:1664–9.
92. Stark T, Walker B, Phillips JK, Fejer R, Beck R. Hand-held dynamometry correlation with the gold standard isokinetic dynamometry: a systematic review. *PM R*. 2011;3(5):472–9.
93. O'Shea SD, Taylor NF, Paratz JD. Measuring muscle strength for people with chronic obstructive pulmonary disease: retest reliability of hand-held dynamometry. *ArchPhysMed Rehabil*. 2007;88(1):32–6.
94. Hartmann A, Knols R, Murer K, De Bruin ED. Reproducibility of an isokinetic strength-testing protocol of the knee and ankle in older adults. *Gerontology*. 2009;55(3):259–68.
95. Dourado VZ. Relationship of upper-limb and thoracic muscle strength to 6-min walk distance in COPD patients. *Chest*. 2006;129(3):551–7.
96. Burns SP, Spanier DE. Break-technique handheld dynamometry: relation between angular velocity and strength measurements. *ArchPhysMed Rehabil*. 2005;86(7):1420–6.
97. Burns SP, Breuninger A, Kaplan C, Marin H. Hand-held dynamometry in persons with tetraplegia: comparison of make- versus break-testing techniques. *Am J Phys Med Rehabil*. 2005;84(1):22–9.
98. Bachasson D, Villiot-Danger E, Verges S, Hayot M, Perez T, Chambellan A, et al. Maximal isometric voluntary quadriceps strength assessment in COPD. *Revue des Maladies Respiratoires*. 2014;31(8):765–70.