18 Inspiratory Muscle Training

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18.1 Rationale and Background

Notably, the most prominent exercise-limiting symptom of patients with chronic respiratory conditions is dyspnea [1] which is associated with avoidance of activities, with subsequent deconditioning [2]. Dyspnea is defined as an uncomfortable sensation of breathing [3]. The respiratory muscles play a key role in the perception of dyspnea [4–6] and in limiting exercise tolerance in patients [6–8]. Respiratory muscle dysfunction is moreover frequently observed in patients with chronic lung diseases [9, 10]. Several factors contribute to respiratory muscle dysfunction in these patients, including lung hyperinflation, hypoxemia, hypercapnia, inflammation, malnutrition, long-term use of corticosteroids, physical inactivity, and changes in the fiber type distribution in the respiratory muscles (Fig. 18.[illegible]6–8, 11–13]. Lung hyperinflation is a major cause of respiratory muscle dysfunction in patients with obstructive lung disease since it places the inspiratory muscles at a mechanical disadvantage. In addition, many shared risk factors contribute to both respiratory and limb muscle dysfunction (Fig. 18.[illegible]). Lung hyperinflation causes shortening of the diaphragm, so that the muscle is able to generate less pressure during contraction [14]. At the same time, the inspiratory muscles have to overcome higher elastic and resistive loads, especially during exercise. There are compensatory mechanisms present by which the respiratory muscles of patients adapt to these mechanical disadvantages and increased chronic loading (Fig. 18.[illegible]). With these adaptations the diaphragm partially preserves its ability to generate pressure during normal breathing despite its shortened operating length and becomes more fatigue resistant [2, 15–17]. In response to chronic hyperinflation, for example, the inspiratory muscles adapt by shortening of sarcomeres, such that, at a given lung volume, pressure generation is well preserved or even increased (Fig. 18.[illegible]) [18]. This is however not effective to adapt to acute changes induced by dynamic hyperinflation during physical activities. Other adaptations (e.g., changes in fiber type distribution) are generally believed to be responses to chronic overload (Fig. 18.[illegible]).

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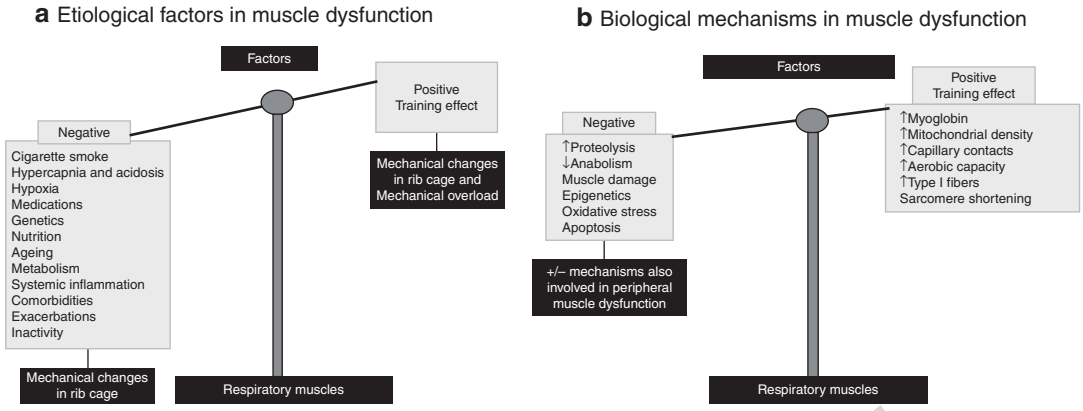

Fig. 18.1 Respiratory muscle adaptations in patients with COPD

In the respiratory muscles, etiologic factors such as alterations in the chest geometry and mechanical overload can to some extent counteract (training effect, right tray of the scales) the deleterious effects of the other etiologic factors of a more systematic nature (left tray of the scales). The factors mentioned on the left tray of the scales also contribute to limb muscle dysfunction in these patients. (b) In the respiratory muscles, several structural adaptation have beneficial effects (adaptive mechanisms, right tray of the scales), which partly counteract the deleterious effects of the other biological mechanisms (left tray of the scales). Reproduced with permission from: Arch Bronconeumol 2015;51:384–95 – Vol. 51(8). doi: 10.1016/j.arbr.2015.04.027 Recommendations of SEPAR Guidelines for the Evaluation and Treatment of Muscle Dysfunction in Patients With Chronic Obstructive Pulmonary Disease.

The compensatory mechanisms present are believed to not fully compensate for the deleterious effects on the respiratory muscles, especially in patients with severe COPD (Fig. 18.1) [19]. Moreover they can quickly become overwhelmed when the ventilation requirements are acutely increased during physical activities. Not only are the respiratory muscles not able to adapt to length changes brought about by this acute hyperinflation but they are also not trained to operate at shorter lengths and higher contraction velocities due to avoidance of activities. The resulting imbalances between load and capacity of the respiratory muscles are closely related to the perception of dyspnea in patients with lung disease especially during exercise (Fig. 18.2) [20].

While highlighting these specific mechanisms that contribute to exercise limitation it is however also important to stress that in patients with lung disease, other factors besides dyspnea, mechanical constraints, and ventilatory limitation are relevant. These factors include peripheral muscle dysfunction and inappropriate increase in energy demands due to recruitment of abdominal muscles [21, 22].

Several pharmacological and non-pharmacological treatment options are available to enable the respiratory muscles of patients to better cope with these high loads, either by attempting to decrease the load on the respiratory muscles (e.g., bronchodilation or ventilatory support) or by improving respiratory muscle function [23, 24]. IMT has been frequently applied in the last decades to improve inspiratory muscle function (both pressure generating capacity and endurance) in patients in order to reduce dyspnea and improve exercise capacity [25].

18.2 Evidence

Different methods for respiratory muscle training have been applied in the past during pulmonary rehabilitation (PR). These include methods that predominantly aim to increase muscle strength, such as targeted resistive breathing [26], and

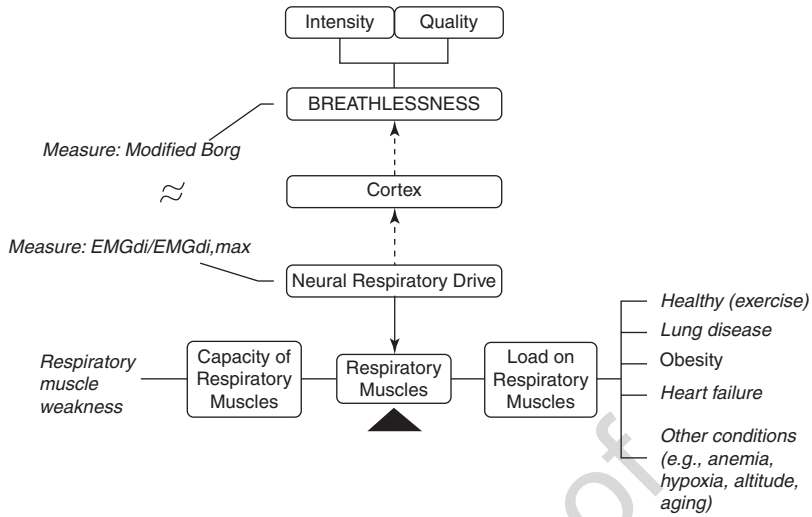

Fig. 18.2 The ventilatory load-capacity balance and dyspnea in COPD (Reprinted with permission of the American Thoracic Society. Copyright© 2016 American Thoracic Society. Jolley CJ, Moxham J. 2016. Dyspnea Intensity: A Patient-reported Measure of Respiratory Drive and Disease Severity. Am J Respir Crit Care Med; 193(3):236–8

threshold loading [27], as well as methods that predominantly aim at increasing muscle endurance, such as isocapnic hyperpnea [28]. Recently a hybrid between threshold loading and targeted resistive loading (tapered flow resistive loading) has gained more popularity [29]. We will discuss the different methodologies in more detail in the following paragraph. In general, the role of the respiratory muscles in respiratory rehabilitation remains controversial, even after more than 40 years of research [30]. The available evidence in patients with COPD will be reviewed first. After that the (more limited) evidence available in other obstructive and nonobstructive respiratory disorders will also be discussed.

18.2.1 COPD

In terms of the demonstrated functional responses to IMT, three meta-analyses have been of key importance in patients with COPD [25, 31, 32]. The first meta-analysis by Smith et al. from 1992 has been very influential and has shaped the perception of effectiveness of this intervention for several years. The review included 17 randomized trials [32]. Across included studies small and non-significant effect sizes were reported: maximal inspiratory mouth pressure (Pimax): 0.12, $p = 0.38$; inspiratory muscle endurance 0.21, $p = 0.14$; exercise capacity −0.01, $p = 0.43$; functional exercise capacity 0.20, $p = 0.15$; and functional status 0.06, $p = 0.72$. This meta-analysis, however, took all studies into account, regardless of whether or not training load was controlled. A subgroup analysis indicated more consistent improvements in inspiratory muscle strength and endurance in those studies where targeted resistive loading with adequate loads was applied [32].

A second meta-analysis by Lötters et al. from 2002 more carefully selected only randomized controlled studies in which training load was adequately controlled during training, restricting intake to 15 studies employing loads of at least 30% of Pimax in comparison with either sham or no IMT intervention [31]. This meta-analysis was subsequently updated by Gosselink et al. in 2011 to include 32 randomized controlled trials (total $n = 830$; IMT: $n = 430$, control: $n = 400$) based on similar selection criteria [25]. On the basis of a methodological framework, a critical review was performed, and summary effect sizes were calculated by applying both fixed and random effect models. This approach more clearly demonstrated the effects of IMT. Indeed, both IMT alone and IMT combined with general exercise reconditioning significantly increased inspiratory muscle function (strength and endurance). Dyspnea symptoms were also reduced. A trend for improved functional exercise capacity after IMT which did not reach statistical significance in the 2002

meta-analysis was found to be statistically significant after inclusion of more studies in the 2011 meta-analysis [25]. An overview of overall results from the 2011 meta-analysis including effect sizes and transformation of observed effects into natural units improvements is provided in Table 18.1. IMT studied in addition to a general exercise program improved Pimax significantly, while additional improvements in functional exercise capacity could not be demonstrated. However, subgroup analysis in studies combining IMT with exercise training demonstrated that patients with inspiratory muscle weakness improved significantly more than patients with preserved muscle function [25]. This observation may be of more general interest. Indeed, so far, most studies in this area have included all COPD patients, instead of selecting COPD patients whose outcomes are more likely related to inspiratory muscle function. Some phenotypes defined by stage of COPD, presence of inspiratory muscle weakness, degree of hyperinflation, severity of dyspnea, level of exercise intolerance, and reduced health status may be other important determinants of the response to IMT [30]. Due to absence of conclusive data it is however still unclear how to best identify patients that are most likely to benefit from the intervention.

A word of caution is required in relation to the interpretation of results from these meta-analyses. Pooling of results is associated with a number of methodological problems. These include differences in populations, study design, training interventions, duration of trials, collection of data, drop out, and other inconsistencies between the studies. A large prospective randomized study is currently ongoing which addresses most of these issues and should facilitate interpretation of outcomes [33].

Most current guidelines are not undisputedly positive on the application of IMT during PR. The most recent ERS/ATS statement on respiratory rehabilitation acknowledges that "current evidence indicates that IMT used in isolation does confer benefits across several outcome areas." [34] It stresses however also the lack of proven added benefit of this intervention as an adjunct to general exercise training in COPD. Based on this (lack of convincing) data the recommendation was formulated that "IMT might be useful when added to whole-body exercise training in individuals with marked inspiratory muscle weakness" [34]. In this context it is worth mentioning that many other add-on treatments to general exercise training, including, for example, lower limb strength training, have also failed to result in additional

AUTHOR 18.1 **Table 18.1** Overall results of the meta-analysis (Gosselink et al. [25])

Outcome	SES	95% CI	*p*-Value	Natural units
$P_{i,max}$	0.73	0.53 to 0.93	0.001	+13 cmH_2O
RMET	1.05	0.62 to 1.49	0.001	+261 s
ITL	0.98	0.72 to 1.25	0.001	+13 cmH_2O
MVV	0.23	−0.27 to 0.72	0.373	+3 L min^{-1}
Functional exercise capacity	0.28	0.12 to 0.44	0.001	6MWD: +32 m
Endurance exercise capacity	0.72	−0.12 to 1.55	0.087	+198 s
V' L min^{-1}	−0.13	−0.38 to 0.11	0.293	−0.04 L min^{-1}
$V'_{O2,max}$ mL min^{-1} kg^{-1}	0.3	−0.02 to 0.63	0.067	+1.3 mL min^{-1} kg^{-1}
$V'_{E,max}$	−0.04	−0.3 to 0.2	0.696	−0.7 L min^{-1}
W_{max}	0.07	−0.16 to 0.3	0.562	+1.7 W
Dyspnoea Borg score	−0.45	−0.66 to −0.24	0.001	−0.9
Dyspnoea TDI	1.58	0.86 to 2.3	0.001	+2.8
Dyspnoea CRQ-Dyspnoea	0.34	−0.03 to 0.71	0.068	+1.1

SES summary effect size, $P_{i,max}$ maximal inspiratory mouth pressure, *RMET* respiratory muscle endurance test, *ITL* incremental threshold loading, *MVV* maximal voluntary ventilation, $V'_{O2,max}$ maximal oxygen uptake, $V'_{E,max}$ maximal minute ventilation, W_{max} maximal power output, *TDI* transition dyspnoea index, *CRQ* chronic respiratory questionnaire

improvements in functional exercise capacity or quality of life in similar study designs. This evidence has recently been summarized in a systematic literature review [35]. Quite in contrast to the similarities in available data the addition of lower limb strength training to PR is however generally encouraged [34]. It has been argued that priority during PR programs in the context of limited resources and time available should be given to the most effective components of the program (i.e., general exercise training) instead of spending too much time on add-on interventions with unproven additional benefit [36]. In the following paragraph innovations in training methods and equipment will be reviewed that might contribute to facilitate implementing well-controlled respiratory muscle training as add-on interventions during PR. Based on the currently available evidence, the recent GOLD guidelines acknowledge the potential benefits of respiratory muscle training especially when combined with general exercise training with evidence level C [37]. To provide additional evidence in support of more clinically relevant effects of IMT as an add-on treatment to PR carefully designed studies implemented in highly selective patient groups using the most appropriate outcomes will be needed [35]. A challenge in conducting these studies will be the considerable sample sizes needed to demonstrate additional effects on functional exercise capacity or quality of life on top of the large effects that will already be obtained in the active control groups (patients participating in general exercise training). It will therefore be necessary to selectively identify and include patients in these studies who are not able to benefit to the fullest from a standard rehabilitation program.

Two additional lines of evidence further support the beneficial effect on inspiratory muscle function with properly controlled IMT. First, Gayan-Ramirez et al. demonstrated in an elegantly designed animal model in rats that intermittent resistive loading resulted in type II fiber hypertrophy in the diaphragm [38]. Second, Ramirez-Sarmiento et al. observed an increase in external intercostal muscle fiber cross-sectional area and an increase in proportion of type I fibers in COPD patients following 5 week of resistive loading [39]. These studies both demonstrated that structural remodeling of the inspiratory muscles occurred with IMT. In any event, an effect of IMT on dyspnea is expected on the basis of the pathophysiological observations made by Redline and colleagues [40]. They demonstrated in normal subjects that the sensation of respiratory force was related to the fraction of Pimax used in breathing maneuvers. Hence, increasing Pimax would be expected to reduce the sensation of respiratory force. Whether these concepts truly apply to patients with COPD has not been convincingly demonstrated. Recent data collected in patients with COPD has provided initial evidence on possible beneficial effects on breathing pattern and operating lung volumes during exercise in response to IMT [41, 42]. The adoption of a more efficient breathing pattern in combination with reduced neural activation of the respiratory muscles should improve neuromechanical coupling and might be related to improvements in exertional breathlessness in these patients in response to IMT [43]. More research on possible mechanisms explaining the reduction in dyspnea after IMT and on identifying the most suitable candidates for this intervention is warranted in the coming years.

The general conclusion for patients with COPD appears to be that, if properly applied, IMT improves inspiratory muscle function. Particularly in patients with compromised inspiratory muscle function these improvements also seem to translate into functional and symptomatic benefits. Based on clinical experience and the available evidence it can therefore at this moment be recommended to select motivated patients with impaired respiratory muscle function in whom dyspnea is an important contributor to activity limitation to participate in add-on IMT interventions during their PR program.

18.2.2 IMT in Other Obstructive Lung Diseases

The consequences of expiratory flow limitation and dynamic hyperinflation on the load/capacity bal-

ance of the respiratory muscles in patients with other obstructive lung diseases (e.g., asthma, cystic fibrosis, or non-CF bronchiectasis) are similar to those observed in patients with COPD. Differences exist concerning the prevalence and severity of respiratory muscle dysfunction between those patient populations. Volume and quality of available data are moreover not comparable to the literature available in COPD. In the following paragraphs the available evidence and applied training protocols in these patient groups will be summarized.

18.2.3 Asthma

Improving respiratory muscle function in these patients could help to prevent overload of respiratory muscles during asthma attacks and should relieve acute symptoms of breathlessness due to dynamic hyperinflation. Respiratory muscle function in non-steroid dependent asthmatics however seems to be on average less impaired than in patients with COPD [44–47]. The available data in terms of randomized controlled trials is less comprehensive and results are less conclusive than in patients with COPD. The results of 5 randomized controlled trials (total $n = 113$) were summarized in a 2013 Cochrane meta-analysis [48]. Except for a statistically significant improvement in Pimax no significant improvements in symptoms or dependency on medical treatment could be demonstrated. All studies applied either flow resistive or mechanical threshold loading with controlled training intensities (40–60% $P_{i,max}$). Vast differences were however present concerning training frequency and duration of IMT programs. With exception of a study by Sampaio and colleagues all subjects were categorized as having mild to moderate persisting asthma [48]. A further study by Turner and colleagues (2011) which was not included in the meta-analysis investigated the effects of 6 weeks of mechanical threshold loading IMT in patients with mild to moderate persisting asthma [49]. Patients trained twice daily at 50% of their $P_{i,max}$ ($n = 7$) or at 15% $P_{i,max}$ (sham-control-group, $n = 8$). The IMT group achieved significant increases in $P_{i,max}$ (+28%), endurance cycling time (+16%), and symptoms of dyspnea on exertion (−16%). No significant changes were observed in the control group. Due to the small number of participants, the between group comparisons did however not reach statistical significance. Larger (multicenter) studies performed in patients with more severe and persisting forms of asthma are needed to find out whether IMT can result in functional and symptomatic benefits in these patients.

18.2.4 Cystic Fibrosis

In analogy to patients with COPD ventilatory needs during exercise are increased for a given workrate in these patients. Airway resistance, increases in intrinsic positive end expiratory pressure, and decreased lung compliance with increasing breathing frequencies increase the load on these muscles [50]. Moreover in patients with CF insufficient uptake of nutrients in combination with a persisting catabolic metabolism due to chronic inflammation can contribute to peripheral and respiratory muscle dysfunction [51, 52]. In analogy to patients with COPD the higher load on the respiratory muscles is thus combined with a reduced capacity [51, 52].

Despite this solid physiological rationale for the application of IMT in these patients, the available database is limited. Only one further study has investigated the effects of IMT in patients with CF following a meta-analysis by Reid and colleagues performed in 2008 [50, 53]. Since this study investigated the effects of a combined general exercise and IMT intervention with a control intervention, it is however less relevant in the current context [54]. In neither of the two randomized controlled studies that were included in the meta-analysis (total $n = 36$) improvements in symptoms or quality of life were observed [55, 56]. Further studies would therefore be needed to find out whether IMT can result in symptomatic benefits in patients cystic fibrosis.

18.2.5 Non-CF Bronchiectasis

In analogy with COPD patients Koulouris and colleagues demonstrated a relationship between negative consequences of expiratory flow limitation on loading of the respiratory muscles, dyspnea, and

reductions in exercise capacity [57]. Moran and colleagues observed reductions in respiratory muscle strength in most patients with NCFB [58]. Owing to these similarities in pathophysiology between COPD and NCFB comparable rehabilitative strategies, including respiratory muscle training, are recommended for both patient groups [59]. The available evidence is however, similar to the situation in asthma and patients with cystic fibrosis, far less comprehensive than in patients with COPD.

Only two studies have so far investigated the effects of IMT in NCFB. Newall and colleagues compared general exercise training in combination with either IMT (twice daily training for 15 min each, starting at 30% $P_{i,max}$ weekly increase of resistance of ~5%, $n = 12$) or "Sham" MTL-Training (fixed resistance of 7cmH2O, $n = 11$) with a control group (usual care, $n = 9$) [60]. Patients were not selected for having respiratory muscle weakness. The larger increase in exercise capacity and respiratory muscle function in the combined exercise training/IMT group in comparison with exercise training /Sham-IMT did not reach statistical significance due to small group sizes. Only differences of both groups with the usual care group could be demonstrated. Liaw et al. investigated the effects of "stand-alone" IMT in comparison with a control group ("usual care") [61]. Patient characteristics and training program were very similar to the study of Newall and colleagues. Statistically significant improvements in respiratory muscle function were observed. Due to the limited group sizes (both $n = 13$) clinically relevant larger increase in 6-min walking distance (42 m) did however not reach statistical significance. These preliminary results found in very small studies are promising. Larger studies will however be needed to investigate whether IMT can truly result in functional benefits in these patients.

18.2 Restrictive Respiratory Disorders: Interstitial Lung Disease

Patients with ILD have to cope with higher elastic loads during breathing. In the ILD group, respiratory muscles, and in particular the diaphragm, are however less disadvantaged compared with patients with COPD, probably owing to the relatively lower EELV and more favorable length–tension characteristics [62–64]. Accordingly, resting MIP and MVV are greater, together with a greater diaphragmatic contribution to increasing ventilation [63]. Specific studies on the effects of IMT in ILD are currently not available. Only the combination of IMT and general exercise training in comparison to a control group has been studied so far [65]. There are however indications that improvements in peak tidal volumes after general exercise training programs in patients with ILD are significantly correlated ($r = 0.78$, $p = 0.001$) with improvements in V′O2peak values [66]. This has been attributed to the repetitive stimulus of high ventilatory demand during exercise sessions in combination with chest expansion during deep-breathing exercises and stretching of the thoracic muscles. This is consistent with a review paper that suggested a beneficial effect of thoracic expansion and stretching on pulmonary restriction in IPF [67]. It is likely that specific inspiratory muscle resistance will have a larger impact on these variables than general exercise training or normocapnic hyperpnea. It might therefore be worthwhile to study additional effects of IMT in this population despite the relatively well-preserved respiratory muscle function.

18.3 Implementation of IMT in Clinical Practice

18.3.1 Patient Assessment

Assessment prior to IMT requires measurements of inspiratory muscle function (strength and endurance) in addition to outcome measures such as dyspnea, exercise capacity, and HRQOL. Both maximum static inspiratory pressure that a subject can generate at the mouth (Pimax) and muscle endurance are often measured in specialized respiratory medicine laboratories [54]. Small handheld devices have however become commercially available for these purposes [68]. These devices have made it easier to perform these tests in less specialized centers or even in the home setting.

18.3.2 Strength

Measurement of Pimax is a simple way to measure inspiratory muscle strength in a clinical setting. Practice attempts are required because Pimax improves significantly with familiarization [69]. To standardize the measurement, it has been recommended to measure Pimax at or close to RV [54]. The test should be performed by a trained operator who should strongly encourage subjects to make maximum inspiratory efforts. Subjects are normally seated and noseclips are not required. Because this is an unfamiliar maneuver, careful instruction and encouraged motivation are essential. Subjects also often need coaching to prevent air leaks around the mouthpiece. Once the operator is satisfied, the maximum value of three maneuvers that vary by less than 10% is recorded. The system requires a small leak to prevent glottic closure during the Pimax maneuver. The inspiratory pressure should be maintained, ideally for at least 2 s, so that the maximum pressure sustained for 1 s can be recorded. The peak pressure is on average higher than the 1 s of sustained pressure but is believed to be less reproducible [54, 70]. The pressure transducers should ideally be connected with a screen in order to display pressure-time curves and computations of the 1-sec plateau pressure. Flanged mouthpieces are readily available in pulmonary function laboratories and although they give values somewhat lower than those obtained with rubber tube mouthpieces, the differences are not usually considered important in a clinical setting [54]. In spite of many assumptions, the recorded pressure is believed to usefully reflect global respiratory muscle strength for clinical evaluation [54]. Sources of variation include type of mouthpiece, presence of a small leak, evaluated pressure (peak or plateau), number of trials performed, and lung volume from which the test is performed. Increases in $P_{i,max}$ have been found in response to specific training in comparison to control groups which indicates that the test is responsive to IMT interventions [25]. Twenty-two studies have been identified that provide reference values for MIP measurements collected in accordance with the abovementioned ATS/ERS measurement guidelines [71]. These data have recently been synthesized to provide age-specific reference values (Table 18.2) [71].

Comparison of $P_{i,max}$ before and after IMT allows clinicians to determine whether the training load was adequate to induce a training-related improvement in inspiratory muscle strength. A lack of change in $P_{i,max}$ is likely to indicate inadequate training loads. Improvements in muscle endurance have also been demonstrated after high flow, low pressure endurance training methods (e.g., isocapnic hyperpnea, for description of technique see next paragraph). There are however indications that higher training resistances tolerated during training result in larger improvements in endurance parameters [29].

18.3.3 Endurance

External loading protocols are frequently used to measure respiratory muscle endurance. These tests are characterized by the imposition of either incremental or constant submaximal inspiratory loads, sustained until symptom limitation [72]. Loads that have typically been applied in these tests include threshold loads [54, 72], or a hybrid between flow resistive loads and threshold loads (tapered flow resistive loading) [73]. Since performance during these

Table 18.2 Age-specific reference values for maximal respiratory pressure (average peak plateau pressure (95% CI) over 1 s measured from RV and expressed in cmH_2O)

Pi,max	18–29	30–39	40–49	50–59	60–69	70–83
Male	128 (116–140)	129 (118–139)	117 (105–129)	108 (99–118)	93 (85–101)	76 (66–86)
Female	97 (89–105)	89 (85–94)	93 (78–107)	80 (75–85)	75 (67–83)	65 (58–73)

Sclauser Pessoa et al. Can Respir J 2014;21(1):43–50

tests is influenced by breathing pattern (both timing components and inspiratory volumes), it has been recommended that these parameters should be controlled during tests [72, 74]. Since this adds complexity to the procedure, measurements of inspiratory muscle endurance have until recently been regarded as being beyond the scope of usual clinical practice [75]. It has been argued that these problems might be overcome to some extent by registering mouth pressure, flow, and inspiratory volumes during the test [54]. External work performed during the test has been put forward as the most dominant determinant of endurance time (t_{lim}), regardless of the pattern of breathing [54]. With the advance of new handheld devices capable of continuously registering flow, volume, and pressure responses, it has become feasible to monitor breathing pattern and external work of breathing during these tests [29, 73]. This has created an opportunity to implement well-controlled endurance tests into the standard clinical evaluation of IMT interventions. The protocol that will be presented here has recently been successfully implemented into a large multicenter trial evaluation of respiratory muscle function [33]. In short, during this constant load test patients are asked to breathe against a submaximal inspiratory load until task failure due to symptom limitation. It has been proposed that inspiratory loads should be selected that result in a t_{lim} of less than 7 min at baseline [72, 73]. In this way maximal post-intervention test durations can be limited to 15 min without important ceiling effects [72, 73]. Longer baseline t_{lim} data have previously been shown to result in ceiling effects. This lowered effect sizes of a constant load test (small to medium effect size of 0.44) in comparison to an incremental threshold endurance test (medium to large effect size of 0.68) in response to IMT [76]. Based on these data it was concluded that the threshold test might be more responsive to IMT interventions. Data from a large multicenter RCT however demonstrated a large effect size in endurance time (0.77) measured with the constant load protocol ensuring shorter baseline t_{lim} (less than 7 min) in response to IMT (Fig. 18.2) [33].

Standardized breathing instructions should be provided and post-intervention tests should be repeated using an identical load. Improvements in t_{lim} and total external work performed during the tests can be recorded as main outcomes of the test. Typical changes in breathing parameters observed during this test after IMT include [1] higher inspiratory flow resulting in shorter inspiratory time (Ti) and [2] increased inspiratory volume and work per breath [29]. While a shorter Ti could be interpreted as a breathing pattern adaptation that reduces the load on the muscles it also reflects the ability of the muscle to perform faster contractions against high resistances (i.e., improvements in muscle power). The observed increases in inspiratory volume and external work (both total and work per breath) are clearly not in favor of adopting a breathing pattern that would reduce load on the muscles. These changes are rather in support of the presence of true improvements in inspiratory muscle endurance capacity after IMT. They also reflect the standardized instructions given to patients on both occasions (pre- and post-intervention) to perform inspirations as fast, forceful, and as deep as possible. The same instructions are provided during training sessions. In summary, this constant load endurance protocol with standardized breathing instructions and registration of breathing parameters offers a feasible technique for implementing measures of respiratory muscle endurance into clinical practice (Fig. 18.2).

18.3.4 Training Modalities

At this moment, there are few studies available comparing different training devices or training protocols head to head. Recommendations on preferred devices and training protocols for different purposes are therefore not supported by firm evidence. General characteristics along with potential benefits and disadvantages of the different methods will be discussed in the following sections to formulate recommendations. Three different types of loading have been used in most respiratory muscle training programs over the last decades. These approaches are either primar-

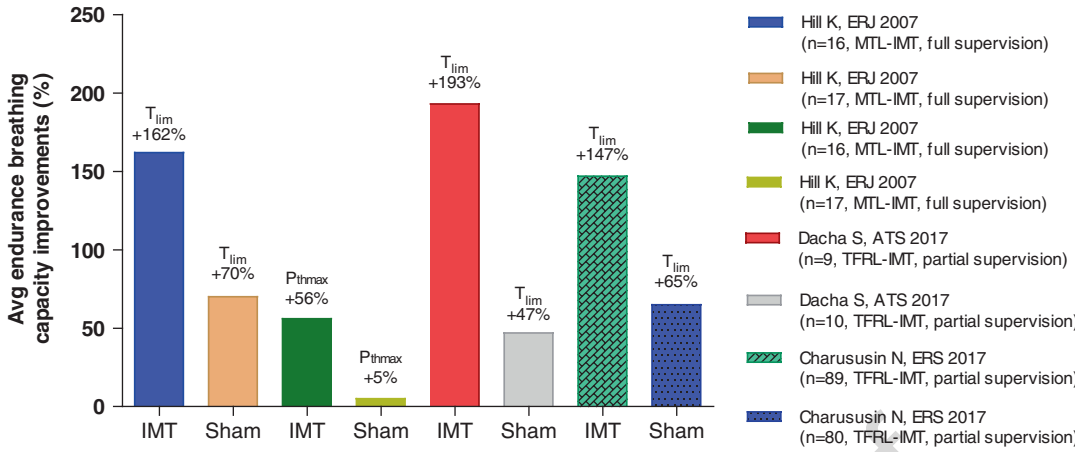

Fig. 18.3 Improvements in endurance breathing time from incremental (Pthmax) or constant load (t_{lim}) tests in response to high intensity IMT protocols in patients with COPD

ily aimed at improving muscle strength (intermediate flow/high pressure approach: targeted resistive loading and threshold loading) or muscle endurance (high flow/low pressure approach: normocapnic hyperpnea). For all these training modalities devices are commercially available that allow to offer controlled home-based training interventions. A fourth type of loading has gained popularity in recent years. This so-called tapered flow resistive loading can be regarded as a hybrid between threshold loading and targeted flow resistive loading. More recently developed electronic devices offer the availability to store data in an internal memory. These recent developments might help to facilitate better monitoring and control of home-based training interventions. A summary of the characteristics of available methods and devices is provided below and in Table 18.3.

18.3.5 Targeted Flow Resistive Loading

In order to generate a sufficient training resistance of at least 30% of the maximal inspiratory mouth pressure patients are instructed to generate high inspiratory flows while breathing through small holes with varying diameters. The smaller the diameter, the larger the resistance that needs to be overcome. Since resistance will be flow dependent devices should be able to register inspiratory flow and to provide feedback on the achieved flow and pressure response ("targeted resistive breathing").

18.3.6 Mechanical Threshold Loading

During this method a known and fixed resistance generated by a spring loaded valve (isotonic threshold load) needs to be overcome before inspiratory airflow can be generated. After overcoming the threshold load an inspiration against this constant load is possible. This resistance, which should also be set at least at 30% of patients $P_{i,max}$ is not dependent on the inspiratory flow rate of the patient. A feedback-system is therefore less necessary. A disadvantage of this method (as with any isotonic muscle training) is the fact that the inspiratory muscles will only receive an optimal resistance (relative to their maximal pressure generating capacity) over a short fragment of their full contraction range. As an example let's assume that the $P_{i,max}$ measured at RV is taken as a reference to determine training intensity (e.g., training at 50% $P_{i,max}$ RV). On initiation of the inspiration at RV the training load will be optimal according to this target intensity. With increasing lung volume, however the constant load will represent an increasingly larger fraction of the maximal pres-

Table 18.3 Overview of different training methods and available devices

Training method	Focus	Costs	Feedback-system	Storage training data	Devices
Mechanical threshold loading	Strength and endurance	Low	NA	NA	Threshold IMT®; POWERbreathe Medic®
Controlled targeted flow resistive loading	Strength and endurance	High	Visual	Yes	Respifit S®
Tapered flow resistive loading	Strength and endurance	Moderate	Visual/accoustical	Yes	Powerbreathe (K-Series)®
Normocapnic hyperpnea	Endurance	High	Visual/accoustical	Yes	Spirotiger®

sure generating capacity. This will eventually limit the ability of the muscle to perform further shortening and might limit volume response especially at higher training intensities (50% $P_{i,max}$ and more). This has implications for the lengths at which the respiratory muscles can be stimulated during training. It is likely to also impact on the perception of inspiratory effort against a given load [29].

18.3.7 Tapered Flow Resistive Loading

This recently developed type of loading combines the beneficial characteristics of the two aforementioned loading approaches. After flow-independently overcoming a threshold load the resistance is subsequently flow dependently tapered down during inspiration. This accommodates the pressure volume relationship of the respiratory system and allows full vital capacity inspirations even at higher training resistances. This has been shown to result in higher inspiratory volumes achieved during training at comparable resistances in comparison with mechanical threshold loading (Fig. 18.4).

The training intensities during an IMT program that could be tolerated by patients in comparison with mechanical threshold loading were higher with this loading approach with comparable perceived respiratory effort scores [29].

18.3.7.1 Normocapnic Hyperpnea

In contrast to the three previously mentioned techniques, this type of training does not apply additional resistances to breathing that need to be overcome. In contrast, by stimulating hyperpnea at around 60% of the subject's maximal voluntary ventilation over a large range of the subject's vital capacity (deep in- and expirations) for longer durations (typical training durations of about 30 min) it stimulates the generation of high inspiratory and expiratory flow rates. This approach is supposed to mainly improve endurance and not strength of the respiratory muscles. To prevent hyperventilation resulting in hypocapnia home training devices have been developed which ensure normocapnia by partial rebreathing of the expired air. The execution of the training is technically challenging and coordination of breathing has to be practiced thoroughly [76]. It is moreover challenging to perform for patients with severe expiratory flow limitation. Based on principles of training specificity, this type of training is not expected to increase maximal pressure generating capacity. This was confirmed in the latest meta-analysis in patients with COPD [25]. Moreover the method did also not result in significant effects on dyspnea symptoms and functional exercise capacity [25]. Finally, advanced and rather expensive home training devices providing both optical and acoustical feedback seem mandatory to efficiently execute this type of training in the home setting.

18.3.7.2 Training Parameters

We recommend the use of either mechanical threshold loading, targeted flow resistive loading, or tapered flow resistive loading to train the inspiratory muscles during PR. Based on available evidence and the complexity of the normocapnic hyperpnea method, this training modality seems

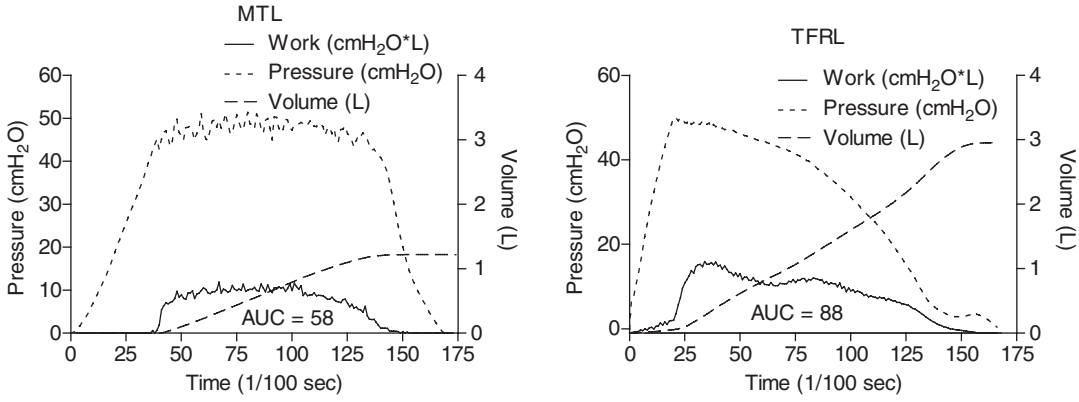

Fig. 18.4 Comparison between two training devices during a typical inhalation against a resistance corresponding to 60% of baseline $P_{i,max}$ (50 cmH_2O). *TFRL* tapered flow resistive loading, *MTL* mechanical threshold loading, *AUC* area under the curve for total external inspiratory work as integrated from mouth pressure (cmH_2O) and volume (L) signals over time

less ideal in this specific setting. Previously many programs were applied that consisted of 30 min of daily strength training at a resistance of at least 30% of the individuals PI,max. Recently, shorter, high intensity programs have been shown to be feasible and effective [29, 77, 78]. These programs reduce daily training time to less than 10 min and use intensities of at least 40% (mechanical threshold loading) or even 50% $P_{i,max}$ (tapered flow resistive loading). They have been studied under both fully and partly supervised conditions (supervision of one training session per week). Since the aim of the intervention is to facilitate breathing during periods of increased ventilatory needs (i.e., during daily physical activities), these shorter training durations should be well adapted to the functional requirements of patients during daily life. Activity monitoring of these patients has revealed that most daily activities of patients are carried out in bouts of less than 10 min [79, 80]. Training durations of 15 or 30 min seem to be less adequate in this context. Moreover these high intensity programs have been proven to result in large changes in $P_{i,max}$ (Fig. 18.5) and comparable improvements in respiratory muscle endurance (Fig. 18.6) in comparison to programs applying longer training durations [29, 77, 78].

One training session typically consists of 30 full vital capacity breaths against resistance and takes an average of 4–5 min to complete. Training takes place with the patient seated. Wearing a noseclip is not obligated. Patients are permitted to lean forward and fix their upper limbs on the arms of a chair or a table if desired. It is recommended that during the rehabilitation period at least one training session per week is supervised in order to permit the training load to be increased and to monitor compliance and progress. In case devices are used with an internal storage for data these supervised sessions offer an ideal opportunity to compare the quality of home-based sessions with supervised sessions. This will enable health care providers to provide patients with specific instructions. It is important to stress the importance of fast and forceful inspirations and the need to achieve the largest possible volume response with every breath. This will maximize gains in muscle power and increase total work performed during training sessions. As with other skeletal muscles, improvements in strength are likely to be dose-dependent [81]. Progression of training intensity by increasing loads over time is therefore mandatory. An initial training load should be selected equivalent to at least 30% of a patient's Pi,max. Loads of less than 30% of $P_{i,max}$ are insufficient to induce improvement in inspiratory muscle strength [25, 32]. A typical example of progression in training loads during IMT in patients with COPD is provided in Fig. 18.6.

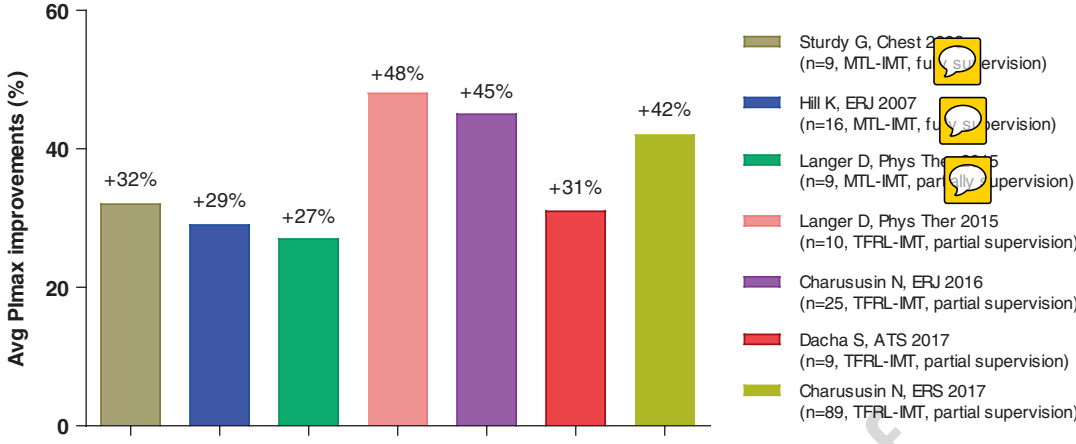

Fig. 18.5 Comparison of improvements in maximum inspiratory mouth pressure (Pi,max) in intervention groups in studies applying short, high intensity IMT protocols

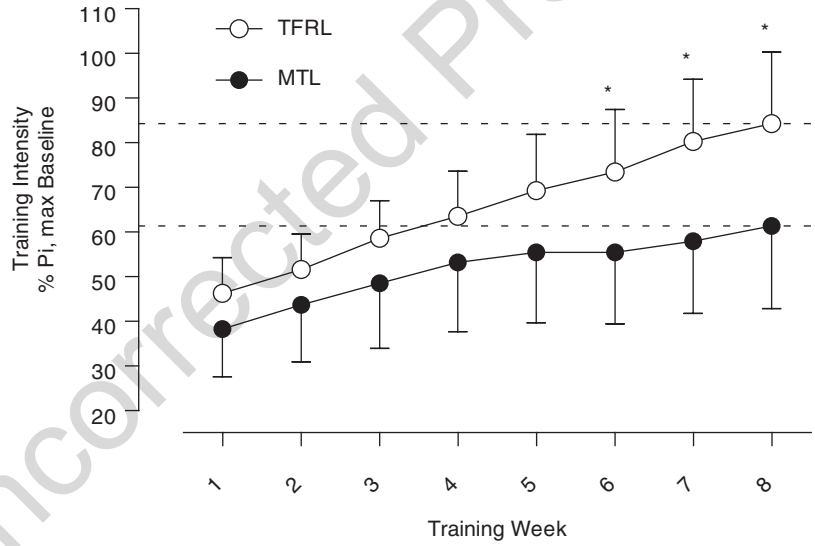

Fig. 18.6 Progression of training intensity expressed as a percentage of baseline Pi, max. *TFRL* tapered flow resistive loading; *MTL* mechanical threshold loading. *$p < 0.05$ between groups. *Dotted lines* represent the highest average training intensities reached in the TFRL and the MTL group, respectively

A symptom-limited approach is recommended to guide the progression of training loads. Selecting loads during which patients describe their respiratory effort at the end of a training session (after 30 breaths) as somewhat hard—that is, between 4–5 on the modified Borg Scale (0–10), seems appropriate. Patients can train at loads corresponding to a higher perceived effort if tolerated. One should aim for the highest tolerable load that still enables full volume expansion dur- ing inspiration. On completion of the first training week, patients are often training at loads equal to approximately 40% of $P_{i,max}$ with the mechanical threshold loading or 50% with flow resistive loading (Fig. 18.6). The inspiratory load usually needs to be increased rapidly during the first 4 weeks of training, largely because of neural adaptations to training [81, 82]. Weekly adaptation and supervision is therefore strongly recommended during this initial period in order to optimize training response. Thereafter, the rate of increase often slows, and further increments in muscle function are likely to reflect gains resulting from muscular hypertrophy [39].

In the beginning of the program patients should be informed about the physiological rationale underlying the training (i.e., facilitating exercise breathing and reducing perceived breathing discomfort during endurance exercise training sessions and daily physical activities). They should also be informed about the expected training effects and physiological adaptations that take place in response to the training. When initiating the training the patients should not only receive information about the correct technical execution of the exercises, but also about hygienic measures that should be taken to maintain the equipment. Daily cleaning of mouthpieces and breathing valves by flushing these parts with tap water and regular disinfection of these parts are recommended to ensure hygienic training circumstances and optimal functioning of the breathing devices.

18.4 General Conclusions and Recommendations

Until recently well-controlled respiratory muscle training interventions were mostly restricted to the laboratory setting or specialized hospital environment and required extensive supervision in order to be performed effectively. Technical progress in training equipment and modifications in training regimens have however been made in recent years. These developments have been shown to result in effective and well-controlled training programs that can be offered largely unsupervised. These recent developments have the potential to reduce time investment for both health care providers and patients and are believed to contribute to facilitate implementation of respiratory muscle training interventions into PR programs in the coming years. Current guidelines acknowledge the potential added value of respiratory muscle training within the framework of PR mainly for selected patients with more pronounced respiratory muscle weakness. The additional effects on outcomes beyond improvements in respiratory muscle function when IMT was studied as an add-on intervention to general exercise training have mostly been reported in this selected group of patients. Better identifying those patients who are most likely to benefit from the intervention will be the most important challenge in the years to come.

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