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New tools in pulmonary rehabilitation

P.J. Wijkstra and J.B. Wempe

ABSTRACT: In patients with more severe chronic obstructive pulmonary disease (COPD), the benefits of rehabilitation might not be clear and, therefore, new treatment options have been developed to increase the benefits of rehabilitation. This review provides an overview of new approaches being developed as an addition to exercise training. In turn, the benefits of adding ventilatory support, oxygen, anabolics or neuromuscular stimulation to a rehabilitation programme will be discussed. While positive benefits for a number of these approaches have been found, many questions remain unsolved. Therefore, at present, we cannot recommend these new tools as part of the routine management of patients with COPD who start a rehabilitation programme.

KEYWORDS: Anabolics, neuromuscular stimulation, oxygen, rehabilitation, ventilatory support

AFFILIATIONS
Dept of Pulmonary Diseases,
University Medical Center Groningen,
University of Groningen, Groningen,
The Netherlands.

CORRESPONDENCE
P.J. Wijkstra
Dept of Pulmonary Diseases,
University Medical Center Groningen
University of Groningen
Post box 30001
9700 RB Groningen
The Netherlands
E-mail: p.j.wijkstra@long.umcg.nl

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Current literature has shown that pulmonary rehabilitation is effective in patients with chronic obstructive pulmonary disease (COPD) by improving dyspnoea, exercise tolerance and quality of life [1–3]. However, in patients with more severe COPD the benefits of rehabilitation might be less; therefore, new treatment options have been developed to increase rehabilitation results. In this review, we will provide an overview of the new approaches to pulmonary rehabilitation that are an addition to exercise training.

VENTILATORY SUPPORT DURING EXERCISE OR EXERCISE TRAINING

Advanced COPD is generally characterised by severe airflow limitation, which is frequently associated with hyperinflation. This will especially worsen during exercise when the absence of any flow reserve requires the subject to breath at a higher lung volume to adjust to the increased ventilatory requirements. The work of breathing will be increased, primarily to overcome the intrinsic positive end-expiratory pressures. As during exercise, the increased ventilatory requirements are difficult to sustain, new approaches are needed to assist patients with the mechanical output during exercise. During recent decades, a number of studies have investigated this topic by applying different types of ventilator support during exercise. In 1990, PETROF *et al.* [4] demonstrated that continuous positive airway pressure (CPAP) reduced inspiratory muscle effort, as indicated by the pressure–time integral of transdiaphragmatic and oesophageal pressure. In addition, they found that dyspnoea improved with CPAP in five out of the eight patients and that the amelioration of dyspnoea was directly related to reductions in the pressure–time integral of the oesophageal pressure. O'DONNELL *et al.* [5] showed that by applying 4–5 cmH_2O of CPAP to patients with COPD (mean forced expiratory volume in 1 s (FEV_1) 1.2 L), less breathlessness was experienced during steady-state submaximal exercise. In addition, they showed that similar levels of CPAP administered to patients with even more severe COPD (mean FEV_1 0.9 L) improved the patient's endurance capacity during constant power cycle exercise by 48% [6]. A study comparing inspiratory pressure support (IPS; mean airway pressure 12–15 cmH_2O), CPAP (6 cmH_2O) and oxygen (2 $L \cdot min^{-1}$) during exercise showed that only IPS increased walking distance compared with control (62% increase, range 14–533 m; $p=0.01$) [7]. Patients experienced less breathlessness at iso-time during IPS rather than during control exercise. A newer technique is proportional assist ventilation (PAV), which is a form of synchronised ventilatory assistance. A specific characteristic of PAV is that the ventilator generates pressure in proportion to

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the patient's instantaneous effort. This means that if the patient makes a greater inspiratory effort the machine will generate more pressure. Thus, in PAV, the ventilator amplifies the patient's inspiratory effort without any pre-selected target volume or pressure. The aim of PAV is to allow the patient to attain whatever ventilation and breathing pattern seems to fit their ventilatory control system. The influence of PAV has been compared with pressure support ventilation (PSV) and CPAP in 15 stable patients with COPD (FEV1 32% predicted, mean arterial oxygen tension 52 mmHg and mean arterial carbon dioxide tension (P_{a,CO_2}) 52 mmHg) [8]. The patients underwent randomised submaximal cycle endurance testing at 80% of their maximal workload, receiving either sham ventilation (1 cmH_2O), CPAP (6 cmH_2O), PSV (inspiratory positive airway pressure 12–16 cmH_2O and expiratory positive airway pressure (EPAP) 1 cmH_2O) or PAV (8.6±3.6 and 3±1.3 cmH_2O of volume and flow assistance, respectively, and EPAP 1 cmH_2O). CPAP, PSV and PAV increased endurance time compared with sham ventilation (9.6, 10 and 12 min, respectively, *versus* 7.2 min). In addition, PAV increased endurance capacity more than the other interventions. More recently, a study by DREHER *et al.* [9] showed that by applying high inspiratory pressures, the walking distance could be increased in patients with severe COPD. In this study, it was remarkable that the high inspiratory pressures needed by the patients during the night did not have to be adjusted during walking. If this is really the case, this would be a big step forward for patients as it would provide an easy way to use the ventilator during exercise.

A recent study has provided some insight into the mechanism of improved exercise with ventilatory support by showing that IPS delayed the increase of serum lactate during exercise in patients with severe COPD [10]. Lactate increased at 2.96 $mmol \cdot L^{-1}$ during unassisted walking and at 2.42 $mmol \cdot L^{-1}$ ($p<0.01$) with IPS. The duration of exercise was increased with IPS compared to control (13.6 *versus* 5.5 min; $p<0.01$). This latter observation may be relevant to the application of exercise rehabilitation for patients with severe COPD. Two studies are relevant to mention in this respect. HAWKINS *et al.* [11] investigated the effects of exercise training with and without PAV during a 6-week programme. 19 COPD patients with a mean FEV1 of 0.8 L (26% pred) were included in this study: 10 patients were randomised for training with PAV while nine trained without PAV. After the programme, the mean training intensity at maximal cycle test was 15% higher in the PAV group compared with the non-PAV group. The lactate concentration at an identical workload in the PAV group was 18% lower compared with the non-PAV group. In addition, the authors found a significant relationship between the reduction in plasma lactate at an equivalent workload and the increase in peak workload after training ($r= -0.6$, $p<0.01$). Thus, confirming that true physiological adaptions can be achieved by applying PAV during training. The study of VAN'T HUL *et al.* [12] is also interesting in this respect. In their study, 29 COPD patients (mean FEV1 1.1 L, 41% pred) with ventilatory limitation during exercise completed an 8-week cycle exercise programme. The authors demonstrated that an IPS of 10 cmH_2O significantly increased training intensity compared with an IPS of 5 cmH_2O, resulting in an improved shuttle walking distance and cycle endurance capacity.

In summary, ventilatory support during exercise may decrease dyspnoea and improve exercise capacity among patients with COPD. However, current evidence comes from studies with small sample sizes. Applying ventilatory support during training also showed physiological benefits, which means that this can be used as an additional tool to improve the well-known benefits of rehabilitation. However, this has only been shown in small studies and its long-term benefits have not been elucidated. Therefore, before widespread use of ventilatory support during training can be advocated, larger clinical trials are needed in order to identify the most effective means of ventilatory support during exercise training and which patients will benefit most.

NOCTURNAL VENTILATORY SUPPORT IN ADDITION TO EXERCISE TRAINING

One of the first studies investigating the additional value of nocturnal noninvasive positive-pressure ventilation (NIPPV) with rehabilitation was published in 2000 by GARROD *et al.* [13]. 45 patients with severe stable COPD (mean FEV1 1.0 L) were randomised to either the combination of domiciliary NIPPV and exercise training (n=23) or to exercise training alone (n=22). After an 8-week training programme, the authors found a significant improvement in mean shuttle walk test in the NIPPV+exercise training group compared with the exercise training alone group of 72 m. In addition, they found a mean significant improvement between both groups for the Chronic Respiratory Disease Questionnaire of 12.3, which is clinically significant. They concluded that domiciliary NIPPV can be used successfully to augment the effects of rehabilitation in severe COPD. Remarkably, in this study NIPPV was applied to patients who were normocapnic, suggesting that ventilation was not the primary limitation during exercise. In addition, the compliance for NIPPV was low as the mean usage time was 2.1 h and only 50% of the patients used NIPPV for <2 h. Although we do not know what the minimal effective time is, 2 h is generally considered as too low.

In a more recently published study, DUIVERMAN *et al.* [14] investigated the benefits of nocturnal ventilatory support in addition to rehabilitation in hypercapnic patients. 72 patients with COPD were randomly assigned to nocturnal NIPPV in addition to rehabilitation (n=37) or rehabilitation alone (n=35). Outcome measurements were assessed before and after the 3-month intervention period. While the primary outcome, the Chronic Respiratory Questionnaire (CRQ) total score, improved 15.1 points with NIPPV+rehabilitation, the CRQ improved to 8.7 points with rehabilitation alone; the difference of 7.5 points was not statistically significant between groups ($p=0.08$). However, compared with rehabilitation alone, the difference in the fatigue domain of the Maugeri Respiratory Failure questionnaire was greater with NIPPV+rehabilitation (mean difference 3.3 points; $p<0.01$), as was the improvement in total score (mean difference -10%; $p<0.03$) and its cognition domain (mean difference -22%; $p<0.01$). Furthermore, the addition of NIPPV improved daytime P_{a,CO_2} (mean difference -0.3 kPa; $p<0.01$) and daily step count (mean difference 1,269 $steps \cdot day^{-1}$; $p<0.01$). This was accompanied by an increased daytime minute ventilation (mean difference 1.4 L; $p<0.001$). This study is unique as it has a long-term follow-up (to be published) and included only patients who were hypercapnic at rest. A number of other issues are also important to mention.

1) Patients were ventilated with relatively high inspiratory pressures (20 cmH_2O). While these are lower than the pressures

used by WINDISCH *et al.* [15], they are higher than the pressures used in the older randomised controlled trials [16]. This might explain why the study by DUIVERMAN *et al.* [14] found a significantly improved gas exchange that was not the reported in the older studies. 2) The drop in P_{a,CO_2} was related to the time for which patients were using the ventilator: more hours of nocturnal ventilation led to a significant drop in P_{a,CO_2} during the daytime. 3) Probably the most important part of this study was the monitoring of gas exchange during the night, which is crucial in order to be able to individually adjust ventilator settings and to achieve effective nocturnal ventilation.

Another study in this field with a comparable design was performed by KOHNLEIN *et al.* [17]. This was a prospective, observational, nonrandomised study carried out in COPD patients in Global Initiative for Chronic Obstructive Lung Disease stage IV. 40 patients combined nocturnal NIPPV with rehabilitation for a mean of 29 days. Their results were compared with 40 matched control patients who underwent the same rehabilitation programme. Patients in the NIPPV group received pressure support ventilation for ~8 h with a mean inspiratory pressure of 17.5 cmH_2O and a mean expiratory pressure of 4.5 cmH_2O. Significant between-group differences were found for the 6-min walking test, FEV1 and lung hyperinflation, while significant within-groups differences were found for blood gasses and quality of life in the NIPPV group. Remarkably, these positive effects were also found for patients who were normocapnic, thus the authors suggest that NIPPV should be started early in the course of COPD.

In conclusion, nocturnal noninvasive ventilation might be an effective tool in increasing the benefits of rehabilitation as positive benefits have been found in several clinically relevant outcomes. However, several issues are still open for discussion. 1) For what type of patient (hypercapnic *versus* normocapnic) is NIPPV useful? 2) What is the minimal time required on NIPPV for positive effects? 3) What is the underlying mechanism of the positive effects of NIPPV (improved gas exchange, muscle rest or sleep quality)? As long as these questions remain unsolved, in combination with the lack of adequately powered studies, NIPPV cannot be advocated as part of routine management in patients with COPD who start a rehabilitation programme.

Oxygen

Hyperoxia increases endurance time in patients with COPD, probably due to an increase of inspiratory capacity or, in a different way, a decrease of dynamic hyperinflation at a certain level of exercise [18, 19]. In addition, hyperoxia reduces hyperinflation during recovery after exercise [20] and may prevent hypoxic vasoconstriction [21]. COPD patients with low fat-free mass (FFM) show lower levels of oxidative stress with supplemental oxygen [22]. Therefore, it has been hypothesised that patients with COPD are able to achieve a higher work rate during exercise training, which will positively affect training results after several weeks. It is generally recommended that COPD patients who are already hypoxaemic at rest should use oxygen during exercise, aiming at a rather arbitrary oxygen saturation of >90%. As far as we know, six randomised controlled trials have been published on the effect of oxygen in COPD patients with or without desaturation during exercise training (table 1) [23–28].

It can be concluded that hyperoxia has no clear effect on the results of exercise training in COPD patients with or without documented desaturation during exercise. Only in the study by EMTNER *et al.* [27] was a significant, and clinically relevant, improvement seen, which is associated with a well-demonstrated higher work load during rehabilitation. Whether the intensity of training in this study really differed from the other studies cannot be concluded from the literature. It should be mentioned that the total number of studied subjects was only small. In addition, it

TABLE 1 Exercise training and oxygen

First author [ref.]	Active/ control n	Inclusion criteria	Oxygen treatment	Exercise training	Main outcome parameters	Results active/ placebo
ROOYACKERS [23]	12/12	P_{O_2} >8.5 kPa, nocturnal S_{O_2} >90%, $S_{O_2,max\ exercise}$ <90%, $\Delta P_{A-a,O_2,rest\ max\ exercise}$ >2 kPa	4 L·min^{-1}	Strength + endurance (cycling), S_{O_2} >90%: 10 weeks, 5 days·week^{-1}, 80 min·day^{-1}	CWRT, 6MWD, CRQ	NS
FICHTER [24]	5/5		35%	Cycling: 4 weeks, 5 days·week^{-1}	$W_{max,cycle\ ergometry}$	NS
GARROD [25]	11/11	FEV1 <40%, $S_{O_2,exercise}$ <90% and ΔS_{O_2} >4%	4 L·min^{-1}	Cycling/walking: 6 weeks, 3 days·week^{-1}, 1 h·day^{-1}	ISWT, CRQ	NS
WADELL [26]	10/10	$S_{O_2,6MWD}$ <92%, P_{O_2} >7.8 kPa	5 L·min^{-1}	Walking, S_{O_2} >90%: 8 weeks, 3 days·week^{-1}, 30 min·day^{-1}	6MWD	NS
EMTNER [27]	14/15	FEV1 <50%, P_{O_2} >7.3 kPa, $S_{O_2,CWRT}$ >88%	3 L·min^{-1}	Cycling: 7 weeks, 3 days·week^{-1}, 45 min·day^{-1}	CWRT	14.5/10.0 min*
SCORSONE [28]#	7/9		40%	Cycling; 8 weeks, 3 days·week^{-1}, 40 min·day^{-1}	$W_{max,cycle\ ergometry}$, CWRT	NS

P_{O_2}: partial pressure of oxygen; S_{O_2}: oxygen saturation; Δ: change; P_{A-a,O_2}: alveolar–arterial oxygen gradient; FEV1: forced expiratory volume in 1 s; 6MWD: 6-min walk distance; CWRT: constant work rate test; CRQ: Chronic Respiratory Questionnaire; W_{max}: maximum work; ISWT: Incremental Shuttle Walk Test; NS: not significant. #: three-arm study: 40% O_2, heliox (He 60%/O_2 40%) and air, presented results 40% O_2 *versus* air. *: $p<0.05$.

may be that different COPD phenotypes respond differently to hyperoxia. In this respect, it was recently shown that comparable correction of exercise-induced desaturation resulted in different effects on exercise responses, such as endurance time, minute volume or heart rate [29]. The overall disappointing results of hyperoxia in exercise training are in line with the absent effect of supplemental oxygen in daily life. In a recent randomised controlled trial, MOORE *et al.* [30] studied the effect of oxygen supplementation of 6 $L \cdot min^{-1}$ during activities and exercise for 12 weeks in 143 COPD patients (partial pressure of oxygen >7.3 kPa; Medical Research Council score $\geqslant$3). They found no effect of oxygen therapy on dyspnoea, functional status and health status. Moreover, no prognostic factors for a beneficial effect of oxygen could be demonstrated, including desaturation ($\leqslant$88%) during exercise. More studies are definitely needed on the role of supplemental oxygen, for instance, on the oxygen concentration, intensity of exercise programmes and effects in different COPD phenotypes.

Heliox

Heliox (a mixture of helium and oxygen) has beneficial effects on pulmonary mechanics, such as improved lung emptying, reduced flow turbulence and reduced airflow obstruction, and improved gas exchange. Heliox results in an increase of exercise time in constant work rate tests, which is associated with delayed dynamic hyperinflation and lower work of breathing [31, 32]. The effect of heliox during exercise training in the rehabilitation setting was investigated in two studies. JOHNSON *et al.* [33] included 32 COPD patients with an FEV_1 of <50% pred and a mean diffusing capacity of the lung for carbon monoxide ($D_{L,CO}$) of 39% pred in a randomised three-arm study. Subjects trained twice a week for 6 weeks on the treadmill with air, heliox (He 79%/O_2 21%) or NIPPV. Endurance time and peak work load improved in all treatment arms, with no difference between the arms. SCORSONE *et al.* [28] studied 30 COPD patients with an FEV_1 of <60% pred and a mean $D_{L,CO}$ of 85% pred. Subjects underwent cycling training three times a week for 8 weeks with either room air, 40% oxygen or heliox (60%/40%). Endurance time and peak oxygen consumption significantly improved in the three treatment arms, with no difference between the arms. The use of heliox appeared safe and was well tolerated. Despite these positive studies, it can be concluded that more studies are needed to define the position of heliox in routine practice.

Anabolics

COPD patients show changes in hormonal status and, in particular, low levels of testosterone may be prevalent, which

TABLE 2 Exercise training and anabolics

First author [ref.]	Active/placebo n	Inclusion criteria	Active treatment	Exercise training	Main outcome parameters	Results active/placebo
SCHOLS [37]#	213, numbers per treatment arm and sex not reported		Nandrolone decanoate 50 mg (M) or 25 mg (F) every 2 weeks for 8 weeks	Endurance training: 8 weeks, 5 days·$week^{-1}$	FFM (BIA), weight, $P_{I,max}$, arm circumference	FFM and $P_{I,max}$ (NN *versus* P)
FERREIRA [38]	10 M/7 M	BMI <20 $kg \cdot m^{-2}$, $P_{I,max}$ <60% pred	Testosterone 250 mg at start then stanozolol 12 $mg \cdot day^{-1}$ orally for 27 weeks	0–9 weeks: none, 9–18 weeks: inspiratory muscle training, 18–27 weeks: endurance training	BMI, LBM (DEXA), extremity circumference, $P_{I,max}$, 6MWD, $V'_{O_2,max}$	LBM 3/0 kg* Thigh circumference 2/0%* Other NS
CREUTZBERG [39]	33 M/30 M	<70 yrs, P_{O_2} >7.3 kPa	Nandrolone decanoate 50 mg every 2 weeks for 8 weeks	Endurance training: 8 weeks, 5 days·$week^{-1}$	FFM (deuterium method), isometric leg strength, $P_{I,max}$, SGRQ, W_{max} and $V'_{O_2,max}$	FFM 1.7/0.3 kg* Other NS *Post hoc* oral corticosteroid users larger effects on W_{max} and $P_{I,max}$
CASABURI [40]¶	12 M/11 M	FEV_1 <60% pred, serum testosterone <400 $ng \cdot dL^{-1}$	Testosterone enanthate 100 mg once a week for 10 weeks	Resistance training: 10 weeks, 3 days·$week^{-1}$	LBM (DEXA), 1RM leg press	Total LBM 3.3/0.2 kg Leg lean 1.4/0.5 kg* 1RM 27/17%*
SVARTBERG [41]	15 M/14 M	FEV_1 <60% pred	Testosterone enanthate 250 mg every 4 weeks for 29 weeks	None	6MWD, FFM (DEXA), SGRQ, sexual QoL questionnaire	FFM 1.1/–0.8* Sexual QoL improved Other outcomes NS
SHARMA [42]	8 (5 M and 3 F)/ 8 (4 M and 4 F)	FEV_1 <50% pred	Nandrolone decanoate 50 mg (M) or 25 mg (F) every 2 weeks for 16 weeks	Resistance/endurance training: 16 weeks, 3 days·$week^{-1}$ unsupervised	CRQ, LBM (DEXA), 6MWD	NS

M: male; F: female; BMI: body mass index; $P_{I,max}$: maximal inspiratory pressure; % pred: % predicted; P_{O_2}: partial pressure of oxygen; FEV_1: forced expiratory volume in 1 s; FFM: fat-free mass; BIA: bioelectrical impedance analysis; LBM: lean body mass; DEXA: dual-energy X-ray absorptiometry; 6MWD: 6-min walk distance; $V'_{O_2,max}$: maximal oxygen uptake; SGRQ: St George's Respiratory Questionnaire; W_{max}: maximum work; 1RM: one repetition maximum; QoL: quality of life; CRQ: Chronic Respiratory Questionnaire; NN: nutrition + nandrolone; P: placebo; NS: not significant. #: three-arm study: placebo, nutrition (420 $kcal \cdot day^{-1}$) and nutrition + nandrolone; ¶: four-arm study: placebo/no training, testosterone/no training, placebo/training and testosterone/training. *: $p<0.05$, comparison between the training arms.

may negatively affect muscle mass and strength [34, 35]. In healthy young males a positive effect of testosterone 600 mg weekly for 10 weeks was found on FFM, thigh circumference and strength, alone or in combination with strength training [36]. Several randomised controlled trials have been performed in COPD following a rehabilitation programme [37–42], these are summarised in table 2. The subjects in the study of SVARTBERG *et al.* [41] did not follow a rehabilitation programme, but the study was added as it yields useful data on specific aspects of quality of life.

In their three-arm study, SCHOLS *et al*. [37] showed after a *post hoc* analysis that the response to anabolics depends on body composition. Depleted subjects (low weight and/or low FFM) showed an increase in arm circumference with nandrolone/nutrition *versus* placebo, but not *versus* nutrition alone, whereas in the subjects with normal body composition, the nutrition/nandrolone and nutrition alone arms gained more weight than the placebo arm. The authors suggested that anabolic steroids may, in particular, be relevant for subjects with low FFM, but the improvements in outcomes were small. It is suggested that anabolics are particularly effective in patients using oral glucocorticosteroids [39], but no randomised controlled trial currently exists. Although anabolics are potentially hazardous, as they may increase haemoglobin concentrations, induce liver function disorders or exaggerate prostate cancer, no serious side-effects have been reported in the aforementioned studies. Finally, it should be noted that most studies included only males.

In summary, anabolics in combination with training appear to increase lean body mass, but do not consistently increase muscle strength. To date, no effect has been found on exercise tolerance or quality of life, except in one study for sexual quality of life.

NEUROMUSCULAR ELECTRICAL STIMULATION

Neuromuscular electrical stimulation (NMES) is a technique aimed at externally stimulating contractions of peripheral muscles to improve peripheral muscle function in patients with severe COPD. It has been tested in COPD patients with severe peripheral muscle weakness and in bed-bound patients. To date, only five small controlled studies have used this technique in patients with COPD. In the study by NEDER *et al.* [43], NMES consisted of a symmetrical biphasic square pulsed current at 50 Hz with pulses of 300–400 μs using the highest tolerable amplitude (beginning with 10–20 mA at the start of the training session and increasing up to 100 mA). In the first week it was performed for 2 s on and 18 s off (10%), while at the end it was performed for 10 s on and 30 s off (25%). This training protocol was applied to each leg (15 min in the first week and 30 min thereafter), five times per week for 6 weeks (a total of 30 sessions). After 6 weeks, home-based programme patients showed significant improvements in muscle function, maximal and endurance exercise capacity, and dyspnoea. In addition, the improvements in muscle performance and exercise capacity correlated well with a decrease in perception for leg effort. BOURJEILY-HABR *et al.* [44] used a similar training programme of NMES consisting of sessions of 20 min, three times a week for 6 weeks. The authors found a significant improvement in both quadriceps and hamstrings muscle strength compared with the sham group. While there was no change in lung function and peak workload, the training group showed a significantly better shuttle walking distance [44]. ZANOTTI *et al.* [45] investigated, in a 28-day study, the additional benefits of NEMS with exercise training in bed-bound COPD patients receiving mechanical ventilation due to chronic respiratory disease. Adding NEMS resulted in an increase in muscle strength, a reduced respiratory rate and a decrease in the number of days spent in bed before able to get out of bed or the chair. VIVODTZEV *et al.* [46] showed that the combination of exercise training and NEMS led to a greater improvement in quadriceps strength and dyspnoea during performance of daily tasks in patients with very severe COPD with low body mass index. DAL CORSO *et al.* [47] investigated the effects of 6 weeks of high-frequency NMES (50 Hz) in 17 COPD patients (FEV_1 50% pred) compared with sham treatment in the quadriceps femoris. A modest increase in type Π cross-sectional area was found, which was not associated with increased muscle strength or walking capacity. Recently, a systematic review on the effects of NMES was performed based on the five previously discussed studies [48]. While significant increases were found for muscle peak torque and walking distance, the authors conclude that modest effect sizes following NMES in combination with a small number of included patients preclude firm evidence to apply this therapy as a standard therapy in COPD. They also conclude that the patients with less severe COPD might have less benefit by applying NMES.

In conclusion, at present there is not enough evidence to start NMES routinely in patients with COPD and further studies should focus on the optimal parameters of NMES and investigate which type of patient will have the most benefit from NMES. Nevertheless, the practice guideline of the European Respiratory Society/American Thoracic Society suggests that NMES may have beneficial effects in addition to exercise training especially in those COPD patients who have weak muscles [49].

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STATEMENT OF INTEREST

Statements of interest for both authors can be found at www.erj.ersjournals.com/site/misc/statements.xhtml

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