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Nonpharmacological treatment and relief of symptoms in COPD

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ABSTRACT: Evidence-based guidelines for chronic obstructive pulmonary disease (COPD) have recently been developed.

Nonpharmacological treatments have evolved rapidly as an essential part of COPD therapy. They are especially important as complementary interventions in severe or very severe disease, when there is loss in function, a reduction in quality of life and when psychological impairments further complicate the disease.

The present article discusses the most used nonpharmacological treatments for severe COPD patients (rehabilitation, long-term oxygen therapy, surgery, noninvasive positive pressure ventilation and supportive nutrition) and their evidence-based usefulness in promoting strategies that relieve symptoms.

All of these interventions are used during end-stage disease, to promote self-efficacy, relieve symptoms and prevent further deterioration. These therapeutic options support physicians and allied professionals in improving symptom management for their patients.

KEYWORDS: Dyspnoea, noninvasive mechanical ventilation, nutrition, oxygen, rehabilitation, thoracic surgery

Chronic obstructive pulmonary disease (COPD) affects 6–10% of the adult population and is a leading cause of morbidity and mortality worldwide [1]. Since the mid-1990s, evidence-based guidelines concerning the risk factors, pathogenesis, diagnosis and treatment of patients with COPD have been developed [2]. Disease severity and complications significantly influence the prognosis of these patients. In particular, the survival of COPD patients requiring intensive care unit (ICU) admission is reduced, and, in survivors, there are high levels of disability and reduced quality of life (QoL) [3, 4]. The ability to perform activities of daily living and QoL are often further complicated by psychological dysfunction.

In a Dutch study [5], severe and very severe disease, assessed by post-bronchodilator forced expiratory volume in one second (FEV_1), accounted for 15 and 3%, respectively, of physician diagnoses of COPD. In an Italian study of prevalence rate across the general population, Global Initiative for Chronic Obstructive Lung Disease (GOLD) [2] stages III and IV showed rates of 4.5 and 0.4%, respectively, in males and 2.2 and 0.3% in females [6]. A similar prevalence was reported in five cities of South America [7].

Pharmacological therapy accounts for a substantial part of the resources used in the long-term management of these patients [8], increasing with disease severity [9] and especially during acute exacerbations of COPD (AECOPD) [10]. However, nonpharmacological treatments have gained in popularity as an essential part of therapy, to promote self-efficacy and relieve symptoms. Such options also improve QoL and are cost effective [11, 12]. Current guidelines make only few recommendations regarding care that might be specific for the most severe patients with COPD [2]. Patients with severe COPD often

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require ICU admission due to complications, AECOPD and worsening of their status. The 6-yr mortality of COPD patients requiring admission to an ICU is high, with survivors showing a worse QoL did prior to their ICU admission [13]. Nonetheless, many patients remain self-sufficient and may benefit from patient-centred long-term therapeutic options, such as pulmonary rehabilitation (PR), long-term oxygen therapy (LTOT), surgery and noninvasive positive-pressure ventilation (NPPV), all of which have been effective when applied to a carefully defined population [14]. In the present article, the most important nonpharmacological treatments and strategies used to relieve symptoms in the subset of very severe or severe COPD patients, *i.e.* GOLD stages III and IV with chronic respiratory failure, are defined.

REHABILITATION

Patients with COPD demonstrate reduced levels of spontaneous physical activity compared with healthy controls. Furthermore, patients receiving LTOT exhibit an even lower level of domestic activity than those not receiving LTOT but with COPD of similar severity [15]. PR is an evidence-based multidisciplinary intervention comprising exercise training, education and psychological support, and aimed at reducing disability and improving QoL [16]. PR addresses exercise deconditioning, social isolation, altered mood states, such as anxiety and depression, muscle wasting and weight loss [17]. Table 1 shows the main components and appropriate location of PR delivered to severe and very severe COPD patients.

Regular physical activity may reduce lung function decline and risk of developing COPD in active smokers [18] and the risk of hospital admission in patients with established COPD [19]. Training the peripheral muscles counteracts the increased exercise-induced oxidative stress [20] and improves exercise capacity and dyspnoea [21]. In severe COPD, there is a close association between changes in a systemic and multidimensional index of performance and functional status (body mass index, airflow obstruction, dyspnoea and exercise capacity index) induced by PR and patient outcomes [22]. Several strategies have been suggested to maintain these benefits in the long term [23].

In a multicentric study of 1,047 COPD patients, PR improved outcomes in patients both with and without chronic respiratory failure [24]. Additionally, COPD patients in the ICU benefit from PR [25, 26]. A subgroup of very impaired, deconditioned, patients receiving long-term ventilation responded to whole-body and respiratory muscle training in terms of improving strength, weaning outcome and functional status [27]. The role of PR during an AECOPD remains unclear.

Transcutaneous neuromuscular electrical stimulation

Within the framework of PR, transcutaneous neuromuscular electrical stimulation (NMES) of the lower limb muscles increases muscular oxidative capacities [28]. Small controlled studies with this technique in severe and even bed-bound COPD patients have been reported [29–35]. NMES must be delivered according to specific protocols of intensity, frequency, duration and waveform of the stimulus in order to target optimal muscle response. The intensity of the electrical stimulus (*i.e.* amplitude) is related to the force developed by muscle contraction. The intensity of the stimulus is generally prescribed according to individual patient compliance or as a fraction of the amplitude inducing the maximal voluntary muscle contraction. Stimulus amplitudes of up to 100 mA are used most since they lead to muscle contraction being well tolerated. The stimulus duration is the total time of each electrical impulse and the pulse frequency is the number of stimuli per unit of time. The duration of groups (trains) of pulses and the interval between trains of pulses are also chosen. Additionally, as for any form of muscle training, the total duration of each session, number of training sessions per week and total training duration must also be specified. Clinical benefits of NMES have been demonstrated in patient populations other than COPD with a broad range of frequencies and session durations ranging from as few as 10–15 muscle contractions·day^{-1} up to 8–12 h continuous

TABLE 1 Main components and location of pulmonary rehabilitation for severe or very severe chronic obstructive pulmonary disease patients

	Ambulatory	Hospital	ICU
Muscle training	Upper/lower limb	Upper/lower limb	Upper/lower limb
	Assisted with O_2	Assisted with O_2 and/or NPPV	Assisted with O_2 and/or NPPV/IPPV
		Passively assisted by NMES	Passively assisted by NMES
	RMT	RMT	RMT
Chest physiotherapy	MATs	MATs	MeATs (IPV, in-/ex-sufflator)
Education	Self-care	Self-efficacy	Self-efficacy
			Assistance to relatives
			End-of-life decisions
Body composition	Assessment	Assessment	Assessment
		Nutritional implementation	Nutritional implementation
Psychosocial support	Selected cases	Selected cases	Assistance to relatives
		Assistance to relatives	End-of-life decisions

ICU: intensive care unit; NPPV: noninvasive positive-pressure ventilation; IPPV: invasive positive-pressure ventilation; NMES: neuromuscular electrical stimulation; RMT: respiratory muscle training; MAT: manually assisted technique; MeAT: mechanically assisted technique; IPV: intrapulmonary percussive ventilation.

stimulation·day^{-1} and 3–7 sessions·week^{-1} for periods ranging from 10 days to 6 weeks [36].

NMES has been used among patients with severe exercise limitation due to congestive heart failure (CHF), with skeletal muscle dysfunction similar to that found in COPD. NMES delivered to the quadriceps and calf muscles for 1 h·session^{-1}, 5 days·week^{-1} and 5 weeks at a frequency of 10 Hz and the maximal tolerated amplitude, without any additional exercise training, led to significant improvements in muscle mass, exercise tolerance and delay in reaching the anaerobic threshold [37]. NMES delivered at a frequency of 50 Hz and an amplitude chosen to induce muscle contractions at 25–30% of maximal voluntary contraction induced significant increases in the strength and cross-sectional area of the thigh muscles in CHF patients awaiting heart transplantation [38]. Subsequently, additional studies have confirmed the benefits of NMES in CHF patients [39, 40].

A number of studies have evaluated NMES in severe COPD patients with significant baseline exercise impairment [30–34]. The electrical stimulus frequency ranged 10–50 Hz. In a randomised controlled double-blind trial of NMES of the quadriceps and calf muscles in stable outpatients with severe COPD, poor baseline exercise tolerance and low ventilatory reserve, NMES led to a significant improvement in maximum quadriceps and hamstring strength, an increase in incremental shuttle walking test distance and reductions in dyspnoea, compared with a sham-treated group [31]. NEDER *et al.* [30] randomised severely breathless COPD patients to either 6 weeks of NMES of the leg muscles or a 6-week control (no NMES) period before undergoing NMES. NMES induced significant improvements in maximal isokinetic strength, a reduction in muscle fatigue and an increase in exercise capacity with improved exercise-related dyspnoea. Patients undergoing AECOPD during the study period were able to continue NMES. Recently, malnourished COPD patients and those with severe deconditioning following hospitalisations due to AECOPDs achieved greater improvements in leg muscle strength and dyspnoea during daily activities following treatment for 4 weeks with NMES and usual rehabilitation compared with usual rehabilitation alone [33]. In the study of ZANOTTI *et al.* [32], the effects of NMES were evaluated in bed-bound COPD patients with chronic hypercapnic respiratory failure receiving mechanical ventilation. NMES added to active limb mobilisation significantly improved muscle strength, respiratory frequency and the time required to transfer from bed to chair compared with active limb mobilisation alone [32].

The major advantage of NMES is considered to be the lack of ventilatory stress during passive muscular activity, due to the reduced muscle mass involved. Furthermore, NMES may be used even after an AECOPD, a condition associated with loss of muscle strength and mass [33]. It is theoretically worthwhile to attempt NMES during an AECOPD, but studies are required to confirm this before it can be advised. However, there are negative studies in which no significant change in neurophysiological aerobic performance or clinical status occurred following electrostimulation [35]. Therefore, the studies on NMES must be considered preliminary, and this innovation should still be considered an experimental tool in PR.

OXYGEN

LTOT is one of the main treatments for patients with advanced COPD suffering from chronic respiratory insufficiency. The primary goal of LTOT is to increase the baseline arterial oxygen tension (P_{a,O_2}) to $\geqslant$7.9 kPa ($\geqslant$60 mmHg) at rest. LTOT administered continuously (>15 h·day^{-1}) to hypoxaemic COPD patients increases survival [41, 42]. It is generally introduced in severe COPD and implemented according to international recommendations [43, 44]. The prescription of LTOT should always include the source of supplemental oxygen (gas or liquid), method of delivery, duration of use, and flow rate at rest and during exercise and sleep. Oxygen therapy during exercise in patients normoxaemic at rest improves exercise endurance and dyspnoea [45–48], but may not have a direct enduring effect on exercise capacity. Despite previous studies of COPD patients trained while using supplemental oxygen failing to demonstrate benefits [49–51], supplemental oxygen during exercise training may enable individuals with COPD to tolerate higher levels of exercise activity with fewer exertional symptoms, ultimately improving their QoL, although larger studies are required in order to establish its effect on functional outcomes [52]. A randomised study failed to find an advantage in QoL of ambulatory oxygen over placebo in COPD patients who did not meet the criteria for mortality reduction with LTOT, thus not supporting the general off-label application of this treatment in patients not meeting recognised criteria for LTOT [53].

Supplemental home oxygen is a costly component of outpatient therapy for adults with COPD [54]. Healthcare systems in many countries include public funding of LTOT for eligible applicants [55]. The role of LTOT and of acute oxygen supplementation during an AECOPD are described elsewhere in the current series [56].

SURGERY

Surgical interventions for end-stage COPD are likely to be of value in only a small percentage of patients. Nevertheless, there are specific indications that, when added to PR, they result in further advancement of exercise capacity and QoL.

Bullectomy

Bullectomy is an established surgical procedure for bullous emphysema. By removing a large bulla that does not contribute to gas exchange, the adjacent lung parenchyma is decompressed. Nowadays, bullectomy can also be performed as a thoracoscopic procedure. In carefully selected patients, this procedure is effective in reducing dyspnoea and improving lung function [57]. In considering the possible benefit of surgery, it is important to estimate the effect of the bulla on the lung and the function of the remaining (nonbullous) lung. Some investigators have recommended that the bulla occupy $\geqslant$50% of the hemithorax and produce definite displacement of the adjacent lung before surgery can be recommended [58].

Lung volume reduction surgery

Lung volume reduction surgery (LVRS) is a surgical procedure in which parts of the lung are removed, to reduce hyperinflation, making respiratory muscles more effective by improving their mechanical efficiency and improving overall gas exchange [59–62]. In centres with adequate experience, the

perioperative mortality of LVRS has been reported to be <5% for both median sternotomy and thoracoscopy [63].

LVRS in an unselected population with severe COPD had no effect on mortality, and, in patients with an FEV1 and diffusing capacity of the lung for carbon monoxide of <20% of the predicted value, there was an increased risk of death [64], whereas, in selected patients with upper lobe disease and a low exercise capacity, LVRS improved mortality, exercise capacity and QoL [65, 66]. LVRS reduces the frequency of COPD exacerbations and increases the time to first exacerbation. One explanation for this benefit may be the post-operative improvement in lung function [67].

Given the increased risk of such procedures among patients with the most severe disease, alternatives have been studied. These include bronchoscopic LVRS and endobronchial valve placement [68, 69]. Both have shown preliminary results in which improvements in exercise capacity and dynamic hyperinflation have been reported [70]. Given the cost-effectiveness of LVRS, it is still considered a palliative surgical procedure for patients with advanced COPD [71]. Experimental studies of biological lung volume reduction, using biological reagents to remodel and shrink damaged regions of the lung, are encouraging for patients with advanced heterogeneous emphysema [72]. All of these techniques are promising, but have not been studied thoroughly to date.

Lung transplantation

Lung transplantation (single or double) is an option for a more limited number of patients, with highly impaired lung function, hypercapnia and secondary pulmonary hypertension [73]. A COPD patient may be considered for transplantation when FEV1 is <25% pred and/or arterial carbon dioxide tension (P_{a,CO_2}) $\geq$7.2 kPa ($\geq$55 mmHg) [74]. Despite the progress since the early 1980s, the short- and long-term outcomes of lung recipients are not as good as those for other solid organs [75]. Pulmonary function improves, but exercise capacity may still be limited due to peripheral muscle dysfunction [76, 77]. PR further improves exercise and QoL after lung transplantation [78]. According to the International Society for Heart and Lung Transplantation's registry, survival for emphysema is 85.7% at 1 yr and 68.3% at 3 yrs [79], significant complications still impair survival [80].

NPPV

NPPV, delivered by nasal or face mask, avoids the risks associated with invasive ventilation. It assists ventilation by improving inspiratory flow rate, correcting hypoventilation, resting respiratory muscles and resetting the central respiratory drive [81]. The benefits of NPPV in stable patients are equivocal, with little evidence to support NPPV in addition to LTOT in the treatment of chronic hypercapnic COPD [82]. Two large multicentric trials have focused on NPPV in this population [83, 84]. One trial [83] indicated that there was no overall survival benefit from NPPV plus LTOT, despite a slight improvement in survival for patients aged >65 yrs. An Italian 2-yr multicentric trial showed that NPPV plus LTOT improved daytime P_{a,CO_2}, dyspnoea and QoL, although survival was similar to that in the control (LTOT alone) group [84]. In this and another observational controlled study [85], ICU admissions were reduced during NPPV compared with the LTOT regimen. In one randomised controlled study, home nocturnal NPPV, added to daytime exercise training, significantly increased exercise capacity and QoL compared with exercise training alone [86].

In a systematic review of short- and long-term NPPV in stable hypercapnic COPD patients, 15 studies met the inclusion criteria, six randomised trials and nine nonrandomised controlled trials, with no improvements identified in the former. Hyperinflation and diaphragmatic work of breathing were reduced in a subset of patients. Therefore, although NPPV may have an adjunctive role in the management of chronic respiratory insufficiency through attenuation of compromised respiratory function and improvement in health-related outcomes, there is little evidence supporting its use in the routine management of stable hypercapnic COPD patients [87]. Reported inconsistency in the effectiveness of all assessed outcomes may be due to the variability in degree of lung hyperinflation, differences in severity of hypercapnia, and in the setting and duration of use of ventilatory support.

NPPV as a coadjuvant of PR

In the most compromised patients, extreme breathlessness and muscle fatigue limit training at the highest levels of exercise intensity prescribed in PR programmes. Increased inspiratory muscle work also contributes to dyspnoea and exercise limitation [88]. NPPV during exercise reduces dyspnoea and increases exercise tolerance [29, 89, 90]. Inspiratory support provides symptomatic benefit by unloading the ventilatory muscles, and continuous positive airway pressure counterbalances the intrinsic positive end-expiratory pressure. Nevertheless, the role of assisted ventilation during exercise training remains controversial, since its beneficial effects are inconsistent compared with unassisted training alone [91–93]. Larger prospective controlled studies are required in order to better define the role of ventilatory support in COPD [94]. Furthermore, it has been reported that, in chronic hypercapnic COPD under long-term ventilatory support, high-intensity NPPV can also be administered during walking, with ventilator settings unchanged compared with those used at rest, resulting in improved oxygenation, decreased dyspnoea and increased walking distance. Therefore, NPPV during walking could prevent hypoxia-induced complications [95].

NPPV in AECOPD

AECOPD are important events in the natural course of the disease [96], leading to deterioration in lung function and QoL [97, 98], and, when associated with acute ventilatory failure, severe short- and long-term prognosis [3, 99]. Frequency of AECOPDs increases with disease severity, as represented by airflow obstruction [100], although the relationship between AECOPD frequency and severity of airflow obstruction is not particularly close and new evidence indicates a possible role of extrapulmonary factors in the genesis of exacerbation [101]. Indeed, the most severe COPD patients, especially those with several comorbid conditions, are prone to more severe exacerbations and are likely to require hospital admission, especially during the winter months, when respiratory viral infections are common [102].

The pharmacological management of AECOPDs is described elsewhere in the current series [56]. Stepwise drug therapy is recommended for both home and hospital management. Hospital management includes proper assessment of severity, diagnosis of cause, controlled oxygen therapy and/or mechanical ventilation with an early noninvasive approach as first line of intervention [103]. A very severe life-threatening episode requires direct admission into the ICU. Several prospective randomised controlled studies, systematic reviews and meta-analyses show a good level of evidence for clinical efficacy of NPPV in the treatment of acute-on-chronic respiratory failure due to AECOPD [104]. Compared with standard medical therapy alone, NPPV improved survival, reduced the need for endotracheal intubation and the rate of complications, and shortened the hospital and ICU length of stay. Based on these observations, NPPV has been proposed as the first-line ventilatory strategy in this condition, with different timing and location according to acute respiratory failure severity [105].

NPPV in palliative care

NPPV is an alternative to invasive ventilation for symptom relief in end-stage COPD [106–108], and a recent European survey of respiratory intermediate care units reported a frequency of use and its role in almost a third of patients among those with poor life expectancy [109]. NPPV reduces dyspnoea even in the absence of hypercapnic respiratory failure [110]. The Society of Critical Care Medicine has recently charged a task force with the development of an approach for considering use of NPPV in patients who choose to forgo endotracheal intubation. In acute respiratory failure, this can be classified as follows: 1) NPPV as life support with no preset limitations on life-sustaining treatments; 2) NPPV as life support when patients and families have decided to forgo endotracheal intubation; and 3) NPPV as a palliative measure when patients and families have chosen to forgo all life support and receive only comfort measures. The goals of NPPV use and parameters for success and failure should be discussed by experienced personnel in appropriate healthcare settings [111].

NUTRITIONAL STATUS

Survival studies have consistently shown significantly greater mortality rates in underweight and normal-weight than in overweight COPD patients [112, 113]. Hospitalisation is associated with negative energy balance and further deterioration in nutritional status [114]. The association between underweight and mortality in COPD patients remains significant after adjusting for possible confounders, such as FEV_1 [115]. This observation is common to chronically ventilated hypercapnic COPD patients with a body mass index of <20 kg·m^{-2} [116]. In particular, muscle wasting and depletion is a common problem in COPD patients [117], and it is mainly caused by an imbalance between low-energy intake and high-energy requirements [118].

Nutritional implementation

Nutritional implementation may improve survival since a gain in body weight and muscle mass and strength has been associated with better exercise tolerance and survival [119, 120]. The pharmacological approach, such as use of anabolic steroid, growth hormone or testosterone supplementation, has been disappointing to date [114, 121, 122].

Nutritional support is also important for patients whom it is difficult to wean from mechanical ventilation in the ICU [123]. Specific nutritional deficiencies, such as hypophosphataemia [124] and impaired lipid synthesis [125], can also be associated with acute respiratory failure and with an abnormal increase in fat mass, respectively. Patients often complain of dietary problems, such as ''anorexia'', ''dyspeptic symptoms'', ''slimming'', ''fear of gaining weight'', ''dyspnoea'', ''diarrhoea'' and ''depression, anxiety, solitude'', which may interfere with energy intake [126].

The oral dietary intake should be carefully evaluated in long-term ventilated tracheostomised COPD patients, who often report swallowing dysfunction due to tracheostomy *per se* and/or multiple associated factors, which include things such as acute illness, medications, such as steroids, neuromuscular blocking agents and general sedatives, prolonged inactivity of swallowing muscles and injury arising from endotracheal intubation [127]. In some such patients, meals may increase respiratory frequency, end-tidal carbon dioxide tension and dyspnoea [128].

Oral or tube feeding enable nutritional intake to be maintained or increased when the normal intake is inadequate. In COPD patients, enteral nutrition in combination with exercise and anabolic pharmacotherapy has the potential to improve nutritional status and function. Frequent small meals are preferable, in order to avoid post-prandial dyspnoea and satiety [129]. However, a meta-analysis provided no evidence that nutritional support had a significant effect on anthropometric measures, lung function or exercise capacity in patients with stable COPD [130].

INTERVENTIONS TO IMPROVE SYMPTOMS AND NEUROPSYCHOLOGICAL FUNCTIONS

Dyspnoea

Dyspnoea is the most important complaint in severe COPD. It is mainly evoked by exercise but may also be present at rest, especially during the AECOPD of end-stage disease, and can be incapacitating. Several strategies may be considered and have recently been described elsewhere [131, 132]

Drug therapy

The most effective treatments for dyspnoea are bronchodilators, although a nonpharmacological approach such as LVRS may also improve dyspnoea. In end-stage disease, one option may also be to reduce ventilatory demand by decreasing the central drive with opiates. These have been shown to decrease minute ventilation at rest and during submaximal exercise, thus reducing the sensation of breathing and its associated anxiety [133]. There is also speculation that opiates act directly on opioid receptors in the airways [134]. Therapeutic doses of opioids induce collateral effects, such as peripheral vasodilation and baroreceptor response inhibition, which need to be carefully evaluated. Despite safety concerns, these drugs have a place in the management of patients in the terminal phase of their disease.

It has recently been reported that epidural methadone infusion at chest level can effectively improve dyspnoea, exercise

capacity and QoL, without deterioration in respiratory control or lung function [135]. No consistent improvement in dyspnoea over placebo has been shown with anxiolytics, although statement guidelines on dyspnoea still recommend ''a trial of anxiolytic therapy on an individual basis'' [136].

Breathed mixtures

Hypoxia contributes to dyspnoea by stimulating minute ventilation. Supplemental oxygen during exercise reduces exertional breathlessness and improves exercise tolerance in hypoxaemic COPD patients by reduced hypoxic stimulation of the carotid bodies, pulmonary vasodilation and an increase in P_{a,O_2} [137]. Reduced hyperinflation also plays an important role in the oxygen-related relief of dyspnoea [138]. Reducing the gas density with heliox has also been shown to reduce ventilation and improve exercise capacity [139]. The reduction in ventilation improves expiratory flow and reduces dynamic hyperinflation, thereby decreasing the operational lung volume and reducing the work of breathing [140].

Psychological consequences and cognitive status

Psychological complaints or mental disorders are often overlooked and rarely treated in these patients, since they are regarded as complications of the pulmonary disease [141]. In countries such as the UK, the prevalence of depression in COPD is estimated to be 40%, and there is a suggestion that anxiety symptoms may have a prevalence of up to 36% [142]. Severe COPD patients experience a greater prevalence of depression compared with patients with mild or moderate disease [143, 144]. Other studies show that, despite treatment, many patients still meet criteria for a depressive and/or anxiety picture [145].

Evidence for the benefit of antidepressant therapy in older COPD patients with depression is inconclusive [146]. Studies with the selective serotonin reuptake inhibitors fluoxetine and paroxetine were unsuccessful in COPD patients [147, 148]. These studies identified the difficulties in treating frail and elderly COPD patients with antidepressants. In light of this, clinicians, caregivers and patients should be careful in the prescription and consumption of benzodiazepines due to the risk of precipitating a severe episode of hypercapnia.

KUNIK *et al.* [149] found a significant improvement in anxiety and depression scores with cognitive behavioural therapy compared to education alone. PR improves depression and anxiety in some COPD patients [150–152], but not all PR programmes include psychological therapy for those patients with high levels of depression and anxiety symptoms.

Neuropsychological function

Few studies have examined the neuropsychological complications associated with end-stage pulmonary disease. COPD patients surviving acute-on-chronic respiratory failure and requiring mechanical ventilation suffer worsened cognitive function than stable COPD patients on LTOT who have never previously required ICU admission. After discharge, their cognitive status may improve to levels similar to those of stable COPD patients on LTOT [153]. In one study, more than half of the end-stage COPD patient candidates for lung transplantation suffered from impaired immediate free recall and consistent long-term retrieval deficits, whereas fewer of these patients suffered from deficient long-term retrieval [154].

CONCLUSIONS

Severe chronic obstructive pulmonary disease is a clinical and resource burden [1]. The literature concerning the healthcare needs of patients in the end stage of chronic obstructive pulmonary disease is sparse, and there is no commonly accepted definition of their healthcare needs [155]. Despite a poor prognosis, such patients still benefit from most of the nonpharmacological interventions. Symptom relief and meaningful improvement in quality of life are the main goals of treatment. Treatment interventions, even for chronic obstructive pulmonary disease patients with end-stage disease, are designed to promote self-efficacy, relieve symptoms and prevent further deterioration. The above therapeutic perspectives should assist healthcare professionals in addressing the clinical challenges associated with severe chronic obstructive pulmonary disease.

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