



Managing severe COPD

Much can be done

Key points

- Management of patients with severe COPD is challenging, but with a combination of therapeutic approaches much can be achieved.
- Pulmonary rehabilitation may improve symptoms and quality of life and reduce exacerbations in patients at all stages of disease severity.
- Detecting and managing comorbidities, including cardiac disease, osteoporosis, anxiety and depression, are important in improving patient outcomes.
- Oxygen therapy improves prognosis in patients with chronic hypoxaemia.
- Noninvasive ventilation is useful in managing acute hypercapnic exacerbations of COPD.
- Clear communication focusing on likely disease trajectory, prognosis, goals of care and advance care planning is essential.
- Patients with very severe COPD may require palliative care, ideally provided by their usual care providers, but some patients require specialist palliative care referral.

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Severe COPD may be challenging to manage as patients often experience debilitating symptoms that fail to respond completely to disease-specific treatment. Clear communication about the goals of care combined with management of symptoms and comorbidities should enable patients to enjoy a better quality of life.

Chronic obstructive pulmonary disease (COPD) is a common and progressive disease associated with significant morbidity and mortality. Access Economics estimated in 2008 that more than one million Australians had moderate COPD, with a further 150,000 having severe COPD.¹ A careful history and clinical examination may suggest a diagnosis of COPD, but they do not reliably predict airflow obstruction and spirometry is essential to confirm the diagnosis.

COPD is defined as severe in spirometric terms when the postbronchodilator forced expiratory volume in 1 second (FEV₁) is less than 40-50% predicted,^{2,3} with very severe disease defined by a post-bronchodilator FEV₁

less than 30% predicted.³ Although the FEV₁ correlates well with prognosis, the degree of airflow obstruction alone may be poorly predictive of symptoms. Guidelines recommend assessing symptom burden (especially the degree of dyspnoea), degree of activity limitation and frequency of exacerbation, along with FEV₁, when determining treatment needs.³

This article discusses the management of patients who are severely symptomatic with an FEV₁ at the 'very severe' or 'severe' end of the COPD spectrum. The specific management of acute exacerbations of COPD has been discussed in the article 'COPD exacerbations – improving outcomes', published in the April 2013 issue of *Medicine Today*,⁴

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although the use of acute noninvasive ventilation for hypercapnic exacerbations is discussed briefly here.

MANAGING SYMPTOMS IN SEVERE COPD

Patients with very severe COPD may have symptoms as debilitating as those with advanced cancer.⁵ A cardinal feature of very severe COPD is profound dyspnoea. Cough, fatigue, poor social functioning, high rates of depression and anxiety and poor quality of life are also prominent symptoms.^{6,7} Carers of people with very severe COPD also have significant morbidity.⁷ Despite intensive treatment, disease-specific symptom relief may be inadequate and many patients receive inadequate palliative care.⁸

Throughout the range of disease severity, treatments for COPD are largely directed at:

- improving symptoms
- preventing deterioration, notably through reducing exacerbations, with their known impact on disease progression and quality of life.

Both nonpharmacological and pharmacological therapies have a role.

NONPHARMACOLOGICAL THERAPIES

Smoking cessation

In patients with mild-to-moderate COPD, smoking cessation reduces lung function decline and mortality⁹ and improves respiratory symptoms and health-related quality of life.¹⁰ Although similar long-term studies are not available in those with severe COPD, health benefits are likely from smoking cessation at all stages of the disease, and counselling (with additional pharmacotherapy if needed) should be offered to all patients.

Physical activity and pulmonary rehabilitation

Patients with COPD typically reduce their participation in activities that induce breathlessness and fatigue; none more so than those with very severe disease.

Continued limitation of daily activities and worsening symptoms (despite reduced activities) induces deconditioning. This results in an ongoing dynamic of symptoms affecting activities, and vice versa, often referred to as the 'dyspnoea spiral' or downward cycle of deconditioning with worsening symptoms and further restriction of activity.

Regular physical activity is recommended for all people with COPD, and has been associated with reduced hospital admissions.¹¹ Pulmonary rehabilitation is an evidence-based, multidisciplinary program involving graded exercise, education, behaviour modification and psychosocial support, typically provided on an outpatient basis, two or three times weekly over six to eight weeks. Pulmonary rehabilitation improves dyspnoea, exercise capacity and health-related quality of life as well as improving symptoms of anxiety and depression and reducing health care utilisation.¹²

Although patients may be hesitant to consider exercise when their dyspnoea is severe, support from their primary care physician is key,¹³ and even patients with very severe COPD can achieve benefits. Pulmonary rehabilitation programs in Australia are generally run through hospital outpatient departments or community health centres. Information about local programs can be obtained through Lung Foundation Australia's website (<http://lungfoundation.com.au>).

Vaccination

Influenza vaccination reduces acute exacerbation of COPD, although its effect on health care utilisation and mortality is unclear. Guidelines recommend yearly influenza vaccinations and up-to-date pneumococcal vaccination for all people with COPD.²

PHARMACOTHERAPY

Inhaled therapies

Titration of inhaled therapy for COPD is recommended using a stepwise approach

to enable evaluation of each additional medication before adding another and to minimise side effects.^{2,3} Treatment should be based on the patient's symptoms, exacerbation risk and response until, ideally, adequate disease control is achieved. Short-acting beta agonists (SABAs) or anticholinergics (SAMAs) are effective in providing acute symptom relief,^{14,15} while longer-acting beta agonists (LABAs)^{16,17} or anticholinergics (LAMAs)¹⁸⁻²¹ may improve quality of life and reduce exacerbation frequency.

The inflammatory response in COPD is relatively corticosteroid-insensitive. Although inhaled corticosteroids may reduce exacerbation frequency and decline in quality of life when prescribed in combination with LABAs for patients with FEV₁ less than 50% predicted and frequent exacerbations (two or more in 12 months), the improvement over LABA alone is of questionable significance. In addition, benefits need to be weighed against the known increased risk of pneumonia with their use.²² There is some evidence that the combination of a LAMA and LABA is better than either monotherapy.²³ However, evidence for triple therapy (LABA, LAMA and inhaled corticosteroid) is conflicting. It is important to note that using more than one agent from each class does not confer additional benefit and should be avoided, suggesting the need for careful and regular review of patients' pharmacotherapy.

When changing pharmacotherapy, the clinician should consider treatment response in terms of dyspnoea, functional status, history of exacerbations and patient preference. In an individual with severe COPD, decisions about which therapies to continue will likely be based on various factors, including:

- severity of symptoms
- frequency of exacerbations with or without the need for hospitalisation
- device preference
- adverse effects
- potential long-term benefits

- other comorbidities and their treatments
- cost and minimisation of polypharmacy.

Longer-term therapeutic trials are needed to determine the impact of changing therapies on exacerbations.

Inadequate device use is very common in patients with COPD, and many primary care as well as specialty physicians and nurses are inadequately equipped to instruct patients in proper inhaler use.²⁴ Health professionals should ensure they are capable of instructing patients and caregivers on inhaler use, and review should be repeated at each visit to ensure maintenance of proper technique.²⁴

Other therapies

Unfortunately, patients with severe COPD may continue to experience significant symptoms despite the use of evidence-based therapies. Theophylline is considered a third- or fourth-line bronchodilator because of its narrow therapeutic window and significant side effects. Although it may be helpful in some individuals with severe COPD, its role in patients who are already receiving various combination therapies is unclear.

Mucolytic drugs may be beneficial in decreasing sputum viscosity and reducing disability and exacerbations, but their role in patients who are already receiving inhaled corticosteroids is, similarly, unclear.²⁵

MANAGING SYSTEMIC EFFECTS AND COMORBIDITIES

COPD is often associated with comorbidities, many of which share common systemic inflammatory features with COPD. Most common among these are systemic hypertension, dyslipidaemia, diabetes, coronary heart disease, heart failure and osteoporosis.

Some of the management principles described above can also be applied to preventive and therapeutic interventions for these common comorbidities. Smoking

cessation, exercise and rehabilitation all have the potential to benefit a range of chronic diseases. Specific treatments such as the use of statins to manage hyperlipidaemia have provoked considerable interest because of studies suggesting they may have beneficial effects in patients with COPD over and above their impact on cardiac risk.²⁶ Prospective studies are awaited.

Cardiovascular disease

Cardiovascular disease is the most frequent and important of all COPD comorbidities and may contribute significantly to disease burden. Beta blockers have proven mortality benefits in the management of cardiac disease but their use is limited in patients with COPD because of their potential to cause acute bronchospasm, increase airway hyper-responsiveness and worsen respiratory symptoms. Concerns have been allayed to some extent by a recent meta-analysis suggesting that cardioselective beta blockers are safe in patients with COPD, even in those with severe airflow obstruction.²⁷ Nonetheless, the included studies were of short duration and the absolute numbers included were small, thus providing little guidance about long-term safety and potential morbidity. European Society of Cardiology guidelines state that COPD is not a contraindication to the use of beta blockers; however, low-dose initiation and gradual up-titration is recommended.²⁸

Osteoporosis

Osteoporosis is a major comorbidity in COPD and patients are at increased risk even in the absence of corticosteroid use. Although no clear association has been demonstrated between the inhaled corticosteroids most commonly used in Australia and increased bone fragility, regular courses of oral corticosteroids will further increase osteoporosis risk. Index of suspicion should be high and treatment should proceed according to standard guidelines.

Anxiety and depression

Patients with COPD have an increased prevalence of both anxiety disorders and depression compared with the general population. These conditions increase disability and social isolation and impair functional status, resulting in reduced quality of life and poorer prognosis.

Standard management principles apply, although evidence for the effectiveness of specific pharmacotherapy is limited in patients who also have COPD and further clinical trials are needed.³ Exercise in the context of pulmonary rehabilitation has proven beneficial in management.²⁹

Other comorbidities

Other comorbidities that may compromise survival and add considerably to the overall burden of COPD include diabetes mellitus, hypertension and vasculopathy, as well as systemic consequences of COPD, such as weight loss and muscle dysfunction due to inactivity and deconditioning. The metabolic and vascular issues should be investigated and treated appropriately, and pulmonary rehabilitation is again important in managing the consequences of inactivity and deconditioning.

Although low body weight is associated with a poorer prognosis, and nutritional advice should be provided, the effects of nutritional supplementation in underweight patients with COPD have been disappointing.³⁰ In the absence of guidelines for the management of multimorbidities, other comorbidities should be managed according to relevant disease-specific guidelines.

OXYGEN THERAPY

Long-term continuous oxygen therapy

Oxygen therapy may be appropriate in patients with severe COPD for the management of hypoxaemia. When PaO₂ is 55 mmHg or below, or PaO₂ is 59 mmHg or below in the presence of pulmonary hypertension, right heart failure or

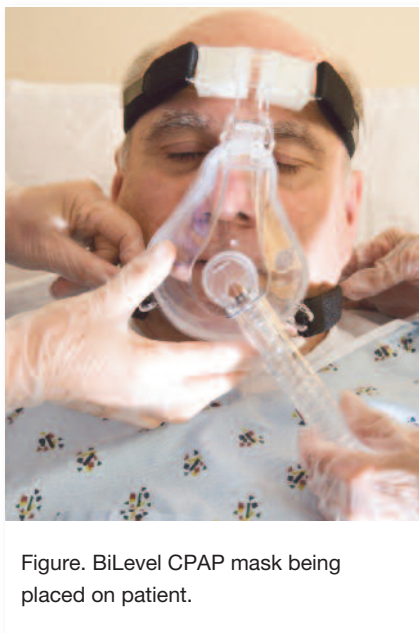


Figure. BiLevel CPAP mask being placed on patient.

polycythaemia, continuous oxygen therapy for at least 15 hours per day (or as long as 24 hours, if tolerated) has been shown to prolong life.^{31,32}

Right heart failure presenting as ankle oedema or raised jugular venous pressure in a patient with COPD should flag the need for arterial blood gas measurement. Other indicators suggesting a need for measurement of arterial blood gases include the presence of cyanosis or polycythaemia, known very severe COPD with FEV₁ less than 30%, and pulse oximetry reading less than 92%.³ Australian guidelines recommend oxygen therapy should only be provided to those who have ceased smoking.³³

In patients with COPD, low flow rates of oxygen (2 L/minute) via nasal cannula are generally sufficient to raise oxygen saturations to satisfactory levels and there is usually no requirement to increase flow rates nocturnally.³⁴ It is important to explain to patients that the indication for long-term oxygen use is the presence of hypoxaemia but that there may be no improvement in dyspnoea through its use. In addition, a recent randomised controlled trial found no benefit over

placebo air in terms of breathlessness for patients who are not hypoxic.³⁵

Ambulatory oxygen

Ambulatory oxygen may be used for patients with COPD requiring continuous oxygen in order to maximise relief of hypoxaemia throughout the 24-hour period and to increase mobility. Portable cylinders are available through a range of government-supported schemes (which vary between states and territories)³⁶ and are generally used with a conservation device. Generally, portable oxygen concentrators are not provided through government-subsidised programs, but many patients find the concept of these light-weight, battery-operated devices, attractive, even though they are expensive. It is, as yet, unclear what role they offer in terms of long-term oxygen use.

Although laboratory-based studies have shown that supplemental oxygen can reduce ventilation and improve exercise capacity in breathless patients with COPD who do not fulfil criteria for the requirement of continuous oxygen therapy, use of oxygen in the ambulatory setting for relief of breathlessness is of questionable benefit. A recent large, randomised controlled trial demonstrated no benefit of oxygen therapy over medical air in relieving breathlessness or improving exercise capacity or quality of life.³⁷ The indistinguishable benefits over the period of the study of both oxygen and air raise the possibility that inhaled therapy with either gas provides a powerful placebo effect.

Nocturnal oxygen therapy

Hypoxaemia may occur during sleep in patients with severe COPD due to hypoventilation or worsening ventilation-perfusion. Clinical consequences of isolated nocturnal hypoxaemia are unknown and results of clinical trials of nocturnal oxygen therapy in such patients have been contradictory. Further studies are needed, but current consensus suggests

that nocturnal oxygen therapy may be indicated in patients whose nocturnal arterial oxygen saturation repeatedly falls below 88% or who have evidence of hypoxia-related sequelae. Any contributing factors such as obstructive sleep apnoea or cardiac failure must first have been treated optimally.

NONINVASIVE VENTILATION

Noninvasive ventilation (NIV) is any form of ventilatory assistance delivered without the need for an endotracheal tube.³⁸ It consists of an electronically powered device, fitted to the patient via a mask, which provides ventilatory support. Some authors include continuous positive airways pressure (CPAP), in this definition, while others include only BiLevel CPAP (Figure). CPAP provides a single pressure throughout the respiratory cycle whereas BiLevel CPAP alternates between two pressures; a higher pressure at inspiration and a lower pressure at expiration. Most BiLevel devices have the capacity to respond to the patient's respiratory efforts or to provide extra 'breaths' if the patient's respiratory rate is low.

NIV in acute respiratory failure

NIV plays a key role in the routine management of patients with acute hypercapnic respiratory failure requiring ventilatory support due to acute exacerbations of COPD. Before the availability of NIV, such patients often required invasive ventilation in the ICU, with consequent poor acute outcomes. Used in combination with other treatments for acute exacerbations of COPD, NIV is clearly superior to intubation in terms of mortality, morbidity and length of stay.^{39,40} In addition, complications associated with intubation, such as ventilator-associated pneumonia, are much reduced.^{39,40} NIV can be delivered outside the ICU setting and may be a more agreeable option for patients compared with intubation as they are able to eat, talk and receive physiotherapy during

the period of NIV support. The utility of NIV in relieving breathlessness is less certain.⁴¹

NIV in chronic respiratory failure *NIV in overlap syndrome*

Both obstructive sleep apnoea (OSA) and COPD are common diseases, and the occurrence of both in a single patient is termed the 'overlap syndrome'. The morbidity and mortality of the overlap syndrome is greater than that of either COPD or OSA alone.⁴² A recent observational trial of CPAP in patients with overlap OSA/COPD found decreased hospitalisations and mortality in the treated group.⁴³

The impact of coexistent OSA on the natural history of COPD is not yet known. When evaluating a patient with either OSA or COPD, a high index of suspicion is crucial to diagnose the overlap syndrome. Daytime hypercapnia and pulmonary hypertension out of proportion to the severity of the disease in patients known to have only one disease (either OSA or COPD) should prompt assessment for the other disorder. Currently, CPAP (with oxygen therapy as needed) is the treatment of choice for the overlap syndrome.

Home nocturnal NIV in COPD

Patients with severe COPD may develop significant oxygen desaturation and hypoventilation nocturnally.^{44,45} Respiratory muscle fatigue is believed to contribute to both gas exchange abnormalities and symptoms, and some studies have found both sleep and respiratory failure parameters are improved by domiciliary nocturnal NIV.^{46,47} However, the reported impact on daytime function, breathlessness, quality of life and mortality of home-delivered nocturnal NIV has been contradictory. For instance, a large Australian trial found that although nocturnal NIV improved survival, this was at the expense of decreased quality of life, tempering enthusiasm for the use of NIV in this population.⁴⁸ The decision

to initiate chronic nocturnal NIV remains contentious and is generally made by specialist providers, often following an inpatient admission for acute hypercapnic respiratory failure. Ongoing research is required to delineate the role of NIV for COPD in the home setting.

SURGERY AND DEVICES

Occasional patients with severe, disabling COPD may be suitable for consideration of lung transplantation (younger patients with fewer comorbidities), whereas those who have predominant upper lobe emphysema with marked hyperinflation or 'gas trapping' may benefit from lung volume reduction surgery. Alternative nonsurgical approaches include a type of 'bronchoscopic lung volume reduction'. Discussions about such highly specialised palliative approaches necessitate referral of patients to a specialist centre.

ADVANCE CARE PLANNING IN COPD

Advance care planning (ACP) is the process by which patients, families and health professionals discuss and establish future goals of care according to the patient's values and preferences. It includes clarifying a patient's understanding of their illness and treatment options, identifying their wishes and appointing a substitute decision maker.^{49,50} It is an ongoing process, and decisions may change as COPD progresses.

ACP can improve patient and family satisfaction with care,^{49,50} limit burdensome treatment at the end of life in line with patient preferences,^{49,50} and reduce stress, anxiety and depression in surviving relatives.⁵¹ Many patients with COPD and their families want information about the diagnosis, its likely progress and prognosis and what dying might be like, and they want to participate in ACP.⁵² Despite this, many patients with advanced COPD lack knowledge about the disease and its likely time course and may be unaware that the disease will progress and may be fatal.⁵³

Patients expect their doctors to initiate conversations about ACP,^{54,55} and appreciate it when they do. Some doctors may find these conversations difficult, and may be unsure as to how to get started. The Victorian Quality Council has recently developed 'The Next Steps' program to assist doctors in undertaking ACP conversations. Materials including videos of patient scenarios and access to a patient ACP e-simulation are available on the council's website (<http://www.health.vic.gov.au/qualitycouncil/activities/training.htm>).

PALLIATIVE CARE

Definition of palliative care

Palliative care is an approach that improves the quality of life of those facing life-threatening illness, through early identification, assessment and treatment of pain and other problems, physical, psychosocial and spiritual.⁵⁶ Importantly, palliative care and end of life care are not synonymous. A palliative approach, focusing on symptom relief, may be applicable for quite some time before death. End of life care refers to the period just prior to death.

Need for palliative care in COPD

The need for palliative care in COPD is increasingly being recognised. As dyspnoea may be difficult to relieve in patients with very severe COPD despite maximal standard therapy, evidence-based symptom-directed therapy may be appropriate. Treatment may include nonpharmacological therapies such as fans or the use of low doses of opioids that have a demonstrated role in the palliation of intractable dyspnoea.^{57,58} Other common symptoms include fatigue, xerostomia, cough and chest pain. The Australian *Therapeutic Guidelines: Palliative Care* offers excellent practical guidance regarding symptom-directed strategies.⁵⁹

COPD is characterised by repeated exacerbations, any of which might be fatal.

Patients' palliative care needs may increase during exacerbations and decrease afterward, and access to palliative care should be on the basis of need rather than prognosis. Specialist palliative care involvement may vary to accommodate these changing needs but some changes in service models are required.⁶⁰ (For example, models of care are required that facilitate shared care involving specialist palliative care providers when needs are especially high or complex and other providers when needs are less.)

Usual care providers (GPs, community nurses and specialist physicians) may be best placed to provide most patients' palliative care needs,⁶¹⁻⁶² but may need additional training to do so.⁶⁴⁻⁶⁸ Specialist expertise should be reserved for treating complex symptomatology or for discussions when there are complex psychosocial factors impeding care. Clear, effective communication is important and excellent Australian guidelines may aid such conversations.⁶⁹

When to refer to palliative care

There is no consensus on when to refer patients with COPD to palliative care, but clinical pointers include:

- repeated hospital admissions
- being housebound or chairbound
- an FEV₁ less than 30% predicted
- on long-term oxygen, or
- a BMI below 20 kg/m².⁷⁰

An exacerbation requiring NIV might also prompt referral, given the one-year survival after such an episode is only 50%.⁷¹ In addition, referral may be considered for patients with difficult-to-manage symptoms, who are unresponsive to usual therapy or with complex psychosocial situations and/or complex ACP needs.

END OF LIFE CARE

Although some patients die of COPD, many die with the disease.^{72,73} However, patients with COPD are more likely to die in the ICU than those with lung cancer, despite having an equal desire to

die at home.⁷³ This may be due to the final, fatal exacerbation being indistinguishable from previous exacerbations, compounded by a medical and social culture that strives for restitution of pre-morbid health.⁷⁴

End of life care for patients with COPD requires clear communication about the goals of care, assessment and management of symptoms and attempts to promote and maintain dignity. This implies the ability to 'diagnose' dying,⁷⁴ which can be challenging in patients having a COPD exacerbation. A time-limited trial of usual exacerbation treatments (antibiotics, corticosteroids, bronchodilators and/or ventilatory support with NIV or even invasive ventilation) may be appropriate.^{75,76} If the patient fails to improve, the diagnosis of dying is made and comfort becomes the focus. The Liverpool Care Pathway for the Dying Patient may be helpful to guide such care.⁷⁷

Although a detailed discussion of end of life care is beyond the scope of this article, medications that may be used include opioids for breathlessness, antipsychotics and benzodiazepines for agitation and anticholinergics for the management of terminal secretions. Guidance may be found in *Therapeutic Guidelines: Palliative Care*.⁵⁹

CONCLUSIONS

Patients with severe COPD require maximal tolerated standard treatment for their disease targeted at symptom control, prevention of exacerbations and treatment of comorbidities, including cardiovascular disease, anxiety and depression. Hypoxaemia may warrant consideration of long-term oxygen therapy. Pulmonary rehabilitation improves exercise capacity and dyspnoea, even in patients with severe COPD.

Intractable breathlessness may be treated by nonpharmacological methods and/or the judicious use of pharmacological treatments. A palliative approach to COPD care focusing on symptom

relief should be considered as exacerbations become more frequent and symptom control becomes more difficult. Specialised palliative care services may be involved at this stage.

End of life care in COPD requires clear communication about the goals of care, ideally should involve the patient and their caregivers and should be initiated through advance care planning. Discussions should preferably occur well before death is imminent, and continue through to the end of life. **MI**

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References are included in the pdf version of this article available at www.medicinetoday.com.au.

COMPETING INTERESTS: Dr Detering: None.

Dr Smith: None. Professor McDonald has received reimbursement in the past three years for Advisory Board Membership and speakers fees from GlaxoSmithKline, Novartis, Boehringer Ingelheim and Pfizer; her Department has received a small equipment grant for a student research project from GlaxoSmithKline and she has received funding to attend an educational meeting from Nycomed.

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Managing severe COPD: much can be done

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