Advanced respiratory disease

Updates in symptom control in the last years of life

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Symptoms in advanced respiratory disease are varied and commonly include breathlessness, fatigue and cough. Symptom control can be complex and difficult to navigate, particularly in the last few years of life as the disease progresses and patients' needs escalate. Management is best optimised through holistic multidisciplinary approaches, with management of individual symptoms alongside treatment of the underlying disease process.

Management of advanced respiratory disease has increasingly shifted to primary care and community settings, owing to a growing focus on supported, home-based care and preferences to avoid hospital presentation. Symptoms in advanced respiratory disease are varied, and can be complex to manage, particularly in the last years of life as the disease progresses and patients' needs escalate.[1] The symptoms discussed in this article are most common in chronic obstructive pulmonary disease (COPD) but are also relevant to other chronic conditions such as pulmonary fibrosis, bronchiectasis and lung cancer. Breathlessness in particular is also highly prevalent in advanced cancers and heart failure.[2]

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Defining the last years of life in advanced respiratory disease

Despite well-recognised fluctuation in chronic respiratory conditions (often with periods of exacerbation), indicative prognostic characteristics have been established. In particular, the question 'Would I be surprised if this patient did not survive the next 12 months?' is a useful clinical prompt.[3,4] This question has been found to have high specificity and is a simple prompt for clinicians to actively focus on symptom control, in combination with ongoing disease-directed management of the underlying condition.[3,4]

The nature and intensity of symptoms also signal a patient's changing needs. A modified Medical Research Council (mMRC) breathlessness scale score of 3 ('breathless after walking a few minutes or 100 metres on the flat') or 4 ('too breathless to leave the house or breathless when dressing or undressing') indicates severe breathlessness.[5,6]

Hospitalisation with an acute exacerbation of COPD has long been recognised as a prognostic indicator of advanced respiratory disease.[6,7] Mortality risk varies across studies;

Key points

- Symptoms in advanced respiratory disease are varied, complex and require specific attention to improve patient experiences.
- Key symptoms include the cluster of chronic breathlessness, fatigue and cough, as well as depression and anxiety, insomnia, cachexia, pain and dry mouth.
- Clinical care is best optimised through a holistic, multidisciplinary approach, with individual symptoms targeted through additional management strategies when symptoms persist despite maximising treatment of the underlying disease(s).
- Nonpharmacological interventions for breathlessness are effective and are the main approach to manage chronic breathlessness. These include mobility aids, activity pacing, breathing techniques and the use of a handheld fan to move airflow on the face.
- The psychological impact of advanced respiratory disease is often overlooked and needs to be directly addressed in best practice care.
- Early introduction of advance care planning (ACP) offers patients the opportunity to document their care preferences and address evident lack of support for chronic lung disease in the final stages of disease. The conversation around ACP should be ongoing as patients' preferences evolve throughout disease progression.

however, a 2017 retrospective study reported one- and five-year mortality of patients hospitalised for COPD as 26.2% and 64.3%, respectively, with mechanical ventilation further increasing these risks.[7] Acute hospitalisation is therefore recommended as an opportunity to discuss and plan for future care.[7,8] Low body mass index (less than 21.75 kg/m^2) and cachexia are also reliable prognostic indicators in advanced respiratory disease.[9,10]

Although the ability of prognostic indicators to predict death varies considerably across patients, its utility lies in the opportunity to prompt an additional care focus – notably the treatment of symptoms as a specific treatment goal.

Management of key symptoms

Symptoms in advanced respiratory disease vary; however, key symptoms may occur as a 'respiratory cluster', including chronic breathlessness, fatigue and cough. Other important symptoms include depression, anxiety, insomnia, cachexia, pain and dry mouth.[1] Comprehensive, individualised assessment of the underlying illness, symptoms and the needs of the patient and their carers is essential. This needs assessment usually occurs iteratively over time.[11] Although a broad and holistic approach to symptom management is recommended, individual symptoms should be addressed if they persist despite optimal management of the underlying disease.[1] A useful summary of evidence-based approaches to individual symptom management of COPD is presented in Box 1.[1,11]

Breathlessness

Chronic breathlessness is extremely distressing for patients with chronic respiratory disease, and highly prevalent in people with severe COPD. Both GPs and specialists often voice a lack of confidence in its management.[12,13] Breathlessness is multidimensional and defined as 'an unpleasant subjective experience of discomfort with breathing that worsens as underlying disease processes increase in severity; in its chronic and severe state, breathlessness can lead to significant disability, progressive inactivity, social isolation and substantive suffering'.[14] In addition, 'chronic breathlessness' is defined as breathlessness that 'persists despite optimal treatment of the underlying pathophysiology and that results in disability'.[15,16] A comprehensive approach to the evaluation and treatment of breathlessness is helpful and includes addressing reversible contributing causes, including anaemia, pleural effusion or anxiety; and implementation of evidence-based nonpharmacological interventions.[11]

Nonpharmacological interventions

Nonpharmacological interventions for breathlessness are effective and accessible; therefore, they should be offered to all patients with chronic breathlessness.[1,11] For example, activity pacing, mobility aids and adjusting a patient's living environment can assist in conserving energy for valued activities.[1,11] Increased physical activity and personalised exercise programs (such as pulmonary rehabilitation) can improve stamina and breathlessness.[11] Breathing exercises, such as pursed lip breathing, slow relaxed deep breathing and yoga breathing have been shown to be safe and to improve breathlessness for some people with advanced lung disease.[17,18] Hand-held motorised fans (Figure and videos) are similarly low harm, low cost, easy interventions that directly target and reduce the sensation of breathlessness.[1,11,19] Breathing retraining, accessed through specialist physiotherapy services, can also help improve associated dysfunctional breathing patterns.

Anxiety associated with breathlessness can lead to avoidance of those physical activities that address deconditioning.[1] Psychological and counselling therapies, including cognitive behavioural therapy (CBT), discussed below, can address negative thought processes and reluctance to engage in helpful activities.[1,20] Similarly, education and supported self-management can help patients improve self-efficacy, which in turn can reduce anxiety and depression, increase activity and social contact, and boost quality of life.[1]

Opioids

The 2024 European Respiratory Society Clinical Practice Guideline on symptom management for people with serious respiratory illness recommended against the use of opioids to treat chronic breathlessness.[11] This recommendation is based on the findings from a systematic review undertaken for the Guideline.[21] This systematic review identified that although clinical trials administering one to two doses of opioids in an exercise laboratory-setting led to improved exertional breathlessness during standardised exercise testing, when opioids were administered regularly at home over several days or weeks, there was no beneficial

1. Evidence-based approaches to managing symptoms in patients with COPD[1,11]

Breathlessness
- Smoking cessation
- Pulmonary rehabilitation
- Multicomponent breathlessness services
- Breathing techniques
- Facial airflow from a hand-held fan
- Activity pacing
- Cognitive behavioural therapy
- Tai Chi
- Yoga
- Support and education for family and caregivers

Anorexia
- Nutritional supplementation (for patients with evidence of malnutrition)
- Megestrol acetate

Fatigue
- Pulmonary rehabilitation or graded exercise therapy
- Self-management education programs
- Activity pacing and good sleep hygiene

Pain
- Principles of WHO analgesic ladder

Depression
- Complex interventions
- Cognitive behavioural therapy
- Multicomponent exercise training
- Antidepressant drugs
- Psychological interventions including cognitive behavioural therapy

Cough
- Complex Physiotherapy and Speech and Language Intervention
- Pregabalin and speech pathology treatment
- Gabapentin

Anxiety
- Psychological therapies
- Pharmacological interventions

Daytime sleepiness and insomnia
- Non-invasive positive-pressure ventilation for hypercapnic patients with stable disease
- Establish good sleep hygiene
- Cognitive behavioural therapy
- Benzodiazepines

Dry mouth
- Topical therapies (e.g. oxygenated glycerol triester spray)

Sexual dysfunction
- Exercise therapy and education, advice on positioning
- Pharmacological management

Adapted from Maddocks M, et al. Palliative care and management of troublesome symptoms for people with chronic obstructive pulmonary disease. Lancet 2017; 390: 988-1002.[1]

impact on breathlessness experienced in daily life.[21] Importantly, adverse effects (nausea, constipation and drowsiness) were significantly increased amongst people receiving opioids, and serious adverse events (including hospitalisation and death) occurred in approximately one-third of people receiving opioids in one clinical trial.[21] Additionally, many patients express concerns regarding taking opioids for chronic breathlessness because of concerns regarding medication safety, impacts on the ability to drive, dependence, addiction, stigma and the associations with substance misuse and death or dying.[21]

Importantly, the data for this recent systematic review were predominantly drawn from clinical trials undertaken in people with COPD.[21] As such, there is little evidence regarding the use of opioids to treat chronic breathlessness in people with other advanced, nonmalignant, respiratory illnesses.[21] Opioids may therefore be considered on an individual basis in people at the end of life or with other non-malignant respiratory illnesses with severe persisting breathlessness (despite optimisation of disease-directed treatment and nonpharmacological interventions for symptom management).[21] When opioids are prescribed to treat chronic breathlessness, clinicians must weigh up the potential harms versus benefits, ensure the treatment aligns with the patient's values and goals, and carefully discuss this treatment as part of shared decision-making.[21]

Other pharmaceutical approaches

Benzodiazepines are not recommended to treat breathlessness, except as second- or third-line therapy, or at the very end of life.[22] A recent multisite, randomised, double-blind, placebo-controlled, clinical trial evaluating the effectiveness of mirtazapine on chronic breathlessness in people with severe breathlessness (mMRC score of 3-4) and COPD or interstitial lung disease (ILD), failed to demonstrate any benefits.[23] However, the trial was substantially underpowered because of difficulties with recruitment during the pandemic. It should be noted that there were more adverse effects in the people receiving mirtazapine (64%) compared with people taking placebo (40%); therefore, the authors recommended against the use of mirtazapine to treat severe breathlessness.[23] Further efficacy trials for anxiolytics are needed; however, in the interim, all patients receiving such agents should be monitored for benefit and adverse effects when treated with these or other symptom relief measures.[2,22]

Fatigue

Fatigue is defined as 'a profound feeling of physical and psychological weariness that is not relieved by sleep or rest'.[1] Similar to breathlessness, fatigue is complex and requires a multicomponent approach to management, including physical conditioning (individualised pulmonary and graded exercise programs), psychological support, supported self-management and resilience training.[11,24] Additionally, treatment for comorbid depression is crucial, as this may compound the experience of fatigue.[1,25]

The recent European Respiratory Society Clinical Practice Guideline on symptom management for adults with serious respiratory illness emphasised the role of physical activity as the primary approach for managing fatigue in people with chronic respiratory conditions. The Guideline recommends graded exercise, which involves 'establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active'.

Occupational therapy-driven management, with a focus on daily life adjustment and maximising participation, has shown promise. Such evidence-based interventions aim to increase patients' understanding of fatigue, identify exacerbating factors and

Figure. A hand-held motorised fan can help alleviate symptoms of breathlessness. The fan pictured is small, inexpensive and lightweight, with soft blades. For further information, watch these videos: https://lungfoundation.com.au/resources/the-benefits-of-hand-held-fans//
Image courtesy of Lung Foundation Australia. © 2021 Copyright Lung Foundation Australia. The fan can be purchased through the Lung Foundation Australia.

facilitate development of fatigue management strategies (Box 2).[11,25,26]

Cough

Chronic cough related to underlying maximally-treated respiratory disease is a significant source of distress for patients.[1] Primary management approaches include physiotherapy, speech and language therapies (such as sputum-clearance techniques, cough control and cough-reflex hypersensitivity training), and psychoeducational counselling (Box 1).[1]

Pharmacological treatments are not well evidenced. However, a recent systematic review and meta-analysis of the neuromodulator gabapentin reported significant improvement in cough-specific quality of life, cough severity and frequency in chronic refractory cough.[27] Antitussive P2X purinoceptor 3 (P2X3) antagonists, which target airway vagal afferent nerve hypersensitisation, may also provide a pathway to mediate cough reflex. Although P2X3 antagonists are not yet available in Australia, preclinical and preliminary trial data are promising and P2X3 antagonists may be the new dawn in addressing this distressing symptom.[28]

Psychological impact

One often overlooked area within advanced respiratory disease is the psychological impact on patients, particularly in light of sustained symptoms.[29,30] The association between chronic respiratory disease and depression and anxiety is well documented, as is social and existential isolation. Psychological issues are reported in as many as 60% of people with COPD.[20,31,32]

Despite disease and symptom management optimisation, for many, a significant burden remains. Raising issues around psychological coping and patient experience provides patients the opportunity and permission to voice the full impact of their condition.

Key treatments for depression and anxiety include behavioural therapies and CBT, as well as pharmacological interventions (Box 1). Multicomponent exercise training has also shown positive impact for patients with advanced respiratory disease and depression.[1] Psychological therapy and counselling are acknowledged as useful, particularly in patients with chronic disease. CBT is a well-established treatment for anxiety and depression that seeks to increase a patient's understanding of their current difficulties and help manage unhelpful thoughts, and has shown promising outcomes for patients with COPD.[20] Of importance, several studies, including a recent large randomised controlled trial, showed that respiratory nurses trained in, and delivering CBT, improved anxiety and healthcare utilisation (emergency department presentations and hospitalisation) among patients with chronic respiratory disease.[29,33] Peer and facilitated support groups have similarly shown improvement in the wellbeing of patients with chronic respiratory conditions.[29] Empowerment through shared experience and collegial support may also improve active engagement with healthcare.[29]

Connecting patients with support and social services is increasingly important.[34] 'Social prescribing', in which primary care services actively link patients to support services within the community and volunteer sectors, can help improve health and wellbeing.[35] Social prescribing activities, including community gardening, group learning, volunteer work and music- and arts-based activities, are of particular value to patients with chronic conditions, such as advanced respiratory disease, in whom disease-related social isolation plays a key role in psychological dysfunction.

2. Practical recommendations for managing patients with respiratory disease-related fatigue[11,25,26]

- Discuss and assess the impact of fatigue on activities of daily living
- Refer for pulmonary rehabilitation with a focus on endurance and fitness training through graded exercise, or consider physiotherapy if pulmonary rehabilitation is not available
- Consider occupational therapy for analysis of daily activities and routines to assess the effort and energy required for different activities
- Provide or refer for education on methods of planning, pacing and prioritising activities to enable participation in valued activities
- Provide or refer for education on simplification skills, body mechanics, environmental adaptations, appropriate assistive devices and rest periods
- Address psychological impact and anxiety through strategies such as relaxation techniques and targeted participation in leisure activities
- Address sleep hygiene and nutritional issues
- Consider referral to specialist nursing or physiotherapy for education on self-management and self-efficacy for self-management of daily fatigue

Adapted from Connolly D, et al. Managing fatigue in patients with chronic conditions in primary care. Fam Pract 2013; 30: 123-124.

Other symptoms

Other symptoms associated with chronic respiratory disease include anorexia, dry mouth and insomnia. Evidence for the management of these symptoms is varied. Anorexia management relies primarily on nutritional supplementation, patient education and dietetic support. For patients with dry mouth, it can be helpful to review inhaler therapies that may contribute to this symptom and consider changing the device or the medication. Additionally, local topical therapies (such as oral lubricants of saliva substitutes)

3. Language to help raise advance care planning[41]

Healthcare professionals, particularly doctors, may find some of the language prompts below helpful when having a conversation with patients about advance care planning.

Introducing the topic: 'I try to talk to all my patients about what they would want if they became more unwell. Have you ever thought about this?'

Speaking for the person: 'Who would you like me to talk to if you were unable to talk to me about important medical treatment decisions?'

Goals and values: 'What does it mean to you to 'live well'? What are your goals at this time?'

Care and treatment: 'What do you understand about where things stand right now with your illness?'

Concluding the conversation: 'Thank you for clarifying your goals, values and acceptable outcomes. Does your family (or carer or friends) know what you would want?'

Reproduced with permission from: Advance Care Planning Australia (2024). Understanding advance care planning: starting the conversation.[41]

can be helpful.[36] Insomnia and daytime sleepiness is treated with sleep hygiene and CBT, and benzodiazepines may be prescribed for short-term intervention.[1] Comorbidities may also contribute to symptoms, thus the approach to management should always be to maximise the treatment of all contributing underlying conditions.

The importance of advance care planning

Despite the life-limiting nature of chronic respiratory diseases, few patients have plans in place for the later stages of disease and care, and less than 18% of patients with COPD in Australia access palliative care in the last 12 months of life.[37-40]

Advance care planning (ACP) is a process and opportunity in which patients 'think about, discuss and record preferences for the type of care they wish to receive and the outcomes they would consider acceptable'.[41] The process involves a series of conversations engaging patients and their family in exploring values, burdens and preferences, and allows healthcare professionals, the patient and their family to develop a shared understanding of how to best provide care that addresses and reflects the person's expressed goals.[41]

ACP increases palliative care involvement, and reduces the likelihood of clinically futile treatments and decision-making in a period of crisis. For patients with COPD, ACP can provide a heightened sense of control, and reduce anxiety and depression.[42,43]

Providing multiple and early opportunities to discuss long-term care wishes and priorities with patients is recommended.[41] These conversations are likely to evolve, as the patient's perspectives may change over time, emphasising the importance of ongoing conversations and willingness for continued discussion of healthcare preferences, even after an advance directive is in place.[41] Advance Care Planning Australia provides information on ACP, and includes language to help raise the conversation (Box 3) and videos for health professionals.[41]

Efficient conversations for long-term care

Patient-driven and patient-led consultations are sometimes erroneously considered too time consuming within the constraints of busy clinical practice.[44] Instead, evidence indicates that interactions commenced with a simple question as to the patient's priorities result in more time-efficient consultations and care that is more strongly aligned with patient's current and ongoing needs.[45] This becomes increasingly important when addressing care within the final years of life. Creating opportunities for patients to voice their priorities for care and ensuring the opportunity is taken to start a longer discussion over several consultations that plans care for now and the future, rather than attempting to address all issues raised, is essential.[44,45]

When to start a palliative approach in COPD

The recent European Respiratory Society Clinical Practice Guideline: Palliative care for people with COPD or ILD recommends that a palliative care approach should be considered 'when people with COPD or ILD and their informal caregivers have physical, psychological, social or spiritual/existential unmet needs'. And that 'needs should be assessed using report from the person with illness, or their informal caregiver report, but surrogate markers of disease severity and/or health service utilisation may help identify those likely to have unmet needs.'[46]

Healthcare professionals often hesitate to consider a palliative approach 'due to the uncertain disease trajectory, lack of a clear transition to "end of life", normalisation of living with COPD, and lack of professional awareness of the potential role of palliative care'. However, early engagement with palliative care is recommended and has been shown to improve survival and quality of death in patients with COPD.[46,47]

Involvement of specialist palliative care teams may be of benefit for patients experiencing unresolved symptoms and challenging situations.[6] Reasons for referral may include: management of persisting refractory symptoms; psychosocial, spiritual or existential care; co-ordination of care; active management of the terminal phase (at home or in a hospice); and emotional care and bereavement support of relatives and carers.[47] Patient and caregiver reluctance and misunderstanding of palliative care (as specific to cancer and the final days of life), compounds referral challenges; however, once referred, acceptability is high.[46]

Conclusion

Management of respiratory symptoms is best optimised through holistic approaches that address individual symptoms in addition to the underlying disease. Symptom burden commonly escalates in the last years of life as the disease progresses. Identifying patients within this category is crucial for well-managed and planned care. Key prognostic indicators for chronic disease include the question 'would I be surprised if this patient did not survive the next 12 months?'. Similarly, discussing patients' priorities for care and early engagement with ACP can better facilitate care that addresses their ongoing needs. **RMT**

References

A list of references is included in the online version of this article (https://medicinetoday.com.au/mt/2025/march/supplements/topics-copd-collection).

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