Advanced COPD

Symptom management and advance care planning

KAREN M. DETERING MB BS, FRACP, MHEth
DAVID C. CURROW BMed, MPH, PhD, FRACP, FAHMS

Patients with advanced chronic obstructive pulmonary disease (COPD) experience chronic breathlessness, have progressively limited function and often have unmet needs. Access to advance care planning and palliative care are often limited. Worsening of chronic breathlessness is closely associated with prognosis.

People with severe COPD experience morbidity, disability and increased healthcare utilisation. In the later stages of disease they experience systemic manifestations, more frequent exacerbations of symptoms and functional decline. Systemic manifestations and increased frequency of hospitalisation indicate the transition from chronic disease to chronic progressive disease. This is an important trigger for initiation or review of advance care planning (ACP).

Chronic breathlessness (at rest or on minimal exertion) is a particularly troublesome symptom in many patients with advanced COPD. Chronic breathlessness is often masked well by patients as they avoid activities that increasingly cause breathlessness with ever-decreasing exertion.

RESPIRATORY MEDICINE TODAY 2016; 1(1): 14-17

Dr Detering is a Respiratory and Sleep Medicine Physician and Medical Director of the Advance Care Planning Department, Austin Health, Melbourne, Vic. Professor Currow is Professor of Palliative and Supportive Services, Flinders University, Adelaide, SA.

Key points

- **Advanced COPD becomes a disease with systemic manifestations. More frequent hospitalisations are a signal to consider advance care planning.**
- **Advance care planning (ACP) is a co-ordinated communication process between a person, their family and healthcare providers clarifying the person's values, treatment preferences and goals.**
- **Patients with COPD want information about their diagnosis and expected disease trajectory, treatment, prognosis, what dying might be like and advance care planning.**
- **Two questions likely to elicit the impact of chronic breathlessness are: 'What do you have to do in order to become breathless?' and 'What have you given up in order to avoid breathlessness?'**
- **The Canadian Thoracic Society has proposed a three-step 'ladder' for the treatment of chronic breathlessness: optimise management of the reversible causes; use nonpharmacological supports; and introduce regular low-dose (10 mg/24 hours) extended-release morphine (and regular laxatives) if breathlessness persists and titrate weekly up to 30 mg/24hours.**
- **A recent meta-analysis of trials of morphine in steady state compared to placebo among people with COPD showed a consistent small to moderate effect, with all trials having a point estimate of reduced chronic breathlessness in favour of morphine over placebo.**

Three steps for managing chronic breathlessness in people with COPD include: ensuring all reversible causes contributing to breathlessness are optimally treated; using nonpharmacological interventions, including pulmonary rehabilitation (if the person is capable of participating) and a handheld battery-operated fan; and the regular use of low-dose oral extended-release morphine. This approach can safely and predictably reduce chronic breathlessness for most people with advanced COPD.

Advanced COPD

The typical course of COPD is one of a gradual decline in overall health and physical capacities over years, punctuated by episodic acute exacerbations that may require hospitalisation and are associated with an increased risk of dying. Patients commonly experience a range of symptoms, including chronic breathlessness, persistent cough, pain, difficulty sleeping, anxiety and depression.[1] Studies comparing symptom burden and quality of life among patients who have COPD with patients who have cancer have shown similar or worse outcomes for COPD patients.[2]

COPD in the advanced stages becomes a disease with systemic manifestations such as increasing fatigue and weight loss (of both lean body mass and fat), more frequent exacerbations and increasing functional decline. Often occurring together with increased frequency of hospitalisation, these changes characterise the transition from chronic disease to chronic progressive disease and are the signal to consider an evolving care plan. Such a plan includes discussion with the patient and his or her caregivers that covers advance care planning; assessments to optimise functional independence at home for as long as possible and a greater focus on symptom control, with a particular emphasis on treating chronic breathlessness as a specific goal of care.

About 25 to 50% of people with COPD will die within one year of a hospital admission for an exacerbation of COPD.[3] With each exacerbation, the person is less likely to recover to their previous level of functioning. This typical disease trajectory makes the exact timing of death hard to predict, and death may seem unexpected for both families and clinicians, particularly given that the patient may have survived similar episodes previously.

Determining prognosis can be difficult as there is wide variation in disease progression among patients. The severity of chronic breathlessness may be an excellent prognostic factor by itself and a better predictor of mortality even than severely impaired lung function (forced expiratory volume in 1 second [FEV_1] of less than 30% predicted).[4] FEV_1 may correlate poorly with the patient's symptom burden or disease course. Indices that also capture the systemic manifestations of COPD, such as the BODE index (body mass index, airflow obstruction, dyspnoea and exercise capacity) may also be useful in considering overall prognosis.[5]

Advance care planning

ACP is a co-ordinated communication process between a person, their family and healthcare providers that aims to clarify the person's values, treatment preferences and goals of medical treatment. Although completion of documents (advance care directives) may be a desired outcome, the discussions that are central to the ACP process are valuable in their own right, and help to prepare the patient and the decision makers for future decision-making. ACP should be revisited regularly, especially as the patient's clinical state changes. ACP improves the quality of care, including end-of-life care, decreases the burden experienced by surrogate decision makers and improves psychological outcomes in both surviving relatives and healthcare providers.[6,7]

Perspectives of patients, family and clinicians

ACP is likely to be of particular importance and relevance for patients with COPD, especially considering the unique and uncertain disease trajectory and high burden of debilitating symptoms. Patients with COPD report wanting information about their diagnosis and expected disease process, treatment, prognosis, what dying might be like and planning their future care (ACP).[8,9]

Despite this desire for information, many patients have reported lacking information about their disease and many may be unaware that COPD is progressive and, for a large proportion, ultimately fatal.[10] Studies have found that despite having similar preferences for intensity of care as patients with cancer, patients with COPD are more likely than patients with cancer to die in the intensive care unit or while on a ventilator and not be treated with symptom-relieving medications such as regular low-dose extended-release morphine.[8,9] People with COPD have also reported that their clinicians often failed to discuss the dying process with them, despite this being an important topic for patients and their families, and despite the desire of patients for emotional support and discussing their end-of-life care. Families and caregivers have reported similar needs to these.[11]

Healthcare professionals voice concerns that these types of discussions will harm patients by removing hope and increasing anxiety and depression. Evidence does not support this. Prognostic discussions in patients with COPD decrease anxiety and improve satisfaction with care.[8] ACP has also been shown to have beneficial outcomes in relation to a person's hope, and to reduce anxiety and depression.[12]

Clinicians need skills to discuss topics such as ACP and end-of-life care. There are several resources available to assist with learning (Box 1). Nondoctor facilitators such as nurses have been shown to be effective in conducting ACP and end-of-life conversations with patients, and this is a feasible option, with the potential to increase opportunities for patient access to ACP.

Incorporating advance care planning into routine COPD management

Most patients do not initiate ACP discussions but will wait for clinicians to do so. Given the typical disease trajectory in COPD, characterised by episodic deteriorations and partial recoveries, ACP can be opportunistic, and specific events or circumstances, such as a recent hospital admission, significant weight loss or functional decline, may act as prompts for initiating or revisiting ACP.

1. Advance care planning online resources

Advance Care Planning Australia
Resources to assist with ACP, including state and territory-specific information
– www.advancecareplanning.org.au

Decision assist
Resources for general practitioners regarding ACP and palliative care
– www.decisionassist.org.au

Victorian Department of Health and Human Services
'Next steps' (videos showing general practitioners having conversations with patients about ACP)
Advance care planning: resources for doctors and health professionals (set of ACP learning modules for doctors)
– www2.health.vic.gov.au

The advance care planning process

An ACP conversation is a structured discussion that follows a broad outline. The order of discussion will vary depending on the patient and clinician, the current clinical situation and how the discussion progresses. Patients and family need time to think and reflect, so it is expected that the ACP process will extend over time. The key components of an ACP discussion are outlined in Box 2.

Patients may not wish to have an ACP discussion, and those who do differ in the extent to which they want to receive information regarding their prognosis. Thus, prior to an ACP discussion it is important to seek permission and to ascertain how much information the patient would like to be given.

Evaluating breathlessness in advanced disease

In evaluating breathlessness, clinicians often ask 'Are you breathless?', to which many patients will reply 'No'. This answer comes despite the fact that the person sitting in front of you is working very hard at breathing as they have walked from the waiting room to the consultation room and are now struggling to talk. Two questions that are likely to elicit very different answers are 'What do you have to do in order to become breathless?' and 'What have you given up in order to avoid breathlessness?'. The modified Medical Research Council breathlessness scale identifies the patient group about whom we are talking: those who are too breathless to leave the house and breathless while dressing (level 4) and those who have to rest while walking along the flat at their own pace (level 3). Both reflect serious levels of impaired day-to-day functioning that substantially limit most activities of daily living.[13]

What is a clinically significant reduction in chronic breathlessness?

On a 0 to 100 mm visual analogue scale, a reduction of 9 mm is the change required for patients with chronic breathlessness to notice improvement of their symptoms.[14] Given that people rate their breathlessness on average as 50 mm in clinical trials, this represents approximately a 20% reduction from baseline. This is in contrast to the reduction (a 2-point reduction on a 0 to 10 cm numerical rating scale) required for patients with acute breathlessness to notice an improvement.[15]

Management of chronic breathlessness

Breathlessness ladder

The Canadian Thoracic Society has proposed a three-step 'ladder' to guide treatment of chronic breathlessness.[16]

Step 1. Look for and treat reversible factors that may contribute to breathlessness

- Check haemoglobin and oxygenation. Although most of us would assume that these basic things have been checked, this is not always the case.[17] Any deficiencies in these should be treated (anaemia with blood transfusions or iron or vitamin B_{12} supplementation, depending on causes and severity; and hypoxia with oxygen therapy).
- Diagnose and treat other conditions, such as heart failure.
- Undertake a medication review in order to maximise medications aimed at reducing breathlessness and cease medications that are not likely to influence short or longer-term outcomes. The latter is important so people continue to take the most important medications rather than self-selecting which to take in the myriad of prescribing that occurs.

Step 2. Nonpharmacological methods of relieving breathlessness

- Maintaining current function (especially if this includes independence) is an important goal for most people facing physical decline late in the course of illnesses such as COPD. Pulmonary rehabilitation should be considered for anyone well enough to participate.[18] Although the benefits of pulmonary rehabilitation in COPD are well recognised, breathlessness itself may be a reason for not enrolling in or completing pulmonary rehabilitation.[19,20] People who cannot participate in rehabilitation should undergo review by a physiotherapist.
- Use of a handheld battery-operated fan, directed at the face, is a simple, inexpensive and convenient option for easing breathlessness and is acknowledged by patients to improve breathlessness and give a sense of control.[21,22]
- Other evidence-based approaches include activity pacing, using a walking frame to help change the mechanics of the chest wall and transcutaneous muscle stimulation (which has been shown to help improve level of function in people who are quite debilitated).[23] Of note, there is often pressure on clinicians to prescribe long-term oxygen therapy for people at home who are either not hypoxaemic or mildly hypoxaemic. Randomised, controlled trial data do not support any additional symptomatic benefit over and above room air also supplied through nasal cannula at 2 L/min.[24]

Step 3. Pharmacological management of chronic breathlessness

- There is good evidence recommending the use of regular low-dose extended-release morphine to relieve chronic breathlessness. Extended-release preparations are chosen because they minimise peak concentrations and provide much more even delivery of drug compared with immediate-release solution. Low dose is up to 30 mg/24 hours, with most people responding to 10 mg/24 hours.[25,26]

Evidence for pharmacological management

A recent meta-analysis of people with COPD who have participated in double-blind, randomised controlled trials of morphine compared with placebo showed a consistent small to moderate reduction in chronic breathlessness (standardised mean difference, 0.33), with all trials having a point estimate of benefit in favour of morphine over placebo in steady state.[27] The magnitude of benefit equates to a clinically meaningful reduction in breathlessness, with emerging evidence that patients derive the most benefit during their worst breathlessness.

In terms of safety, there have been no recorded episodes of respiratory failure with use of morphine to treat breathlessness. Where carbon dioxide has been measured, there has been no worsening of carbon dioxide retention. One large cohort study demonstrated no increase in hospital admissions or mortality when low-dose opioid therapy (≤30 mg morphine equivalent/24 hours) was commenced in people with oxygen-dependent COPD.[28] More recently, however, a very large cohort from Canada found an association between opioid treatment being commenced and both hospital admissions and death, although in this series more than 98% of people were given opioids for pain, mostly at much higher doses than 30 mg of morphine equivalent/24 hours.[29] This Canadian study did not include any data on respiratory depression or obtundation. Low-dose extended-release morphine is well tolerated except for causing constipation, which should be treated expectantly by commencing aperients concurrently with morphine. In people who are already established on opioids for the relief of pain, the best available evidence suggests that a dose increase of 25% will relieve concomitant breathlessness.[30] Of note, this is not currently a registered indication, and no medication is registered internationally for symptomatic treatment of chronic breathlessness.

In practical terms, the evidence supports starting 24-hour extended-release morphine 10 mg once daily orally and assessing benefits in terms of worst breathlessness at one week (although benefit may be seen in as little as 48 hours). The dose can be titrated up weekly to a maximum of 30 mg/24 hours.[26] Commence a laxative such as docusate with sennosides at the same time.

Benzodiazepines are often used in people with breathlessness and anxiety. The evidence to date is that they are no better than placebo, and are associated with significant morbidity.[28,31] Results of a large randomised, placebo-controlled trial of the anxiolytic buspirone for breathlessness were also strongly negative.[32] Despite this, in the terminal stages of life, a regular low dose of a benzodiazepine may be indicated.

2. Key components of an advance care planning (ACP) conversation

- Ensure relevant people are present during discussions
  - Having others involved, including surrogate decision makers, provides support for the patient and provides carers with the opportunity to receive information first hand
- Establish how decisions are to be made if the person themself does not wish to make or is unable to make their own decisions
  - This often involves the appointment of surrogate decision makers and establishing how they will make treatment decisions
- Discuss the person's values and beliefs and what it means to them to live well
  - Include discussion of current and future goals and what they would consider to be a 'reasonable outcome' from treatment
- Assess understanding of illness, treatment and prognosis (where desired)
  - This step involves assessing the patient's current understanding of their illness and its likely trajectory. Specific information related to COPD can be provided, while also acknowledging that the uncertainty related to prognosis in individuals with COPD is important. One way to address this is to consider 'hoping for the best and planning for the worst'
- Documentation and dissemination
  - Although documentation in an advance care directive is not essential, it increases the likelihood of a person's wishes being known and respected. Even when a surrogate decision maker has been appointed, completing an advance care directive is useful as it can function to remind the surrogate of the person's wishes and the need to uphold them in decision-making. Documentation is also useful if the surrogate is not contactable in an emergency
- Review and update as appropriate
  - ACP is an ongoing process that requires regular review and updating

Conclusion

Advance care planning and proactive screening and management of symptoms, including breathlessness, must become an important part of routine care for patients with advanced COPD to facilitate a better quality of life. Evidence shows that advance care planning improves outcomes for patients and families. Furthermore, both nonpharmacological approaches and regular low-dose extended-release morphine safely improve chronic breathlessness in people with advanced COPD. **RMT**

References

A list of references is included in the website version of this article (www.medicinetoday.com.au).

COMPETING INTERESTS: Dr Detering: None. Professor Currow is an unpaid consultant to Helsinn Pharmaceuticals, Switzerland and Specialised Therapeutics, Australia, and has received consultancy and IP payments from Mayne Pharma.

Advanced COPD

Symptom management and advance care planning

KAREN M. DETERING MB BS, FRACP, MHEth; **DAVID C. CURROW** BMed, MPH, PhD, FRACP, FAHMS

References

1. Vermylen JH, Szmuilowicz E, Kalhan R. Palliative care in COPD: an unmet area for quality improvement. Int J Chron Obstruct Pulmon Dis 2015; 10: 1543-1551.
2. Solano JP, Gomes B, Higginson IJ. A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. J Pain Symptom Manage 2006; 31: 58-69.
3. Steer J, Gibson GJ, Bourke SC. Predicting outcomes following hospitalization for acute exacerbations of COPD. QJM 2010; 103: 817-829.
4. Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5-year survival than airway obstruction in patients with COPD. Chest 2002; 121: 1434-1440.
5. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med 2004; 350: 1005-1012.
6. Detering KM, Hancock AD, Reade MC, Silvester W. The impact of advance care planning on end of life care in elderly patients: randomised controlled trial. BMJ 2010; 340: c1345.
7. Houben CH, Spruit MA, Groenen MT, Wouters EF, Janssen DJ. Efficacy of advance care planning: a systematic review and meta-analysis. J Am Med Dir Assoc 2014; 15: 477-489.
8. Patel K, Janssen DJ, Curtis JR. Advance care planning in COPD. Respirology 2012; 17: 72-78.
9. Heffner JE. Advance care planning in chronic obstructive pulmonary disease: barriers and opportunities. Curr Opin Pulm Med 2011; 17: 103-109.
10. Gysels M, Higginson IJ. The experience of breathlessness: the social course of chronic obstructive pulmonary disease. J Pain Symptom Manage 2010; 39: 555-563.
11. Currow DC, Ward AM, Clark K, Burns CM, Abernethy AP. Caregivers for people with end-stage lung disease: characteristics and unmet needs in the whole population. Int J Chron Obstruct Pulmon Dis 2008; 3: 753-762.
12. Brinkman-Stoppelenburg A, Rietjens JA, van der Heide A. The effects of advance care planning on end-of-life care: a systematic review. Palliat Med 2014; 28: 1000-1025.
13. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. Thorax 1999; 54: 581-586.
14. Johnson MJ, Bland JM, Oxberry SG, Abernethy AP, Currow DC. Clinically important differences in the intensity of chronic refractory breathlessness. J Pain Symptom Manage 2013; 46: 957-963.
15. Karras DJ, Sammon ME, Terregino CA, Lopez BL, Griswold SK, Arnold GK. Clinically meaningful changes in quantitative measures of asthma severity. Acad Emerg Med 2000; 7: 327-334.
16. Marciniuk DD, Goodridge D, Hernandez P, et al. Canadian Thoracic Society COPD Committee Dyspnea Expert Working Group. Managing dyspnea in patients with advanced chronic obstructive pulmonary disease: a Canadian Thoracic Society clinical practice guideline. Can Respir J 2011; 18: 69-78.
17. Dudgeon DJ, Lertzman M. Dyspnea in the advanced cancer patient. J Pain Symptom Manage 1998; 16: 212-219.
18. McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y. Pulmonary rehabilitation for chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2015; (2): CD003793.
19. Corhay JL, Nguyen D, Duysinx B, et al. Should we exclude elderly patients with chronic obstructive pulmonary disease from ambulatory pulmonary rehabilitation programme? J Rehabil Med 2012; 44: 466-472.
20. Harris D, Hayter M, Allender S. Improving the uptake of pulmonary rehabilitation in patients with COPD: qualitative of the experiences and attitudes. Bri J Gen Pract 2008; 58: 703-710.
21. Johnson MJ, Booth S, Lam LTM, Currow DC, Phillips JL. A mixed-methods, randomized, controlled feasibility trial to inform the design of a phase III trial to test the effect of the handheld fan on physical activity and carer anxiety in patients with refractory breathlessness. J Pain Symptom Manage 2016; 51: 807-815.
22. Galbraith S, Fagan P, Perkins P, Lynch A, Booth S. Does the use of a handheld fan improve chronic dyspnea? A randomized, controlled, crossover trial. J Pain Symptom Manage 2010; 39: 831-838.
23. Bausewein C, Booth S, Gysels M, Higginson I. Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases. Cochrane Database Syst Rev 2008; (2): CD005623.
24. Abernethy AP, McDonald CF, Frith PA, et al. Effect of palliative oxygen versus room air in relief of breathlessness in patients with refractory dyspnoea: a double-blind, randomised controlled trial. Lancet 2010; 376: 784-793.
25. Gourlay GK, Plummer JL, Cherry DA. Chronopharmacokinetic variability in plasma morphine concentrations following oral doses of morphine solution. Pain 1995; 61: 375-381.
26. Currow DC, McDonald C, Oaten S, et al. Once-daily opioids for chronic dyspnoea: a dose increment and pharmacovigilance study. J Pain Symptom Manage 2011; 42: 388-399.
27. Ekstrom M, Nilsson F, Abernathy AP, Currow DC. Effects of opioids on breathlessness and exercise capacity in chronic obstructive pulmonary disease. A systematic review. Ann Am Thoracic Soc 2015; 12: 1079-1092.
28. Ekström MP, Bornefalk-Hermansson A, Abernethy AP, Currow DC. Safety of benzodiazepines and opioids in very severe respiratory disease: national prospective study. BMJ 2014; 348: g445.
29. Vozoris NT, Wang X, Fischer HD, et al. Incident opioid drug use among older adults with chronic obstructive pulmonary disease: a population-based cohort study. Br J Clin Pharmacol 2016; 81: 161-170.
30. Allard P, Lamontagne C, Bernard P, Tremblay C. How effective are supplementary doses of opioids for dyspnea in terminally ill cancer patients? A randomized continuous sequential clinical trial. J Pain Symptom Manage 1999; 17: 256-265.
31. Simon ST, Higginson IJ, Booth S, Harding R, Bausewein C. Benzodiazepines for the relief of breathlessness in advanced malignant and non-malignant diseases in adults. Cochrane Database Syst Rev 2010; (1): CD007354.
32. Peoples AR, Bushunow PW, Garland SN, et al. Buspirone for management of dyspnea in cancer patients receiving chemotherapy: a randomized placebo-controlled URCC CCOP study. Support Care Cancer 2016; 24: 1339-1347.