



Recommendations of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR)

## Recommendations for End-of-Life Care in Patients With Chronic Obstructive Pulmonary Disease

Recomendaciones sobre la atención al final de la vida en pacientes con EPOC

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### Introduction

Over the last 20 years, advances in the treatment of patients with chronic obstructive pulmonary disease (COPD) have improved survival even among patients in the most advanced stages of the disease, such as those requiring domiciliary oxygen therapy.<sup>1,2</sup> This improvement—in principle a positive development—has given rise to considerable clinical problems associated with the establishment of a therapeutic ceiling and the difficulty of determining prognosis in some of these patients. In this situation, the clinician should consider introducing palliative care, that is, care aimed at improving symptom control, communication, physical activity, and emotional support, in order to achieve the best possible quality of life for the patient. Palliative care is generally associated with the advanced stages of a disease's natural history, but in the case of COPD it is important to emphasize it does not necessarily mean that death is imminent.

The lack of a generally accepted definition for "end-stage COPD" makes it difficult to compare studies.<sup>3</sup> Table 1 defines the basic concepts.

Improving the management of advanced-stage COPD not only has a direct impact on the quality of care received by the patient, but also has a positive effect on the health care system as a whole in that it reduces hospital admissions shifts the burden of care from the hospital to the community, and reduces unnecessary and unscheduled admissions to intensive care units.<sup>4</sup>

Many patients with COPD remain undiagnosed, and some of those diagnosed do not fulfill the accepted criteria, and it is therefore extremely difficult to establish how many patients actually have very severe COPD, though it is estimated that the proportion may range between 3% and 15% of the total.<sup>5,6</sup>

The concern with broadening the clinician's approach beyond actions taken primarily to prolong the patient's life has developed more recently in the context of COPD in comparison with other diseases. Nonetheless, and despite the lack of precise definitions and the unpredictability of this disease, this broader approach should be an indispensable component of good practice in pulmonology. Figure 1 summarizes the final stages of life in patients with COPD.

### Identifying the Patient With End-Stage Disease: Diagnostic Criteria

The course of chronic diseases follows identifiable patterns.<sup>7</sup> In patients with cancer, the period of decline is shorter. In the case of age-related disability, the starting point is worse, the individual's independence is severely limited, and in many cases cognitive disorders are present. The pattern associated with organ failure, as is the case of COPD, is characterized by progressive deterioration over a long period of time punctuated by severe exacerbations that require hospitalization and may, in some cases, lead to death.<sup>8</sup> In general, these patients are virtually never free of symptoms. COPD is a disease associated with prognostic uncertainty and, furthermore, the health care system does not usually prioritize the care of patients with chronic diseases in the same way it does that of cancer patients.<sup>9</sup> Table 2 lists some of the obstacles to planning end-of-life care in patients with COPD.<sup>10</sup>

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The search for prognostic certainty may paralyze some physicians<sup>11</sup>: as they do not know what will happen, they take no decisions. One way to approach this problem is to ask ourselves whether we would be surprised if the patient should die within the next 12 months. Table 3 lists a number of criteria used to identify patients at risk of death within the next 6 to 12 months.<sup>12-14</sup>

Since it is difficult to predict prognosis in end-stage COPD, it is essential to anticipate the final stages of the disease. Certain characteristics of the disease make it more difficult to be precise in predicting survival in patients with COPD than in cancer patients. Moreover, other factors make the prognosis even more difficult to determine; for example, the lack of any tradition of living wills (advance directives), the inappropriate use of time on the part of both the physician and the patient, whether due to work overload or because of a fear of the uncertainty of the information. All of these circumstances tend to lead both clinicians and patients to find reasons for postponing any discussion about the decisions that must be taken on end-of-life issues.

In addition, the prognostic uncertainty associated with diseases involving organ failure may lead patients to think that they are not being given enough information.<sup>15</sup>

**Table 1**  
Definitions

Advanced COPD	This imprecise term should be avoided
End-of-life care	Care during the period prior to death (for example, the last 12 months of life)
Palliative care	A concept that does allow comparisons to be made Care aimed at preventing or treating symptoms as early as possible and dealing with the psychological and social problems arising from the disease
Terminal care	During the final stages of the disease, the care and treatment undertaken to prevent suffering in the final days or hours of the patient's life. The therapeutic effort should, in these cases, be comparable to that invested in a medical action with a curative aim
Mourning	The process through which the caregiver adapts to the loss

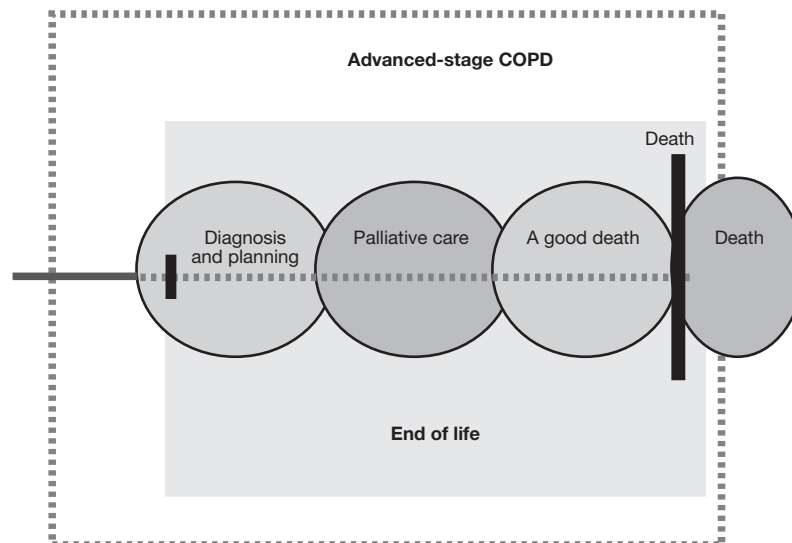
**Table 2**  
Barriers to Planning End-of-Life Care in Patients With COPD

The difficulty of establishing the prognosis and knowing which exacerbation will be the "last" one
A tendency to postpone discussion of the possible options
The lack of awareness on the part of the patients of how far their disease has progressed
The high percentage of caregivers who are also not aware of the seriousness of the patient's situation
The difficulty of deciding in many cases whether a death at home or in hospital is the better option
The lack of communication between the different care providers
A sense of inevitability that leads some physicians to take a passive attitude toward therapy
The fact that palliative care is not as common or intensive in patients with COPD as it is in patients with cancer <sup>10</sup>

**Table 3**  
Profile of the Patient Who May Die Within 6-12 Months

FEV <sub>1</sub> <30%
Scant physical activity
Dependence on caregivers for the basic activities of daily living
Not dressing every day
Inability to walk up a few steps without resting
Walking less than 30 minutes per day
Consumption of healthcare resources
Three or more severe exacerbations (emergency department visits and/or hospitalizations) in the past year
>21 days of hospital care during the previous year
General health affected by disease
Comorbidities
Body mass index <21 kg/m <sup>2</sup>
Dyspnea (3-4 on the modified MRC scale)
A BODE index score between 7 and 10
Personal and social factors
Older age
Depression
Living alone (or without a partner)

Abbreviations: FEV<sub>1</sub>, forced expiratory volume in the first second; MRC: Medical Research Council.  
Adapted from Hansen-Flaschen,<sup>12</sup> Chu et al,<sup>13</sup> and Celli et al.<sup>14</sup>



**Figure 1.** Final stages of chronic obstructive pulmonary disease (COPD).

**Advance Care Planning**

Very few studies have been done on the end-of-life care needs of COPD patients, but it is not reasonable to delegate the care of these patients to other professionals at the end of their lives. The physicians who have cared for the patient throughout the entire process should also take on the responsibility of managing the final stages of the disease. In some cases, the contribution of a team of palliative care experts may provide a useful support for the medical team as they devise the best care plan. Bioethics committees can also play an important role if they are able to respond immediately and help in critical situations with difficult decisions such as whether a patient should be intubated or the desirability of using noninvasive ventilation. The key element in the organization of the whole process is continuity of care (Figure 2). A single team (especially if hospital based) cannot respond to all the patient's needs in every situation. It is, therefore, essential to ensure that all those involved in the patient's care are working together towards the same goals, especially the primary care teams, social workers, and medical support personnel.<sup>16</sup> The provision of home care is a useful way of affording COPD patients direct care and at the same time guaranteeing continuity of health care.<sup>17</sup>

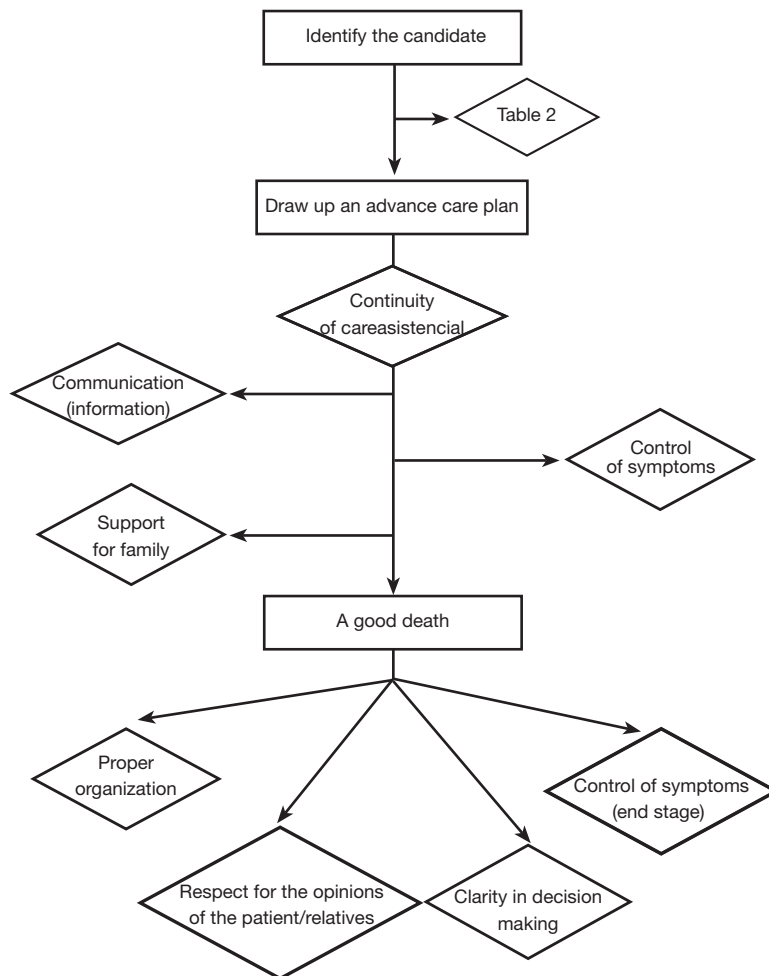
Certain issues that cause great anxiety can be quickly and easily resolved when patients and their caregivers can consult by telephone.

The signs and symptoms of the advanced stages of COPD do not differ substantially from those associated with the final stages of

other chronic processes. Patients with COPD experience dyspnea, sometimes accompanied by pain (flattened vertebrae, immobility), gastrointestinal symptoms (nausea, loss of appetite, constipation), anxiety or depression, sleep disorders, and weight loss. The best care plan should include the following<sup>18</sup>:

- Medical treatment of proven efficacy.
- Interventions that ensure the patient's comfort.
- Continuous, coordinated, and integrated treatment.
- An advance care plan.
- An individualized approach to care that takes the patient's preferences into account.
- Careful and considered use of the patient's and the relatives' resources.
- Support aimed at making the best of each day.
- Consideration of comorbidities, in particular heart or kidney failure and diabetes.<sup>19</sup>

When conventional treatments fail, some patients may turn to complementary medical techniques. There is no evidence that acupuncture improves dyspnea.<sup>20</sup> Patients have the right to turn to alternative medicine, and this choice is often related to 2 evident facts: the inability of conventional medicine to provide solutions to some of their real needs (which go beyond drug treatment and the hope of a cure), and the better communication provided by some alternative medical practitioners in the case of patients whose chief need is for someone to listen to them. Patients who turn to alternative



**Figure 2.** End-of-life care in patients with chronic obstructive pulmonary disease.

medicine often use it to complement conventional care rather than as a substitute.<sup>21</sup> Respiratory specialists should advise patients to avoid any practices that are potentially dangerous and to carefully evaluate the costs and benefits of any supposedly therapeutic intervention.

### Training in End-of-Life Care

The training of residents and other professionals who care for patients with respiratory diseases (personnel with degrees in nursing or physiotherapy) should cover the core competencies of end-of-life care, including symptom control, achieving a reasonable quality of life, effective communication and emotional support, and how to maintain, as far as possible, the patient's ability to independently carry out activities of daily living. Table 4 summarizes the components of the palliative care syllabus.

Palliative care unit rotations for residents have been shown to change their attitudes towards end-of-life care.<sup>22</sup>

### Care for the Caregiver

In the advanced stages of COPD, the impact of the disease also affects caregivers, especially in terms of the limitations it poses on their social relationships<sup>23</sup> and the fact that they must witness the patient's suffering over a long period of time. It is important to involve the caregiver in the end-of-life care planning,<sup>24</sup> but as health professionals we also have a duty to care for the caregiver even before this stage is reached. In some cases, this care should be extended to include support during the process of mourning and adjustment to loss.<sup>25</sup>

### Communication

One of the most complex aspects of end-of-life care for patients with COPD is communication between the doctor and the patient concerning prognosis. Advance directives are useful when the future course of the disease is known (for example in the case of amyotrophic lateral sclerosis or lung cancer). In the case of COPD, however, there is a risk that advance directives will be focused more on the treatments the patient rejects than on the patient's values and preferences with respect to the decisions that have to be made. Moreover, even when advance directives have been drawn up, patients may change their opinions. They tend to judge the impact of a treatment more in terms of how it affects their independence and cognitive state than in terms of survival.<sup>26</sup> Older patients tend to prefer less aggressive treatments, especially when treatment may affect their independence and cognitive functions.<sup>27</sup> When discussing the situation with a patient, it is essential to inform him or her of the probable outcome of non-intervention and to contextualize the concept of risk.

There are decision-making aids, such as videos and books, specifically designed to inform patients and help them to make

choices. Patient support groups can facilitate communication, but individuals must assess their own personal situation and discuss it directly with the physician responsible for their treatment.

Ultimately, the decision regarding the best possible treatment for a specific patient may represent a balance between the patient's independence, the usefulness of the intervention, and distributive justice.<sup>28</sup> Physicians deciding whether or not to propose a transplant or volume reduction surgery face ethical choices that should in some cases be made in consultation with colleagues.

Tools that improve communication skills have been developed for training health care professionals.<sup>29</sup>

### Management Approach

The primary focus of end-of-life care should be to alleviate dyspnea and the effects of anxiety and depression.<sup>30</sup>

#### *Symptomatic Relief of Dyspnea*

Shortness of breath is the most prevalent and incapacitating symptom in patients with advanced-stage COPD. It can be alleviated with bronchodilators, supplemental oxygen, pulmonary rehabilitation, surgery (lung transplantation or volume reduction), and opioids. However, only 50% of patients with end-stage COPD benefit from such measures and consequently many of these patients live—and die—with incapacitating dyspnea.<sup>31</sup>

Before we can effectively treat dyspnea we need to measure the severity of the symptom in a uniform and reproducible way. In a recent review, Baussewin et al<sup>32</sup> recommended "combining a unidimensional scale (eg, a [visual analog scale]) with a disease-specific scale...or a multidimensional scale in conjunction with other methods...to gauge psychosocial and carer distress." The advantage of this combination is that it recognizes dyspnea as a symptom that affects both the patient and the caregiver. Traditional approaches to alleviating dyspnea, which include the use of bronchodilators and oxygen therapy, lie outside the scope of these guidelines. Other measures can be useful in patients already receiving maximum conventional treatment whose short-term prognosis is poor. These include the administration of opioids or benzodiazepines, pulmonary rehabilitation, and noninvasive mechanical ventilation.

*Use of opioids to alleviate dyspnea.* Opioids may be useful in patients with severe COPD who have reached the therapeutic ceiling with conventional treatment. Several randomized clinical trials and 1 meta-analysis<sup>27</sup> report that oral or parenteral opioids can alleviate the sensation of shortness of breath, although it is recognized that these drugs are associated with a number of side effects, in particular constipation. Nebulized opioids were not, however, found to be useful. Since all of these trials were of short duration, the long-term effects of this type of therapy are unknown. The effect of low doses of opioids on respiratory depression is of particular concern. However, the trials included in the meta-analysis cited above did not report any adverse effects on gas exchange, and some international guidelines even include recommendations concerning the use of opioids in patients with severe COPD.<sup>33</sup> The recommended starting dose is 1 to 2 mg of oral morphine or equivalent. The dose can be increased gradually until effective control of dyspnea is achieved. Patients experiencing a severe dyspnea crisis and patients whose advance care plan includes palliative therapy should be offered treatment with parenteral opioids, although the potential of this type of therapy in the management of such a crisis has never been rigorously assessed. Figure 3 illustrates a proposal for a stepped plan for managing dyspnea in patients with COPD.

*Benzodiazepines.* Benzodiazepines can be used in the management of severe dyspnea associated with anxiety, including panic attacks.<sup>34</sup> However, the depressive effect of such medication on the respiratory system in patients with hypercapnia must be taken into account.

**Table 4**  
Components of the Palliative Care Syllabus

Assessment and treatment of pain and dyspnea
Management of general symptoms
Ethical principals
Current legislation
Communication skills
Psychosocial considerations related to death and dying
Multidisciplinary teamwork
Knowledge of available resources (home support, social support, social and healthcare provisions, etc)
Overall assessment of care (and communication with other professionals who have cared for the patient)

**Pulmonary rehabilitation and noninvasive mechanical ventilation.** Combining pulmonary rehabilitation with adjuvant interventions, such as noninvasive positive-pressure ventilation or the administration of supplemental oxygen, could provide additional benefits in patients with advanced-stage COPD. Supplemental oxygen can greatly improve exercise tolerance and reduce dyspnea, even in patients with moderate hypoxemia.<sup>35</sup> However, the results obtained outside the laboratory are less conclusive. Various types of noninvasive mechanical ventilation have also been shown to improve exercise tolerance and reduce dyspnea in patients with severe or very severe COPD undergoing pulmonary rehabilitation,<sup>36</sup> although once again the effect of such treatment outside the context of such programs remains a matter of debate. Pulmonary rehabilitation programs also educate patients in therapeutic strategies and self-management, and include psychosocial support—all components that could have beneficial effects on symptoms.

### The Impact of Anxiety and Depression

Depression and anxiety, occurring separately or together, are common problems in patients with COPD. According to a recent review,<sup>37</sup> the prevalence of generalized anxiety disorder in COPD ranges from 10% to 33%, and panic disorder occurs in between 8% and 67% of these patients. The prevalence of depression in patients with moderate to severe COPD ranges from 7% to 42%. The variations in these estimates are due to differences in the methods and scales used in the different studies. These figures do, however, reveal a considerable overall impact that often goes unnoticed because of the overlap between the symptoms of COPD and those associated with anxiety and depression.

A number of questionnaires are currently available to measure the severity of anxiety-related symptoms.<sup>38-40</sup> Many others evaluate depression, including one developed specifically for use in patients with COPD.<sup>41</sup> These instruments should, however, be seen as screening tools. Specific cases of anxiety and/or depression should be diagnosed by a qualified mental health professional using appropriate methods in a clinical interview.

**Treatment of anxiety.** Only a few studies have investigated the effectiveness of anxiolytics in the management of COPD.<sup>42-45</sup> The results of studies of buspirone, a serotonin receptor agonist, have been inconsistent and inconclusive.<sup>42,43</sup> Nortriptyline, a tricyclic antidepressant, has been reported to reduce anxiety and depression in patients with COPD, but only in a single study of 30 patients.<sup>44</sup> Finally, citalopram, a selective serotonin reuptake inhibitor, has not been shown to be beneficial in patients with COPD.<sup>45</sup>

Among the nonpharmacologic approaches, psychotherapy and progressive muscular relaxation have been evaluated in very few studies and the results obtained have been inconclusive.<sup>37</sup> In contrast, a number of studies have shown that pulmonary rehabilitation reduces anxiety. However, benefit in these cases was always observed when the educational techniques were associated with supervised muscle training; this suggests that benefits are more closely related to such training.<sup>37</sup>

**Treatment of depression.** Pharmacologic treatment should be considered in patients with major depression. The choice of antidepressant therapy will depend on the pattern of depression and, more particularly, on the chronic respiratory condition of the patient because drugs with a sedative action should be avoided. Although respiratory depression is a potential side effect, the oldest antidepressants have been shown to have little effect on respiratory drive.<sup>46</sup> These side effects have not been reported with selective serotonin reuptake inhibitors or the new antidepressants (venlafaxine, duloxetine, and mirtazapine). In a small study with low statistical power, paroxetine was shown to be very effective in COPD, with significant improvements in the emotional function and mastery domains of the Chronic Respiratory Questionnaire, although no differences were observed in the dyspnea or fatigue domains.<sup>47</sup>

### End-of-Life Care: "A Good Death"

Although death is inevitable, it is often experienced as a failure rather than as a natural part of life.<sup>48</sup> Any definition of a "good death"<sup>49</sup> should include the following elements:

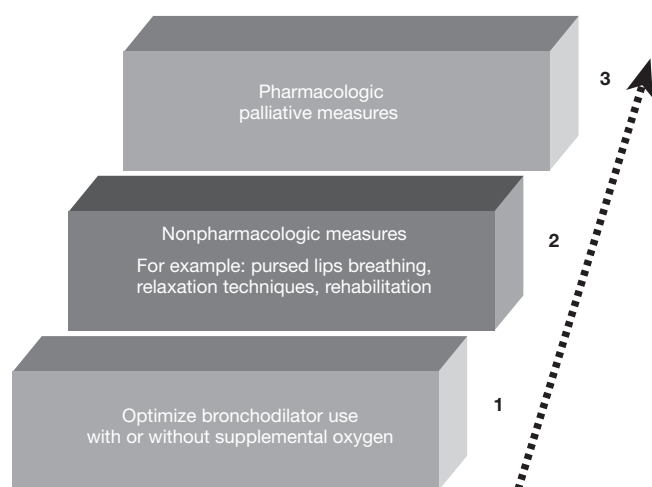
- Control of symptoms.
- Clear decision making.
- Respect for the opinions of the patient and the family.
- Giving those involved the possibility of preparing for the process of dying.
- Freeing the patient from pointless responsibilities.
- Ensuring that both the family and the patient feel that they have completed the entire process as they had planned (goodbyes, will, etc).
- Respect.
- Optimum organization (no unnecessary changes of room or hospital).
- Communication with the whole team who have cared for the patient.

### Advance Directives

Advance directives can be very helpful when taking decisions at these times. These are the documents signed by patients in which they specify their preferences regarding the treatment and care they wish to receive. It is very important to stress that advance directives in no way replace the decisions made by the conscious patient. This document is only used when a patient is no longer able to decide or make his or her decision known, and a patient can revoke the advance directives at any time.<sup>50</sup>

Under Spanish law, instructions that require actions that are illegal under current legislation or contrary to the profession's definition of good practice will not be followed. Advance directives can only be applied in the specific circumstances determined by the patient at the time the document was drawn up.

Notwithstanding these preparations, the decision to withdraw life support is often difficult for clinicians and very hard for family members.<sup>51</sup> Withdrawal of mechanical ventilation in sedated patients does not pose the same problems as the withdrawal of ventilatory support from patients on long-term home ventilation whose condition is deteriorating progressively or who make the decision themselves to discontinue. The clinician's primary aim is to achieve



**Figure 3.** Palliative approach to dyspnea in chronic obstructive pulmonary disease.



effective control of symptoms while avoiding unnecessary measures. Nonetheless, the limits are difficult to establish, especially from the legal standpoint. As Simonds<sup>52</sup> has suggested, there is great variation in clinical practice with respect to the withdrawal of life support.

### The Process of Dying

The medical care team can provide essential support for patients and relatives who are facing difficult decisions.<sup>53</sup> In the final stages of a patient's life, it is important to avoid, whenever possible, delegating responsibility to other professionals. In some cases, after years of treating a patient, a distressing course of events in the final stages of life can destroy all of the efforts of the medical team and leave the family feeling guilty. The quality of the process of dying can be audited, and Thomas and Day<sup>54</sup> have proposed the following criteria for evaluating whether or not the process has been acceptable in a particular case:

1. The patient was free from symptoms (pain, dyspnea, anxiety, pressure sores).
2. Therapeutic strategies were planned in advance.
3. Death occurred in familiar surroundings (hospitalized patients should be accommodated in a private room).
4. The patient was not moved during the last 3 days of life.
5. Relatives were aware that the patient was dying and were present if desired.
6. An autopsy was performed if the cause of death was unclear.
7. The patient's general practitioner was informed of the death by telephone within 24 hours and received a written report within 7 days.

Despite the significant increase in our knowledge in the field of palliative care, there are still barriers that make it difficult to apply what we know. The official policy statement of the American Thoracic Society<sup>55</sup> notes the following obstacles to the provision of end-of-life care: the physician's discomfort with discussion of these problems with patients and their relatives; the uncertain short-term prognosis that is characteristic of nonmalignant diseases; the lack of specific knowledge and skills on the part of the clinician; the considerable investment in time required for palliative care; and, finally, the additional difficulty that, after dealing with a long-term illness, many caregivers are worn out and overwhelmed. In conclusion, the skills and knowledge needed to provide palliative care should carry greater weight in the process of training professionals who will care for patients with advanced respiratory disease.

### References

1. Cooper CB, Waterhouse J, Howard P. Twelve year clinical study of patients with hypoxic cor pulmonale given long-term oxygen therapy. *Thorax*. 1987;42:105-10.
2. Carrera M, Sauleda J, Bauzá F, Bosch M, Togores B, Barbé F, et al. Resultados de la actuación de una unidad de control de la oxigenoterapia domiciliar. *Arch Bronconeumol*. 1999;35:33-8.
3. Habraken JM, Willems DL, de Kort SJ, Bindels PJ. Health care needs in end-stage COPD: a structured literature review. *Patient Educ Couns*. 2007;68:121-30.
4. Gómez-Batiste X, Porta-Sales J, Pascual A, Nabal M, Espinosa J, Paz S, et al; Palliative Care Advisory Committee of the Standing Advisory Committee for Socio-Health Affairs, Department of Health, Government of Catalonia. Catalonia WHO palliative care demonstration Project at 15 years (2005). *J Pain Symptom Manage*. 2007;33:584-90.
5. Hoogendoorn M, Feenstra TL, Schermer TR, Hesselink AE, Ruttenvan Molken MP. Severity distribution of chronic obstructive pulmonary disease (COPD) in Dutch general practice. *Respir Med*. 2006;100:83-6.
6. Ambrosino N, Simonds A. The clinical management in extremely severe COPD. *Respir Med*. 2007;101:1613-24.
7. Murray SA, Kendall M, Boyd K, Sheikh A. Illness trajectories and palliative care. *BMJ*. 2005;330:1007-11.
8. Soler-Cataluña JJ, Martínez-García MA, Román Sánchez P, Salcedo E, Navarro M, Ochando R. Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. *Thorax*. 2005;60:925-31.
9. Murray SA, Boyd K, Kendall M, Worth A, Benton TF, Clausen H. Dying of lung cancer or cardiac failure: prospective qualitative interview study of patients and their carers in the community. *BMJ*. 2002;325:929.
10. Yohannes AM. Palliative care provision for patients with chronic obstructive pulmonary disease. *Health Qual Life Outcomes*. 2007;5:17-22.
11. Murray SA, Boyd K, Sheikh A. Palliative care in chronic illness. *BMJ*. 2005;330:611-2.
12. Hansen-Flaschen J. Chronic obstructive pulmonary disease: the last year of life. *Respir Care*. 2004;49:90-7.
13. Chu CM, Chan VL, Lin AW, Wong IW, Leung WS, Lai CK. Readmission rates and life threatening events in COPD survivors treated with non-invasive ventilation for acute hypercapnic respiratory failure. *Thorax*. 2004;59:1020-5.
14. Celli B, Cote C, Marín JM, Casanova C, Montes de Oca M, Méndez RA, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med*. 2004;350:1005-12.
15. Hansen-Flaschen J. Chronic obstructive pulmonary disease: the last year of life. *Respir Care*. 2004;49:90-7.
16. Seamark DA, Seamark CJ, Halpin DM. Palliative care in chronic obstructive pulmonary disease: a review for clinicians. *J R Soc Med*. 2007;100:225-33.
17. García-Aymerich J, Hernández C, Alonso A, Casas A, Rodríguez-Roisin R, Antó JM, et al. Effects of an integrated care intervention on risk factors of COPD readmission. *Respir Med*. 2007;101:1462-9.
18. Farrero E, Escarrabill J, Prats E, Maderal M, Manresa F. Impact of a hospital-based home-care program on the management of COPD patients receiving long-term oxygen therapy. *Chest*. 2001;119:364-9.
19. Lynn J. Perspectives on care at the close of life. Serving patients who may die soon and their families: the role of hospice and other services. *JAMA*. 2001;285:925-32.
20. Gudmundsson G, Gislason T, Lindberg E, Hallin R, Ulrik CS, Brondum E, et al. Mortality in COPD patients discharged from hospital: the role of treatment and comorbidity. *Respir Res*. 2006;7:109-16.
21. Lewith GT, Prescott P, Davis CL. Can a standardized acupuncture technique palliate disabling breathlessness: a single-blind, placebo-controlled crossover study. *Chest*. 2004;125:1783-90.
22. George J, Ioannides-Demos LL, Santamaría NM, Kong DC, Stewart K. Use of complementary and alternative medicines by patients with chronic obstructive pulmonary disease. *Med J Aust*. 2004;181:248-51.
23. Duong PH, Zulian GB. Impact of a postgraduate six-month rotation in palliative care on knowledge and attitudes of junior residents. *Palliat Med*. 2006;20:551-6.
24. Ibáñez M, Aguilar JJ, Maderal MA, Prats E, Farrero E, Font A, et al. Sexuality in chronic respiratory failure: coincidences and divergences between patient and primary caregiver. *Respir Med*. 2001;95:975-9.
25. Wolff JL, Dy SM, Frick KD, Kasper JD. End-of-life care: findings from a national survey of informal caregivers. *Arch Intern Med*. 2007;167:40-6.
26. Maciejewski PK, Zhang B, Block SD, Prigerson HG. An empirical examination of the stage theory of grief. *JAMA*. 2007;297:716-23.
27. Fried TR, Bradley EH, Towle VR, Allore H. Understanding the treatment preferences of seriously ill patients. *N Engl J Med*. 2002;346:1061-6.
28. Fried TR, van Ness PH, Byers AL, Towle VR, O'Leary JR, Dubin JA. Changes in preferences for life-sustaining treatment among older persons with advanced illness. *Gen Intern Med*. 2007;22:495-501.
29. Simonds AK. Ethics and decision making in end stage lung disease. *Thorax*. 2003;58:272-7.
30. Back AL, Arnold RM, Baile WF, Fryer-Edwards KA, Alexander SC, Barley GE, et al. Efficacy of communication skills training for giving bad news and discussing transitions to palliative care. *Arch Intern Med*. 2007;167:453-60.
31. Rocker GM, Sinuff T, Horton R, Hernández P. Advanced chronic pulmonary disease: innovative approaches to palliation. *J Palliat Med*. 2007;10:738-97.
32. Jennings AL, Davies AN, Higgins JP, Gibbs JS, Broadley KE. A systematic review of the use of opioids in the management of dyspnoea. *Thorax*. 2002;57:939-44.
33. Bausewin C, Farquhar M, Booth S, Gysels M, Higginson IJ. Measurement of breathlessness in advanced disease: a systematic review. *Respir Med*. 2007;101:399-410.
34. O'Donnell DE, Aaron S, Bourbeau J, Hernández P, Marciniuk D, Balter M, et al. State of the art compendium: Canadian Thoracic Society recommendations for the management of chronic obstructive pulmonary disease. *Can Respir J*. 2004;11 Suppl B:7-59.
35. Freeman D, Price D. Primary care and palliative care. *BMJ*. 2006;333:188-90.
36. O'Donnell DE, D'Arigny C, Webb KA. Effects of hyperoxia on ventilatory limitation during exercise in advanced chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2001;163:892-8.
37. Hernández P, Maltais F, Gursahaney A, Leblanc P, Gottfried SB. Proportional assist ventilation may improve exercise performance in severe chronic obstructive pulmonary disease. *J Cardiopulm Rehabil*. 2001;21:135-42.
38. Hill K, Geist R, Goldstein RS, Lacasse Y. Anxiety and depression in end-stage COPD. *Eur Respir J*. 2008;31:667-77.
39. Hamilton M. The assessment of anxiety states by rating. *Br J Med Psychol*. 1959;32:50-5.
40. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol*. 1988;56:893-7.
41. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67:361-70.
42. Kunik ME, Azzam PN, Soucek J, Cully JA, Wray NP, Krishnan LL, et al. A practical screening tool for anxiety and depression in patients with chronic breathing disorders. *Psychosomatics*. 2007;48:16-21.

43. Argyropoulou P, Patakas D, Koukou A, Vasiliadis P, Georgopoulos D. Buspirone effect on breathlessness and exercise performance in patients with chronic obstructive pulmonary disease. *Respiration*. 1993;60:216-20.
44. Singh NP, Despars JA, Stanbury DW, Avalos K, Light RW. Effects of buspirone on anxiety levels and exercise tolerance in patients with chronic airflow obstruction and mild anxiety. *Chest*. 1993;103:800-4.
45. Silvertooth EJ, Doraiswamy PM, Clary GL, Babyak MA, Wilkerson N, Hellegars C, et al. Citalopram and quality of life in lung transplant recipients. *Psychosomatics*. 2004;45:271-2.
46. Borson S, McDonald GJ, Gayle T, Deffebach M, Lakshminaravan S, vanTuinen C. Improvement in mood, physical symptoms, and function with nortriptyline for depression in patients with chronic obstructive pulmonary disease. *Psychosomatics*. 1992;33:190-201.
47. Steen SN. The effects of psychotropic drugs on respiration. *Pharm Ther*. 1976;2:717-41.
48. Lacasse Y, Beaudoin L, Rousseau L, Maltais F. Randomized trial of paroxetine in end-stage COPD. *Monaldi Arch Chest Dis*. 2004;61:140-7.
49. Smith R. A good death. *BMJ*. 2000;320:129-30.
50. Steinhauser KE, Clipp EC, McNeilly M, Christakis NA, McIntyre LM, Tulsky JA. In search of a good death: observations of patients, families, and providers. *Ann Intern Med*. 2000;132:825-32.
51. Ley 41/2002, de 14 de noviembre, básica reguladora de la autonomía del paciente y de derechos y obligaciones en materia de información y documentación clínica. BOE núm. 274, de 15 de noviembre de 2002. p. 40126-32.
52. Prendergast TJ, Puntillo KA. Withdrawal of life support intensive caring at the end of life. *JAMA*. 2002;288:2732-40.
53. Simonds AK. Ethics and decision making in end stage lung disease. *Thorax*. 2003;58:272-7.
54. Goldstein NE, Back AL, Morrison RS. Titrating guidance. A model to guide physicians in assisting patients and family members who are facing complex decisions. *Arch Intern Med*. 2008;168:1733-9.
55. Thomas M, Day R. A good death. Quality of death can be measured outside hospices. *BMJ*. 2000;320:1206.
56. Lanken PN, Terry PB, Delisser HM, Fahy BF, Hansen-Flaschen J, Heffner JE, et al; ATS End-of-Life Care Task Force. An official American Thoracic Society clinical policy statement: palliative care for patients with respiratory diseases and critical illnesses. *Am J Respir Crit Care Med*. 2008;177:912-27.