Mitigating the impact of breathlessness in Chronic Obstructive Pulmonary Disease: can a structured specialty palliative care intervention fill in the gap in our treatment algorithms?

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Abstract

Breathlessness is a distressing symptom, uniformly faced at some point in the disease process in all patients with Chronic Obstructive Pulmonary Disease (COPD). Despite maximal medical therapy and pulmonary rehabilitation, patients with COPD continue to experience refractory dyspnea, pain, poor appetite, limitations of physical activity, emotional distress, depression and overall poor health-related quality of life. Our current GOLD ABE pharmacologic treatment algorithm provides maximal disease specific therapy directed at optimization of physiologic airflow obstruction and exacerbation frequency, however leaving a gap in how best to approach the complex and multifactorial symptom of refractory breathlessness that occurs despite these pharmacologic interventions and pulmonary rehabilitation. The comprehensive and multidisciplinary approach of specialty palliative care may well fill this gap in our treatment algorithms. In this review, we will review the growing body of literature on the definitions and role of primary and specialty palliative care in the treatment of patients with COPD, review the components of a structured palliative care intervention in advanced lung disease, review the current pharmacologic and non-pharmacologic treatments for breathlessness, the identified barriers to palliative care intervention and consider the future direction of palliative care engagement in patients with COPD.
Introduction
Breathlessness is a distressing symptom, uniformly faced at some point in the disease process in all patients with Chronic Obstructive Pulmonary Disease (COPD). For some patients, this presents early in their disease trajectory, and for others, it is much later in their disease progression. Treatment guidelines for patients with COPD have been written annually by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) panel of experts and are determined by dyspnea limitations, using either the Modified Medical Research Council score (mMRC) or COPD Assessment Test (CAT) and the frequency of acute exacerbations of disease. The GOLD disease grouping and treatment model recognizes that symptom burden is independent of formal grading of severity of obstructive lung disease by FEV1 (forced expiratory volume in one second). It also recognizes the impact of recurrent disease exacerbations on disease progression and symptom burden, with many patients not returning to their previous level of function after each exacerbation. The GOLD 2023 revision to the patient classification underscores the impact of the exacerbations on disease progression, moving from an ABCD model (Figure 1a) to an ABE model (Figure 1b), where all patients with recurrent exacerbations are moved to the more severe ‘E’ group, regardless of degree of dyspnea. The GOLD guideline endorses intensification of pharmacologic therapy for either high dyspnea scoring or recurrent exacerbations of disease.

Figure 1. GOLD Assessment Tools
GOLD ABE (2023, 1b) replaces the previous GOLD ABCD assessment (2022, 1a) tool, collapsing groups C and D into one single group, defined by increased exacerbation frequency.

Reproduced from the 2022 and 2023 GOLD Guidelines under the terms of allowed use.

However, despite maximal GOLD directed medical therapy with smoking cessation, short and long-acting inhaled bronchodilators, inhaled corticosteroids, phosphodiesterase 4...
(PDE4) inhibitors, azithromycin and structured pulmonary rehabilitation, patients with COPD continue to experience refractory dyspnea, pain, poor appetite, limitations of physical activity, emotional distress, depression and overall poor health-related quality of life (HRQoL). Patients with COPD have a symptom burden equal or greater than advanced cancer patients, but receive fewer symptom-alleviating treatments (opioids, benzodiazepines). Despite the preferences towards care focused on symptom burden, few patients (0.6-8%) with COPD receive palliative care services with most receiving interventions only at the end of life. The greatest impact on HRQoL in patients with COPD is from refractory dyspnea. The symptom of dyspnea is complex, and is intersectional with psychosocial and physiologic impairments, as research has demonstrated that the treatment of depression and anxiety in COPD can reduce dyspnea, and is likely at least part of the reason that our purely physiologic based pharmacologic interventions fail to address the full spectrum of breathlessness.

The GOLD guidelines have recommended a role for palliative care in the management of patients with severe symptoms since at least 2013. The recommendations have been in the context with end-of-life care recommendations and interlinked in the discussion with hospice care. The GOLD 2017 guideline was the first to address the possibility of outpatient palliative care involvement, though the authors recognized that this opportunity was not widely available. The discussion of the role of palliative care in the management of COPD has remained unchanged within the section of the document related to ‘supportive, palliative, end of life and hospice care’ including the just released 2023 GOLD guideline. Though it may not have been the intent, the location of the discussion of palliative care in the document with hospice and end of life care suggests that this not be introduced until the patient has been defined as end stage disease. Reference within the GOLD document and others to palliative approaches for ‘advanced’ or ‘end stage’ COPD, reinforce the late in disease recommendation for referral to palliative care. There is a significant group of patients with non-end stage disease but significant refractory symptom burden, for whom there is not clear guidance on when and how to engage concomitant palliative care.

Our current GOLD ABE pharmacologic treatment algorithm provides maximal disease specific therapy directed at optimization of physiologic airflow obstruction and exacerbation frequency, however leaving a gap in how best to approach the complex and multifactorial symptom of refractory breathlessness that occurs despite these pharmacologic interventions and pulmonary rehabilitation. There have been dramatic improvements in quality of life, breathlessness and survival when palliative care was added to the standard oncology care for patients with advanced stage lung cancer. As COPD is often co-existent with lung cancer, the dramatic results from trials of palliative care in lung cancer inform us about the potential utility of specialty palliative care in the
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refractory symptoms in COPD that may well fill this gap in our treatment algorithms. In this review, we will review the growing body of literature on the role of palliative care in the treatment of patients with COPD, identify barriers to intervention and consider the future direction of palliative care engagement in patients with COPD.

What defines ‘palliative care’ in lung disease? Before we can discuss palliative care in lung disease, we need to better understand the structure of palliative care delivery as primary palliative care and specialty palliative care. Primary palliative care is ideally incorporated into all outpatient encounters, with effective communication regarding symptoms and management, discussions regarding advanced care planning, education about disease progression and provision of patient and caregiver support. Primary palliative care, when effectively integrated into the continuum of care, is seamless with the evidence-based treatment guidelines specific to medication-based disease management (Figure 2)²⁹-³¹.

Figure 2. Primary and secondary palliative care integration in serious respiratory illness

This figure has three panels. In the top panel, the x-axis denotes patient wellbeing and function, and the y-axis denotes time. The top panel illustrates the hypothetical integration of palliative care cross illness trajectories of lung cancer (red dashed line), pulmonary hypertension (blue line), and chronic obstructive pulmonary disease/interstitial lung disease (COPD/ILD; gold line), each punctuated by declines in
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wellbeing at hospitalizations (stars) and potential lung transplant referral (diamonds). The integration of primary palliative care (orange circles) starts early (see Figure 4 for triggers), and the integration of secondary palliative care (blue circles) is added later, but well before the end of life. In the middle panel, the x-axis denotes palliative care intensity, and the y-axis denotes time. Primary palliative care increases in intensity after initiation (expanding orange triangle) as serious respiratory illness worsens, and secondary palliative care starts later and also increases in intensity but layers on top of secondary palliative care (expanding blue triangle). Through ongoing comanagement, a period of collaborative primary and secondary palliative care (overlapping triangles) should occur as illness severity worsens through the end of life. The bottom panel illustrates how palliative care may evolve across a continuum of serious respiratory illness. When illness is less severe, palliative care occurs concurrent with illness-directed therapies and then shifts focus from cure to end-of-life care (e.g., hospice and bereavement support) near and after death. This figure is adapted by permission from Iyer, AF. The Role of Palliative Care in COPD. Chest 2022;161: 1250-1262.

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However, with disease progression, the symptom management of the primary palliative care according to disease specific guideline-based medication interventions becomes insufficient to meet patient needs. In COPD, the quantifiable cough and breathlessness symptoms are just the tip of the iceberg for patients with advanced lung disease such as COPD, but they are the symptoms that have been the best studied and have validated assessment tools. Other systemic manifestations are individually assessed in non-pulmonary specialties, such as weight loss, depression, anxiety and fatigue, but what about the amalgam of the less easily quantified symptoms burden, including fear, loss of control, increasing dependence on others, cognitive impairment, isolation and caregiver/life partner distress? This is where specialty palliative care (or secondary/tertiary palliative care) is likely the missing piece in our structured care algorithm in COPD, able to address the multifaceted causes of an individual patient’s refractory symptom burden (Figure 2).

It is extremely important to underscore that palliative care should not be perceived to be equivalent with hospice care. Hospice care is provided when curative options are no longer deemed appropriate and there is an estimated 6-month prognosis. Hospice care is provided to help with symptoms such as pain and refractory breathlessness as one nears the end of life, while also preparing patients and families for their death and supporting families with respite care and bereavement. Hospice eligibility (in the United States) requires that two physicians certify that a patient has less than six months to live if the disease were to follow its natural progression. In contrast, palliative care can begin at any time, any stage of illness, at the discretion of the physician and patient. Both services do
have overlapping similarities and philosophies of care, following an interdisciplinary approach while addressing physical, emotional and spiritual pain.

**Structured Palliative Care in COPD**
Palliative care interventions are based on a structured framework outlined by the National Consensus Project Guidelines for Quality Palliative Care across 8 domains that address the physical, psychological, psychiatric, social, spiritual and cultural aspects of care and the care processes needed to address the symptom burden with severe disease. We address the domains both in general, and with items specific to COPD (Figure 3).

<table>
<thead>
<tr>
<th>Domain 1: Structure and Processes of Care</th>
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<tbody>
<tr>
<td>Assessment of disease status, comorbid conditions, and functional status.</td>
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<tr>
<th>Domain 2: Physical Aspects of Care</th>
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<tbody>
<tr>
<td>Medical management of dyspnea, pain, and/or other symptoms identified in Domain 1.</td>
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<tr>
<th>Domain 3: Psychological Aspects of Care</th>
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<tr>
<td>Assessment and treatment of anxiety and depression. This also includes gaining a deeper understanding of the patients’ understanding of their disease and how it impacts both the patient and their family.</td>
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<th>Domain 4: Social Aspects of Care</th>
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<td>Full social history and understanding of the “person” and not the patient.</td>
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<tr>
<th>Domain 5: Spiritual, Religious, and Existential Aspects of Care</th>
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<tr>
<td>Address patients and families hopes, fears and beliefs about death and/or afterlife, and generally explore spirituality as it relates to the patient.</td>
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<th>Domain 6: Cultural Aspects of Care</th>
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<tr>
<td>Communication with the patient and family will be respectful of cultural preferences. Will gain deeper understanding of the patients’ cultural background and how it relates to care.</td>
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<th>Domain 7: Care of the Imminently Dying Patient</th>
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<td>Should the patient be determined to be end of life, the provider will assist the patient and family with end-of-life concerns, hopes, and expectations. Symptoms will be addressed and a hospice referral if consistent with the goals of care.</td>
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<th>Domain 8: Ethical and Legal Aspects of Care</th>
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<tr>
<td>Exploring the patient’s preferences for end of life care, and a discussion about advance care planning should the patient want to discuss.</td>
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**Figure 3. Domains of care for a structured palliative care intervention**
Palliative care interventions are based on a structured framework outlined by the National Consensus Project Guidelines for Quality Palliative Care.

*Domain 1: Structure and Process of care*
Doman 1 focuses on the interprofessional care team that allows access to care for all patients living with COPD in various settings. Early integration and involvement of palliative care alongside with pulmonary specialists and primary care allows for a team-based approach for patients. This relies on the tenants of having primary palliative care skills taught to various specialties to be able to...
provide the basic palliative care needs. This includes providing a comprehensive assessment and care plan that is consistent with the patient’s goals and values, as well as addressing primary non-medical needs. This allows for early referral to various disciplines such as nutrition, social work, PT, OT and mental health to further assist patients and their families.

**Domain 2: Physical aspects of care**

Domain 2 focuses on the easing of suffering experienced by patients living with COPD due to their symptom burden. Initial assessment involves the focus on relieving symptoms of breathlessness, anxiety, depression, fatigue, weight loss and pain while also maintaining a focus on quality of life and patient’s functional status.

**Domain 3: Psychological and psychiatric aspects of care**

Despite ongoing pharmacological management of symptoms for patients with COPD, a large component of existential and complex psychological distress is a confounding factor. Domain 3 focuses on evaluating the psychological and psychosocial aspects including evaluating not only the patient, but also recognizing signs of psychological stress in families and caregivers. Domain 3 moves beyond physical symptoms, and the focus is on treating the person as a whole person and defining what ‘quality’ means to each patient. As the physical symptoms worsen, patients often place high value on achieving a sense of control, strengthening relationships, maintaining dignity and coming to peace spiritually. Lifestyle interventions can be beneficial in improving both anxiety and depression in COPD, earlier cognitive behavioral therapies are now being incorporated into pulmonary rehabilitation programs.

**Domain 4-6: Social aspects of care, spiritual aspects of care and cultural aspects of care**

These 3 domains focus and heavily rely on the use of the interdisciplinary team to address social factors, including identifying a social support network, addressing financial stressors, ensuring access to care, addressing spiritual concerns with disease progression. Palliative care often involves not only discussions and evaluation of the patient but also their caregivers and families, and addressing the influence that COPD has on the family unit and individual family members.

Dignity conserving therapy and spiritual support often helps reduce the loss of self-esteem and the feeling of being a burden on others. Patients who often live with caregivers are shown to have fewer exacerbations than those who live alone, however this can often bring a large emotional toll on caregivers, families and people who are often close to the patient. Support for families and caregivers may include assessment and active treatment for their own psychosocial distresses, feelings of anxiety and depression, providing adequate education about the disease, anticipatory guidance on symptom progression, and providing bereavement support.

Spirituality is multifaceted, multidimensional and includes religious and non-religious factors. Assessing spiritual needs and having spiritual involvement early on addresses
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distress that may be present for those living with COPD. Cultural differences often also arise in patients living with life limiting illnesses, as culture often influences the view with which patients and families perceive ongoing goals of care conversations, and discussion regarding the end of life. It remains important to respect values, beliefs and traditions related to health, illness, family caregiver roles and decision making.

Domain 7-8: Care of the imminently dying and ethical and legal aspects of care

Domains 7 and 8 focus on providing ongoing support to those patients who have COPD and are approaching the end of their life. A key component of palliative care focuses on advance care planning, which includes engaging patient and their caregivers in early, value-based discussions, while also addressing appropriate advance directives and creation of legal documents. Whenever appropriate, early discussions and referrals to hospice should be facilitated and ensuring that the patients have adequate communication about their prognosis, symptom burden as well as providing education and support for families. This often relieves burdens that may be imposed on families in an emotional situation as well as providing them bereavement services after a loved one has died.

Pharmacologic treatment of breathlessness

Most pharmacological based approaches for breathlessness have a limited evidence base and more research is needed, however the main drug class routinely used to palliate breathlessness are opioids. The American Thoracic Society has declared that the use of opioids is not contraindicated for the treatment of chronic dyspnea and can be safely used for individualized treatments. The initial studies on the use of systemic opioids for chronic breathlessness are summarized in a comprehensive meta-analysis of 8 small studies of short duration (less than 6 weeks) that suggested use of opiates, both short acting and sustained release, may improve breathlessness (data was a mix of short and sustained action opiates), and improve exercise induced breathlessness and exercise tolerance, though these studies were not limited to patients with COPD. Multiple subsequent studies demonstrated that opiates could be administered without the development or worsening of hypercapnia in COPD to address one of the barriers to use of opioids in refractory breathlessness. However, the most recent randomized controlled studies of sustained release morphine in COPD patients with refractory breathlessness failed to demonstrate a significant improvement in breathlessness, as did an older randomized control trial. The discordance in the impact on breathlessness between short acting and sustained release morphine may be a direct pharmacological effect, however the smaller, older studies were not limited to patients with COPD, and the significant impact may have been due to patients with non-COPD related breathlessness. The recent much larger studies of sustained release
morphine enrolled only patients with COPD and may more accurately reflect the impact of isolated pharmacologic therapy of morphine on breathlessness. The absence of a significant improvement in breathlessness in response to a single add on pharmacologic intervention supports the principle that the sensation of breathlessness is a complex, intersectional symptom, with a large component of existential and complex psychological distress as a confounding factor, requiring a multi-disciplinary approach for effective treatment.

Benzodiazepines have not been shown to have a significant impact on refractory breathlessness in COPD either alone or in combination with opioids.49,55

**Non-pharmacologic treatments of breathlessness in COPD**

Structured pulmonary rehabilitation programs have been shown to improve refractory symptoms of dyspnea, health related quality of life, improve functional exercise ability and reduce hospital admission.56,57 The American Thoracic Society with the European Respiratory Society published the definition of pulmonary rehabilitation in the ATS/ERS Pulmonary Rehabilitation Statement (2013) rehabilitation as “a comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education, and behavior change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviors.”58 The key components to a complete program outlined in this statement included initial assessments, exercise testing, quality of life measure, dyspnea assessment, nutritional status evaluation and occupational status evaluation and interventions of endurance and resistance training in addition to disease education, self-management training, goal setting, smoking cessation support and home exercise programs. The multidisciplinary approach and structured interventions of a pulmonary rehabilitation program align very similarly with the 8 domains of a structured palliative care program. There is insufficient data to determine if the comprehensive pulmonary rehabilitation program can be partitioned into individual interventions with the same improvements.59

**Barriers to effective palliative care in COPD**

The barriers to the introduction of primary and specialty palliative care include both patient and provider specific barriers. For patients and caregivers, barriers include limited awareness of palliative care60, including lack of knowledge of associated services, uncertainty about care preferences61 and overall poor communication with physicians. Consequently, patients and their families frequently do not understand that COPD is often a progressive and terminal illness.62 Physicians struggle with identification of suitable patients for palliative care due to the uncertain and variable disease trajectory of COPD and therefore there is significant uncertainty in predicting prognosis, that is compounded by lack of time and limited resources.21,63,66.
Physicians also reported hesitancy in prescribing opiates due to concerns with appropriate dosing and ultimately concerns over respiratory depression and hypercapnia with higher or sustained dosing\textsuperscript{67}, fear of scrutiny from drug monitoring boards in the wake of years of unchecked opiate prescribing and a general lack of comfort with dosing. The research in the palliation of breathlessness completed over the intervening years since these initial barriers were identified has demonstrated that opiates are safe to use in COPD without precipitating acute hypercapnia\textsuperscript{43-45,68}. The addition of palliative medicine rotations into physician training programs has increased the comfort level of the more recently trained pulmonary physicians in prescribing opiates for dyspnea, as compared to those who are further from training\textsuperscript{69,70} moves us closer to addressing this barrier to care.

The final barrier to introducing a structured role for palliative care is the national shortage of palliative care physicians nationwide. Despite the increase in fellowship trained palliative care physicians and emerging skills training offered to various healthcare professionals, the current numbers still do not meet patient demand. A 2011 study showed that there is only 1 palliative medicine physician for every 1200 persons living with a serious or life threatening illness\textsuperscript{29}. As the American population ages with chronic and debilitating diseases like COPD, there is an estimated 10,000 or more palliative care clinicians that will be needed to meet the demands\textsuperscript{31,72}. Therefore it remains crucial for all healthcare providers to receiving training in basic palliative care skills, and although specialty palliative care teams can deliver care focused on symptoms, care planning and quality of life, it is not feasible for all patients to be cared by these specialty teams\textsuperscript{73}.

\textbf{Timing of palliative care intervention}

The introduction of specialty palliative care (secondary/tertiary) into the care continuum of patients with lung disease has been overshadowed by the original association with hospice and end of life care by both patients and physicians and other providers. More recently, the American Thoracic Society, jointly with the American Academy of Hospice and Palliative Medicine, Hospice and Palliative Nurses Association and Social Work Hospice and Palliative Care Network, published a policy statement on the integration of palliative care into the continuum of patients with serious respiratory disorders. Their use of ‘serious’, rather than ‘advanced’ or ‘end-stage’, and the absence of any specific additional requirements that must be met, underscores the document content supporting a much earlier integration of palliative care into the comprehensive care of these patients. This document addresses one of the major barriers to earlier integration of palliative care (association with hospice care and end stage disease), with the second statement of fundamental value; ‘primary and specialist palliative care should be provided throughout the course of the illness when needs arise, integrated with illness-directed treatment, and should not be limited to patients in the final months or weeks of life’. It will take time for this very recent recommendation to filter into direct clinical
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These new comprehensive recommendations for early integrated palliative care are an exciting step forward in the management of these patients but does not yet answer the difficult concrete question of what specific criteria should trigger a referral to palliative care. The absence of concrete referral criteria allows for flexibility in referral, and longevity of the document and reflects the absence of data on which to make a more specific trigger recommendation for referral timing. The proposal of multiple thresholds for referral by two recent publications including mMRC, FEV1 and prognosis (BODE index) and a broader model including a spectrum of disease severity including FEV1%, breathlessness assessment, functionality (6MWD, weight loss), hospitalizations, oxygen use, lung transplant referral and extent of support needs underscore the multifaceted unmet needs of patients with lung disease. The impact of incorporation of the FEV1% into these referral models needs to be further evaluated, as FEV1% was removed from the GOLD treatment algorithm for stable COPD, with a shift in focus to unmet symptom burden and exacerbation frequency as better predictors of need for intensification of therapy.

The absence of concrete referral criterion will continue to fuel the uncertainty of some providers in the need for palliative care referral, and for some patients to understand the importance of timely referral for effective symptom management, however these are important steps toward redefining how we provide comprehensive care for patients with COPD.

Conclusion

While we have made significant strides in recognition of the gap in our pharmacologic management of patients with severe COPD and refractory symptoms, and the benefits of introducing specialty palliative care into the treatment algorithm, we have not yet generated sufficient data to be able to provide a clear criterion on when and how a structured specialty palliative care should be introduced into the treatment algorithm. The data we have to date suggests that attempting to compartmentalize the management of refractory symptoms into single treatment interventions, such as the use of opioids and benzodiazepines alone in the treatment of dyspnea is insufficient to provide relief of the multidimensional symptom of breathlessness. Similar to the successes of pulmonary rehabilitation in improving breathlessness and quality of life, it is likely that the best outcomes will be with a comprehensive specialty palliative care intervention encompassing all of the domains of care, and introduced early in the disease process, such that the greatest benefit can be derived in the remaining life years.
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Acknowledgement:
None

Conflicts of Interest Statement:
None

Funding:
None

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