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Chapter

Palliative Care for Patients with Lung Cancer: A Review of the Current Developments in the Field and Perspectives on the Implementation of Care

Yuk-Chiu Yip, Ka-Huen Yip and Wai-King Tsui

Abstract

This chapter aims to explore the key developments in palliative care for patients with lung cancer. Lung cancer has high morbidity and mortality rates and is a leading cause of cancer-related death in the United States. Substantial evidence supports the adoption of a palliative care approach for patients with lung cancer. Palliative care aims at preventing and relieving suffering by identifying and treating debilitating symptoms early, supporting patients and their relatives to optimize coping and active living, and addressing any physical, psychosocial, and spiritual problems. An increasing number of studies show that introducing palliative care at an early stage can be beneficial for patients with advanced malignancies, including advanced lung cancer. Currently, newer palliative care approaches are being adopted, including multidisciplinary clinics and home- or community-based care. Furthermore, alternative care delivery models, such as telephone and telehealth-based approaches and outpatient palliative care, are becoming increasingly popular. However, further research is required to determine the best palliative care approach for patients with lung cancer. This chapter is a valuable contribution for both researchers and clinicians in this field, providing a more profound understanding of the existing findings in many key areas, from the developmental milestones to the adoption of holistic approaches in palliative care services for patients with lung cancer.

Keywords: lung cancer, palliative services, palliative interventions, service models, holistic care, symptom management, models of delivery, candidates for referral

1. Introduction

As a discipline, palliative care (PC) has developed rapidly since the launch of the pioneering hospice movement by Dame Cicely Saunders in the 1960s. It has become inextricably connected to optimal care for patients with serious illnesses and is now widely considered a key component of oncologic therapy in patients with advanced

tumors. Moreover, it is widely agreed that patients with advanced malignancies should be referred to a PC physician at the earliest possible instance [1]. Many studies have shown that PC can improve the quality of life (QoL) of patients and their families and caregivers [2, 3].

Lung cancer is associated with high mortality and morbidity rates. It is the leading cause of cancer-related deaths in the United States, accounting for 25.9% of all cancer-related deaths in 2017 [4]. Currently, the anticipated 5-year survival rate for patients with lung cancer is only 18.1%. Even for patients with stage 1 non-small cell lung cancer (NSCLC), the 5-year overall survival rate is 73–90%, while for those with stage 4 NSCLC, it is a dismal 0–10% [5]. A meta-analysis including more than 5,000 patients with lung cancer showed that the average survival time of patients who do not undergo antineoplastic treatment is approximately 7 months [6]. Although lung cancer incidence and mortality are now declining, its prevalence remains high, with more than 500,000 people in the United States currently living with the disease [7]. For patients with advanced lung cancer, the burden of the disease, its consequences, and treatment side effects can dramatically reduce the QoL.

Lung cancer can take various forms, ranging from a silent or minimally symptomatic illness with a low burden and/or moderate progression to an aggressive and fast-progressing disease with severe symptoms. Survival rates and QoL tend to be worse in patients with advanced lung cancer experiencing severe symptoms [8]. Lung cancer symptoms include pain, nausea, dyspnea, fatigue, anorexia/cachexia, depression, and confusion/delirium [9]. Because of the high prevalence and symptom burden of the disease, the impact of PC on patients with lung cancer has attracted great research attention in recent years.

This chapter is structured to offer readers a coherent, systematic overview of the current developments and practices in the field of PC for patients with lung cancer. It starts with a brief introduction of the concepts underpinning PC, followed by an overview of research evidence that supports the role of PC in patients with lung cancer. Next, we discuss the criteria for identifying potential candidates for PC referral and explore various PC delivery models. Finally, we examine how holistic care is provided to the patients through different interventions.

2. Defining PC

The meaning of the term PC has been widely debated among healthcare professionals and the general public. The term is frequently used interchangeably with hospice care. However, hospice care focuses specifically on end-of-life practices prioritizing patient comfort over prolonging life. Patients undergoing hospice care do not usually receive disease-modifying treatments (such as antineoplastic therapies for patients with lung cancer) designed to prolong survival. This is further complicated by the fact that, in oncology, the term “palliative” is used to describe treatments that are not intended to cure, even if the key objective of the treatment is to prolong survival.

For clarity, the WHO definition of PC is employed here [10]. The WHO defines PC as a treatment approach designed to enhance the QoL of patients suffering from long-term fatal illnesses and their families by identifying, preventing, and relieving suffering as early as possible, as well as addressing physical, psychosocial, and spiritual problems. The key features of PC include a team-based approach that provides pain and symptom relief, supports patients and their relatives to optimize coping and

active living, and addresses the psychological and spiritual aspects of care. PC can be delivered at any stage during an illness and used in combination with treatments designed to cure diseases or prolong survival. Although it is in no way intended to hasten death, PC does involve recognizing that death is a normal process and must be carefully thought out in advance. Specialized PC is ideally delivered by an interdisciplinary team including healthcare providers (physicians and advanced practice providers), nurses, pharmacists, chaplains, social workers, physical therapists, and dietitians.

3. Evidence supporting the role of PC in patients with lung cancer

A growing body of evidence supports using PC in patients with lung cancer. Temel et al. (2010) performed a study on early referral to PC specialists for patients newly diagnosed with advanced NSCLC [2], which is probably the most formative study on PC to date. The findings of this study showed that patients assigned to early PC combined with routine oncologic therapy had a better QoL, lower depression levels, less aggressive end-of-life care, and a significant albeit moderate improvement in overall survival. The advantages of early PC involvement in advanced lung cancer care attracted substantial research interest after this trial.

Numerous studies have found that early PC can have a positive impact on survival and QoL. For example, in the ENABLE randomized control trial, four educational sessions were held with advanced practice nurses trained in PC over the course of a week, which was followed up with monthly phone consultations. The findings showed that patients with advanced cancer undergoing PC had improved QoL [11]. Furthermore, the survival rates were found to be improved in patients with advanced cancer who were given access to a PC specialist at an early stage with monthly follow-ups [12]. Early PC was also found to reduce caregiver depression scores and stress burden [3]. In another randomized controlled trial, medical oncology clinics were randomized into PC team consultation and monthly follow-up groups [13]. The findings indicated significant improvements in end-of-life care and patient satisfaction at the primary 3-month endpoint, as well as vast improvements in the additional QoL metrics at 4 months (secondary endpoint) [13]. A recent retrospective analysis including a large cohort of patients diagnosed with advanced lung cancer who had been referred to a PC provider following their diagnosis found that survival rates were improved (i.e., the likelihood of death was reduced) in acute care settings [14]. Notably, this positive relationship with improved survival was only evident in patients who were seen by a PC specialist more than 1 month after diagnosis (but within a year). Contrarily, a negative relationship was observed among patients who were seen within the first month. Interestingly, patients referred within a month of diagnosis were seen in inpatient settings, which indicates that such appointments may have been in the end-of-life setting. The higher chances of death in such patients may be due to poor functional status, extensive disease burden, and/or poor prognosis, which may have ultimately hastened the PC referral process.

Researchers have investigated the different components involved in a PC visit to determine the optimal ways to achieve the benefits listed above. Many different patient outcomes are impacted by a PC provider's area of focus during each appointment. For instance, outpatient PC consultations can help with symptom management, prognostic information, psychosocial support, and elucidating patients' end-of-life care objectives. A prior study revealed that patients who had more

consultations focusing on coping with symptoms reported better QoL and depression scores, whereas those who had more consultations focusing on treatment decisions were less likely to receive aggressive end-of-life care. Furthermore, patients with more consultations focusing on advance care planning were more likely to relocate to a hospice [15]. Studies have also shown that early PC referral improves prognostic understanding in patients with advanced lung cancer [16].

The above evidence confirms the advantages of early PC introduction. Consequently, there has been a significant increase in the number of patients referred to PC within 1 year of diagnosis of metastatic lung cancer [17]. Nevertheless, despite the increase in the proportion of patients referred to PC from 3% in 2001 to over 30% in 2013, most patients did not receive a PC referral at all, and only one-fifth of those who did, received outpatient PC services [17]. Thus, research indicates that most people with advanced lung cancer are not able to see a PC practitioner regularly, despite the well-documented advantages of this treatment approach.

4. Candidates and timing for PC referral: meeting patients' needs within the boundary of existential challenges

According to the current American Society of Clinical Oncology (ASCO) guidelines, patients with advanced cancer (and their caregivers) should be given access to PC services within 8 weeks of diagnosis and while undergoing treatment [1]. However, in reality, such volume of referrals would rapidly overload the existing PC services and further impede care for patients living in places where access to PC is limited. Moreover, there is currently a global lack of PC providers, further hindering the service.

Many attempts have been made to determine acceptable PC referral criteria for patients with cancer [18, 19] due to the misalignment between the number of patients who are eligible for referral and the number of patients who can actually be seen. For instance, Hui et al. employed a panel of 60 experts worldwide and performed a Delphi analysis to establish the major and minor criteria for guiding outpatient PC referrals [20]. Ultimately, 11 major criteria were identified, namely, (1) severe physical symptoms; (2) severe emotional symptoms; (3) requests for hastened death by the patient; (4) spiritual or existential crisis; (5) a need for help with advance planning and decision-making; morbid complications, such as (6) spinal cord compression, (7) brain or leptomeningeal metastases, or (8) delirium; (9) referral requests by the patient; (10) the passing of 3 months since diagnosis with an expected survival time of less than 1 year; and (11) disease progression following second-line therapy [20]. Moreover, 36 minor criteria were identified in cases where 70% of experts reached an agreement. This further emphasizes the difficulty of creating a list of specific criteria.

A recent observational study examined the feasibility of applying these criteria to specific groups of patients with lung cancer [21]. In this study, the previously defined Delphi criteria were reduced to six, namely, (1) severe physical symptoms; (2) emotional symptoms; (3) brain or leptomeningeal metastases; (4) cord compression/cauda equina; (5) within 3 months of cancer diagnosis and a projected survival time of less than a year; and (6) disease progression after second-line therapy. The findings showed that 82.4% of the 28,164 patients who met the criteria for PC referral based on these indicators obtained PC referral, with a median wait time of 56 days. Thus, the findings of this feasibility study indicate that this condensed list of criteria may be effective if adopted nationally.

The current guidelines proposed by the National Comprehensive Cancer Network and the American College of Chest Physicians recommend that PC be introduced at an early stage for all patients with metastatic NSCLC [22, 23]. The ASCO also advises that PC is initiated early for patients with advanced malignancies [1]. However, there are no recommendations regarding the timing of PC referral, and few studies have explored the effect of varying time points of early referral. In the study of Bakitas et al. [12], patients with advanced cancer referred for PC at the time of diagnosis and those referred 3 months later had similar scores in the QoL, mood, or use of health-care resources evaluations. One of the many reasons for providers to delay referrals until symptoms are deemed refractory may be the absence of well-defined guidelines regarding the timing of PC referral. As a result, the time points at which referrals are made are inconsistent, and in many cases, referrals are tardy.

We propose that a compromise position be adopted, one that recognizes real-world workforce issues and the absence of clear guidelines setting out the ideal referral time point yet considers cancer staging at diagnosis, patients' prognosis, and the burden of symptoms. Assuming resources permit, patients with advanced lung cancer should be referred to the PC team within 3 months of diagnosis. This will give the team the opportunity to treat symptoms as they arise and enable the patient and team to build a relationship, which will be invaluable over time as the patient's condition deteriorates. If this is not possible, patients with a high symptom burden should be prioritized regardless of the prognosis. Other patients who should be prioritized for PC referral include those with complex psychosocial stresses, those with an estimated survival prognosis of no more than 1 year, and those with disease progression following first- or second-line treatment. In our opinion, it is critical that healthcare providers have developed primary PC skills, as they will need to fill the inevitable delay between disease diagnosis and PC referral. In particular, it is recommended that healthcare providers working with patients with lung cancer develop their primary PC skills and make efforts to ensure other members of the team are similarly skilled. Symptom assessments used in oncology practices should be standardized yet modified to meet the conditions of the practice and local resources; furthermore, these should incorporate psychosocial stress assessments that can be administered routinely. Using assessments to detect stressors early can advance referrals to case managers or social workers. Similarly, informed by assessment findings, oncology nurses and advanced nurse practitioners can hold timely consultations regarding care goals and future directives. Combined, these measures would promote communication about the care goals and support patients and caregivers in end-of-life settings.

5. Diverse models of PC delivery: existing trends and future opportunities

When patients with lung cancer are admitted to the hospital, PC is traditionally provided by consultation teams in inpatient settings [24]. As PC can largely reduce hospital expenses, fee-for-service bundled payment systems have a large influence on the development of PC delivery models [25]. Specialist consultation services and inpatient PC facilities, in which the PC team members are the primary patient caregivers, are the two most common models in hospital settings. Consequently, PC is expected to be centered in inpatient settings in the USA [26, 27]. More recent models of PC include multidisciplinary clinics [2, 28–31], home- or community-based care [32, 33], alternative delivery models (such as those that employ telephone and telehealth methods [7, 34, 35]), and outpatient PC clinics [36–38]. These newer

models are favored over traditional inpatient delivery models because the focus is on the upstream incorporation of PC in outpatient settings. Additionally, the care coordination and follow-up settings are better established [39]. Some of these newer PC delivery models are discussed in depth below.

5.1 Multidisciplinary PC or oncology clinics

Although the timing of PC introduction should be based on patients' needs, it is important that assessments include factors such as the patient's prognosis, time from diagnosis to median survival age (based on cancer stage), treatment trajectory (such as first or second line of treatment), and performance status [40]. Delivering PC to patients with lung cancer at the same time as their lung cancer treatment in outpatient oncology clinic settings is a well-established delivery model that has been found to improve patient outcomes [2, 28]. Similarly, breathlessness clinics also provide a multidisciplinary integrated service that often combines respiratory, physiotherapy, occupational therapy, and PC examinations and management as a one-stop treatment paradigm. Although it is not limited to patients with lung cancer, this approach has increased the patients' mastery of breathlessness (i.e., patients' feelings of control over their respiratory condition and its impact on their QoL and function) by 16% as compared with the control group [31]. Furthermore, a systematic evaluation of 37 research articles covering 18 different breathlessness services found a substantial reduction in distress due to lower breathlessness and depression ratings compared with the control groups [41]; however, no variations in the health status or QoL could be identified. PC integration in outpatient multidisciplinary settings could be the most effective model for coordinating the care of patients with lung cancer, particularly if they are also being given disease-directed treatments like radiation or chemotherapy. Nonetheless, there is a major shortage of PC professionals, as well as a lack of capacity in outpatient cancer settings at present, and these have been reported to be significant barriers hindering the widespread implementation of such approaches [26, 42, 43].

5.2 Community-based PC

The interdisciplinary community-based care offered by registered home health or hospice agencies may have influenced the development of this approach. Previous studies have shown that this model can enhance patient satisfaction, reduce care demands in emergency departments, reduce the number of hospital days, and minimize the number of skilled nursing facility days compared to administering PC in general care settings for those with serious illnesses, including approximately 61% with advanced cancer [44]. Moreover, healthcare costs dropped by 45% due to a reduction in the use of healthcare resources. In the future, community-based PC will likely become an increasingly important PC delivery model [33]. Nonetheless, evidence supporting the use of community-based PC for patients with lung cancer is limited.

5.3 Telehealth

Patients and their families, particularly those living in rural areas, have been advised to use delivery models that involve telephone and telehealth technologies to reduce travel demands. In the ENABLE trial, telephone-based assessments were employed to facilitate the delivery of PC in a rural population of patients with

advanced cancer, and the results demonstrated improved QoL [2, 45]. Another study found that a nurse-led, completely telephone-based PC intervention for patients with lung cancer is feasible [35]. Although alternative PC delivery models will almost certainly include a combination of treatments (including telemedicine), existing evidence is limited to observational non-controlled research and a few quasi-experimental studies [46]. A more recent umbrella review revealed that there is still a lack of evidence to support the use of telemedicine techniques in PC [47].

Technological issues are a significant drawback of telehealth approaches, particularly when live video platforms are used. Commonly reported issues include poor connectivity and connection, slow video feed, or problems with understanding how to use the technology (particularly among older patients) [48]. These issues are more prominent among patients from lower socioeconomic groups, non-Caucasians, and those living in rural areas. Moreover, clinicians have reported that the most severely ill patients gained the least benefits from the telehealth symptom management options [49]. Thus, there is a significant research gap regarding the intersection of PC and telehealth. Nonetheless, several well-established innovative PC delivery models have been developed for patients with lung cancer. Inpatient delivery models are preferable for such patients due to the symptom burden and their frequent inpatient clinical encounters. However, research has shown that outpatient models also enable early PC integration and enhance patient outcomes. Thus, combined delivery methods based on available resources and context are critical in providing timely PC based on the guidelines proposed by the ASCO, which recommend that PC is initiated within 8 weeks of diagnosis of advanced lung cancer [1].

Based on the above, further research is required to determine the optimal methods for delivering PC to patients with advanced malignancies. The best approaches are likely to be multidisciplinary in nature and accessible to all patients in need. In order to understand the barriers hindering the universal provision of specialized PC to patients with advanced lung cancer, oncological care providers must be able to identify and address the needs of such patients as much as possible. Standard guidelines outlining the factors involved in PC (specifically in the field of oncology) have been put forward by the ASCO and the American Academy of Hospice and Palliative Medicine [50]. Experts agree that symptoms must be evaluated and managed, with a specific focus on common oncologic symptoms, such as pain, nausea, diarrhea, vomiting, and dyspnea.

6. Patient care and therapeutic interventions in PC services for patients with lung cancer

Although there are benefits to applying PC as an additional or alternative approach to improve patients' QoL even if they are not receiving cancer-directed therapy, directed treatments have been developed to alleviate disease-related symptoms, and these are discussed below.

Pain is one of the most common and debilitating symptoms in advanced malignancies. Additionally, pain tends to be a multifaceted experience of suffering that is related to psychological distress. Thus, in such cases, a multidisciplinary approach is recommended. Opioids are one of the most commonly used medicines for managing cancer-related pain, and an aggressive titration is often necessary to control pain effectively. However, given the widespread opioid abuse problem, it is important that practitioners and/or caregivers remain vigilant about any abuse/misuse while also

avoiding undertreating pain. Pain caused by bone and/or liver metastases, as well as neuropathic pain, can be relieved using low-dose corticosteroids [51, 52].

Disease-related complications, including malignant effusions (pleural and pericardial) and airway obstruction, can cause dyspnea and cough in those with locally-advanced NSCLC or lung cancer metastases. Thoracentesis, pleural drain placement, and pericardiocentesis with a pericardial drain/window are examples of therapeutic procedures that can be performed for palliative reasons [53, 54]. Furthermore, methods such as bronchoscopy, photodynamic treatment, laser therapy, and stent implantation (endobronchial or vascular) can be used to ease airway obstruction [53]. Hemoptysis can be treated with arterial embolization.

Patients with advanced NSCLC, as well as those with lung metastases from other advanced cancers, may experience a sensation known as air hunger. Various pharmacologic and nonpharmacologic therapies can be considered to reduce this discomfort as much as possible. Morphine has been found to alleviate the feeling of air hunger in some people. Other opioids, such as oxycodone and fentanyl, have been examined in this context, but the findings have been conflicting [55]. A motorized fan aimed toward the face can alleviate this symptom for some individuals [56]. In such cases, benzodiazepines can also be administered as an adjuvant or a replacement for opioids to alleviate dyspnea [57].

Anticholinergic medications can be administered to minimize excessive secretions, such as scopolamine, atropine, hyoscyamine, and glycopyrrolate [58, 59]. Patients with substantial appetite and weight loss may benefit from appetite stimulants and dietary counseling. Although the effectiveness of low-dose corticosteroids in stimulating appetite is unknown [52], these drugs are often used for this purpose and as an antiemetic [51].

Fatigue is also a common symptom in those suffering from advanced-stage cancer. Other symptoms, including pain, dyspnea, and depression, can also contribute to this. Endocrinopathies and electrolyte abnormalities are potential metabolic causes that must be adequately investigated and managed. Although various medications have been studied, such as steroids, stimulants, antidepressants, and erythropoietin-stimulating agents, there is no compelling evidence for their efficacy in treating fatigue [60]. Physical activity and exercise have been found to be the most effective interventions for reducing fatigue [61].

Psychological distress and depression are common in patients with advanced cancers, particularly metastatic NSCLC. In a study examining the QoL of patients with advanced NSCLC, major depression was observed in 23% of patients and was also associated with lower median survival in this group compared with the group without depression [62]. Psychological distress has been shown to reduce the QoL, impair responsiveness to medicines, and increase hospitalization rates [63]. Dyspnea has also been found to be related to anxiety, which is often coupled with uncertainty about the course of the disease. The Hospital Anxiety and Depression Scale, Patient Health Questionnaire-4, or Generalized Anxiety Disorder 7-item scale can all be used to evaluate psychological symptoms. Two potential medications that can be used to alleviate symptoms are selective serotonin reuptake inhibitors and buspirone. The former are commonly administered to individuals with panic attacks [63], while breakthrough symptoms can be reduced using benzodiazepines. When it comes to treating anxiety, nonpharmacologic therapies are critical. Cognitive-behavioral therapy should be a key component of any therapeutic plan. Relaxation and panic control techniques, mindfulness training, distraction techniques, and breathing

strategies may also be beneficial [63]. Additionally, patients suffering from social and financial stress are likely to benefit from social work engagement. Support groups can help patients connect with others experiencing similar symptoms. Moreover, the ENABLE II trial found that regular meetings with PC nurses to provide psychoeducation improved the patients' mood and QoL [11].

Spiritual distress is common among patients with a progressive life-threatening illness. Frequent concerns include questions about existence, the meaning of life, regret, and destiny. Spiritual issues may also be important to patients as they approach the end of their lives. The Spiritual Well-Being Scale or the Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being can be employed to evaluate symptoms. In most cases, pharmacologic therapy is not required. Benzodiazepines or barbiturates can be used for sedative purposes in rare and refractory cases. It is important to listen to the patient's concerns actively and offer gentle reassurance, which are examples of nonpharmacologic therapies. Family involvement, pastoral care, and community and religious resources are all critical, as it can be incredibly distressing for individuals to watch a family member suffer from spiritual distress. It is thus critical to assess caregivers for exhaustion.

7. Conclusion

Despite the significant advances in the care-providing approaches for patients with lung cancer in recent years, the morbidity and mortality remain high. Cancer and its treatments can cause incredibly debilitating symptoms. PC, an approach to care for patients with life-threatening illnesses, including those with lung cancer (or any cancer), can reduce this burden. If introduced at an early stage of a patient's illness, PC can alleviate symptoms and enhance the QoL. There is even a possibility that it will increase the chances of survival. In order to provide PC timely, the ASCO guidelines recommend that it be started within 8 weeks of an advanced lung cancer diagnosis. Ideally, the patient should be referred to PC immediately after diagnosis. However, referring all patients for early PC is challenged by understaffed PC teams. Clinicians may make referrals based on their patient's burden of symptoms or psychosocial stresses. Patients with lung cancer would benefit from clinicians with primary PC skills. Therefore, clinicians should take steps to develop these skills and, from the outset, provide routine symptom and psychosocial assessments while the patient awaits the referral. To support the patient's PC needs, advanced practice providers, nurses, and social workers can be trained to provide PC through the oncology practice. Moreover, the PC approach should involve a combination of delivery methods based on available resources. A wide range of pharmacologic and nonpharmacologic tools are available to help patients manage their illnesses. Once treatment has been initiated, the patient's response should be regularly monitored. Providing appropriate holistic care will enable patients to live as long as possible with the best QoL.

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Conflict of interest

The authors declare no conflict of interest.

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