LITERATURE REVIEW

Implementing Palliative and End-of-Life Care in Lung Cancer: When to Start?

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ABSTRACT

Lung cancer is among the most prevalent cancers and the primary cause of cancer-related mortality. Despite advances in treatment, patients often have a poor prognosis, with a limited survival period, particularly in advanced stages. Significant morbidity is linked with lung cancer, and symptoms are frequently inadequately controlled, resulting in a considerable symptom burden for patients and their family caregivers. It is typically accompanied by an overall reduction in one's quality of life (QoL). Palliative care is an established therapy paradigm that successfully enhances symptom management and physical and mental health. It can be initiated as soon as the patient develops symptoms (even in the early stage) or is diagnosed with a late stage. Over the past few decades, palliative care has become a vital part of comprehensive care for people, especially those with advanced diseases. Early palliative care (EPC) integration within the oncology setting is more effective than standard care in enhancing the patient's QoL and length of survival, resulting in less intrusive end-of-life care. When caring for lung cancer patients, medical practitioners must remember their duty to cure occasionally, routinely alleviate, and constantly comfort the patient. Treating physical symptoms, illness comprehension, coping, and psychological and spiritual anguish are all vital components. Intervention strategies by multidisciplinary teams concentrating on the patient and their family and dealing with the circumstances are essential. All health providers should prioritize palliative and end-of-life care to enhance care and assist patients and their families in navigating the final period of life.

INTRODUCTION

Lung cancer is a serious threat to global public health since it is the leading cause of cancer-related deaths in both men and women worldwide. With a five-year survival rate of only 6%, $^{5}/_{6}$ cases were identified at an advanced stage.[1] Despite the progress in diagnosing lung cancer through pathology and developing treatments for the disease, many people continue to suffer from progressively fatal diseases.[2,3] Patients with a life-threatening illness such as lung cancer may experience high emotional anguish. In many cases, a relatively brief survival results in substantial suffering and reduced quality of life (QoL). Patients and their families go through unimaginable suffering between the moment of diagnosis and the time of death.[4] Palliative care is a model that has been used successfully for a long time to reduce suffering. Early palliative care (EPC) and conventional therapy have been proven to positively affect QoL, depression, and the quantity of intensive (rather unnecessary) medical operations at the end of life. Regrettably, palliative care is not undertaken until a late stage in lung cancer progression. Many people consider it a therapy used in hospice or other end-of-life care.[5] This article addressed the significance of EPC and end-of-life care in lung cancer patient treatment. Hence all clinicians are aware of and attentive to the requirements of advanced lung cancer patients.

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Palliative Care: Definition

The modern hospice was first introduced in 1967 by a pioneer in palliative care, Dame Cicely Saunders, and her innovative work has inspired all subsequent ideas in this field.[6] Regrettably, both those working in the medical field and members of the general population have a muddled understanding of what "palliative care" actually means. Sometimes, it is used interchangeably with the phrase "hospice care", which describes a type of end-of-life care that focuses more on providing comfort than extending lives (no longer receiving disease-modifying therapies). We use "palliative" to describe the non-curative treatment, even when the goal is to prolong survival, which adds to the confusion.[7] Palliative care is defined by the World Health Organization (WHO) as "an approach that improves the QoL of patients and their families facing life-threatening illness through the prevention and relief of suffering through the early identification and impeccable assessment and treatment of pain and other physical, psychosocial, and spiritual problems".[8] By avoiding and alleviating suffering, palliative care enhances the QoL for patients and their caregivers confronting life-threatening illnesses.

Time limitations and the absence of aggressive interventions in a hospice are the significant distinctions between hospice care and palliative care. Hospice care is offered when the patient's life expectancy is estimated to be less than six months. However, palliative care is not time-limited and should be chosen to deal with secondary symptoms caused by therapies for a disease with possible, but not guaranteed, recovery.[9] According to the WHO definition, palliative care can be administered to a patient at any time throughout their sickness, in collaboration with other treatments that attempt to prolong the patient's life or even cure their condition.[7]

The Development of a New Perspective on Palliative Care

Early palliative care combines cancer treatment with palliative care for metastatic lung cancer patients. A study by Temel, *et al*. (2017) marked a turning point in the field.[20] After 12 weeks, patients assigned to EPC had a higher QoL and longer median overall survival (OS) (11.6 vs 8.9 months, P = 0.02) than individuals randomized to cancer treatment only. Patients who received EPC had a significantly improved QoL as well. According to Sullivan, *et al*. (2019), palliative care is associated with improved survival and a decreased risk of death in an acute care setting for patients with advanced lung cancer who receive it between 31- and -365 days following diagnosis.[10] Following the publication of the research, EPC was approved by the American Society of Clinical Oncology (ASCO) as a standard management for metastatic lung cancer.[1,10]

Patients with advanced lung cancer usually receive palliative care when standard lung cancer treatments are no longer effective, typically during the later stages of the disease.[11] From 1990 until 2002, WHO cancer resource allocation models showed a rise in palliative care and a decline in disease-modifying drugs (Figure 1). A paradigm change occurred over these past years, which resulted in the recommendation that metastatic lung cancer patients acquire early palliative treatment.[12]

There should be no distinction between palliative care and disease-modifying treatments. Rather, it should be incorporated into treating lung cancer from the onset. It forms a square pillar of care along with diagnostics, systemic therapy, radiation therapy, surgery, and follow-up. Palliative care should be accessible to lung cancer patients and their caregivers throughout the illness and in many healthcare settings. In the end, the assignment should be predominantly based on the seriousness of the patient's condition and diseases (Figure 1).[12]

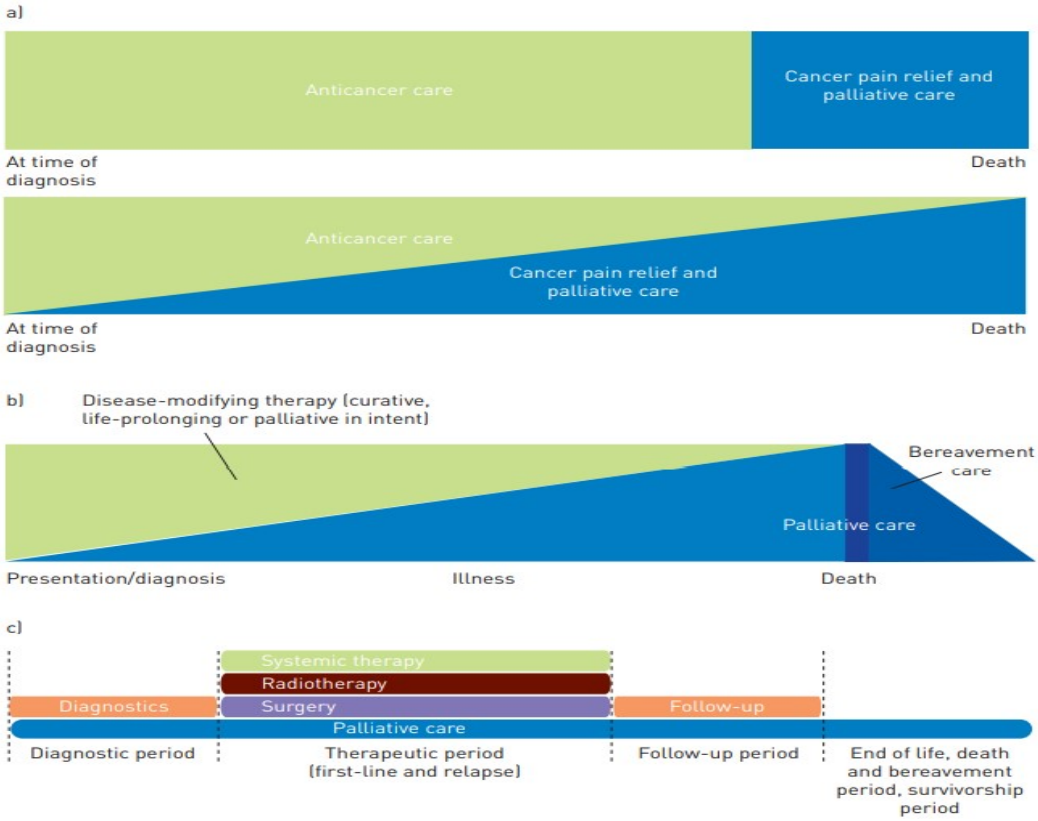

Figure 1. a) 1990 WHO cancer resource allocation model; **b)** 2002 WHO "continuum of care" model for palliative care; **c)** Early integrated lung cancer care concept with diagnostics, systemic therapy, radiation, surgery, palliative care, and follow-up as pillars of lung cancer care.[13]

The Workings of the Early Palliative Care Action Mechanism

Early palliative care is multifaceted and uses several approaches—first, the biological mechanism, commonly known as the immune system's potentially proper anticancer function. Improving one's QoL will reduce chronic stress, which may lead to improved immune system function (Figure 2A and B). There is a correlation between high levels of chronic stress, increased levels of cortisol, and decreased levels of adaptive immunological resistance, a consequence of the altered profile of T helper lymphocytes in the body.[1,14,15] T cells with a changed profile dampen the immune response against tumors. Cortisol levels were lower in individuals with a higher QoL, indicating that there may have been an improvement in immune function. Another key mechanism of action is lowering depressive symptoms caused by multidirectional palliative care early on.[1] Previous studies have identified depression as a potentially clinically relevant predictor of overall mortality in cancer patients.[16,17] Patients suffering from minimal depression are more active, which is good for their health (Figure 2B). They also observe distressing disease and cancer treatment symptoms developing more frequently and rapidly, which may affect the survival rate. Recent studies suggested that physical activity might improve the QoL of patients with lung cancer by lowering the immune system's inflammatory response and boosting the immune cells' activity. This new information means clinicians can obtain a deeper insight into the patient and determine the most appropriate treatment.[1,18]

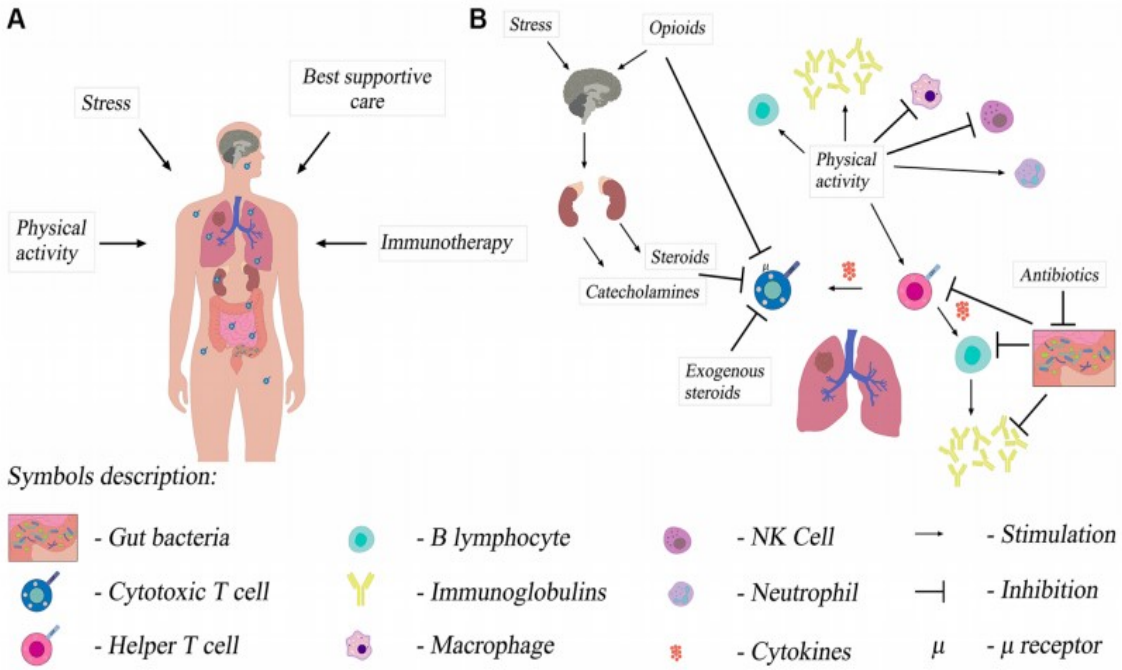

Figure 2. (A) Several factors influence the immune system's function in non-small cell lung cancer (NSCLC) patients; **(B)** Immunosuppressive effects of stress depend on a fundamental mechanism of action. Regular physical activity lowers the inflammatory response and boosts the movement of the immune cells that fight cancer.[1] NK cell = natural killer cell

Candidates Who Would Benefit from Receiving Palliative Care

It is assumed by the very nature of the term "palliative care" that its recipients are terminally ill people or those whose circumstances are terminal. Patients who have lung cancer would consequently be eligible. However, there is a limited supply of materials. Hence, professionals in palliative care have reached an international consensus on the key criteria for its use: (1) Need-based criteria, which include significant mental and/or physical suffering, delirium, and spinal cord/brain/leptomeningeal disease, and (2) time-based criteria, like disease trajectory and advancement (less than one-year median survival, and disease progression despite second-line treatment). This means that palliative care can be provided even to patients who are still at an early stage if the patient is disturbed by mental or physical complaints. By time-based criteria, all patients with advanced small or non-small lung cancer would reasonably be entitled to palliative care because their median survival has consistently been less than a year. Other valid reasons for recommending a patient are the patient's request and aid in decision-making or treatment plan. A reference to organizations that provide palliative care assistance, such as bereavement counselling, can also be highly beneficial to caregivers.[7]

Palliative Care Treatment Options for Patients with Lung Cancer

Palliative care could be delivered with therapies to cure the illness or extend the patient's life during a patient's condition. Palliative care does not seek to speed up the dying process, but it acknowledges that death is a natural process that should be thought about and planned for in advance. Helping patients and families to cope and live actively, consideration of the psychological and spiritual aspects, and using a team-based approach to relieving pain and other painful symptoms are essential to palliative care.[7]

Palliative care is another technique for reducing pain and other unpleasant symptoms. Doctors, nurses, physical therapists, nutritionists, social workers, occupational therapists, and chaplains are common members of palliative care teams. Extensive clinical trials have demonstrated how EPC enhances the QoL, minimizes depressive symptoms, and increases support care. EPC decreased lung cancer patients' treatment in their final stages of life, increased the number of patients who enrolled in hospice care and the length of their stays and improved overall survival. Notably, none of the trials showed any adverse consequences linked with early engagement in palliative care.[19,20]

Patients who have advanced cancer are eligible for palliative care, which consists of the following components: relationship building with the patient and caregivers; management of symptoms, distress, and functional status (such as fatigue, dyspnea, pain, mood, sleep disturbance, constipation, or nausea); education about the disease and prognosis; discussion of treatment goals and coping needs; assistance with making a clinical decision; coordination with another care provider; and referrals as indicated. Palliative care is

provided by improving physical complaints, psychological conditions, and spiritual well-being.[20]

Physical complaints could be improved by surgery, radiotherapy, or systemic therapy.[12] Palliative surgery could afford very effective pain relief in various scenarios. Surgical debulking of large, slow-growing tumors can alleviate discomfort and is appropriate in patients where the procedure's estimated morbidity is low. Individuals in advanced stages may also benefit from palliative surgery. For example, in bone metastases, such patients may benefit from the preventive fixation of a long bone (in terms of reduced pain and risk of fracture). Palliative radiation is frequently utilized in symptomatic lung cancer, metastatic illness, and locally advanced patients who cannot receive curative treatment. Palliative radiotherapy is an effective treatment for lung cancer, with ⅔ of treated patients experiencing symptom reduction or relief and ⅓ experiencing QoL improvement. Systemic therapies are aimed at managing pain and other symptoms. Although subjective, pain rating scales are nevertheless accurate, and, for most patients, they give a number indicating the pain's intensity.

A recent study demonstrated that palliative care might prevent and alleviate pain by early detection, positive evaluation, and pain control, thereby increasing the QoL of patients and families. Other symptoms such as fatigue, dyspnea, mood, sleep disturbance, constipation, or nausea should also be treated to obtain a better QoL.[21,22]

A lung cancer diagnosis will affect the patient's psychosocial and spiritual well-being. Patients may experience anxiety, stress, and even depression due to a serious illness diagnosis and fear of the future. Aside from patients, caregivers of lung cancer patients have a significant incidence of anxiety and depression. Caregivers' stress and emotional states are linked to a patient's QoL, and the caregivers' emotional status is likewise connected to the patient's emotional problems. Studies in lung cancer patients showed that palliative care could significantly reduce the incidence of depression in patients and their caregivers.[5,23]

What is "End-of-Life Care" (EOLC)?

There is no general agreement over the meaning of "end of life" (EOLC) or when it should occur. The final few days, weeks, or even months of a person's life are considered by many people to be their last moments in life. Although the terms palliative care and EOLC or hospice care are frequently used interchangeably, there are distinctions between them. Palliative care is appropriate at any time, even simultaneously with curative-intent treatment. Still, EOLC is only one component of palliative care, provided at the end of life, as the name implies. Hospice care, or EOLC, is a quality, compassionate model focusing on caring, not curing.[24]

Patients regarded to have less than a one-year life expectancy are the focus of the recommendation made by the General Medical Council (GMC) in the United Kingdom. The need for hospice care was defined by the final six months of life in the United States. Many definitions use a period dependent on a patient's survival. However, survival cannot be anticipated with a high degree of accuracy. If we continue to use the old methodology, many patients will require EOLC, and many unmet requirements will go unaddressed. EOLC should be based on the patient's needs, not the time frame.[2,24,25]

EOLC should aim to meet the needs of the patient and the family during the later phases of life. In 2006, the United Kingdom National Council for Palliative Care established a working definition: (1) End-of-life care encompasses the care for patients that are considered to be in the last stage of their lives; (2) It involves the treatment of pain and other symptoms along with the assistance of psychological, social, spiritual, and practical support during the final phase of life and the grieving process; (3) It encompasses the delivery of supportive and palliative care for the patient and the patient's family; (4) It is provided during the final phase of life and continues into the grieving process.[2,25]

When a patient's performance status rapidly declines as they enter an incurable and rapidly progressing phase of their illness, EOLC will be required the most (Figure 3). As a result, clinicians must consider the progression of the disease in advanced lung cancer patients. The disease progresses slowly initially, with patients displaying few symptoms and maintaining a high overall performance status. Eventually, individuals will get to a point where they exhibit more symptoms, creating a more rapid decline that tends to spiral downward until death occurs.[2,26]

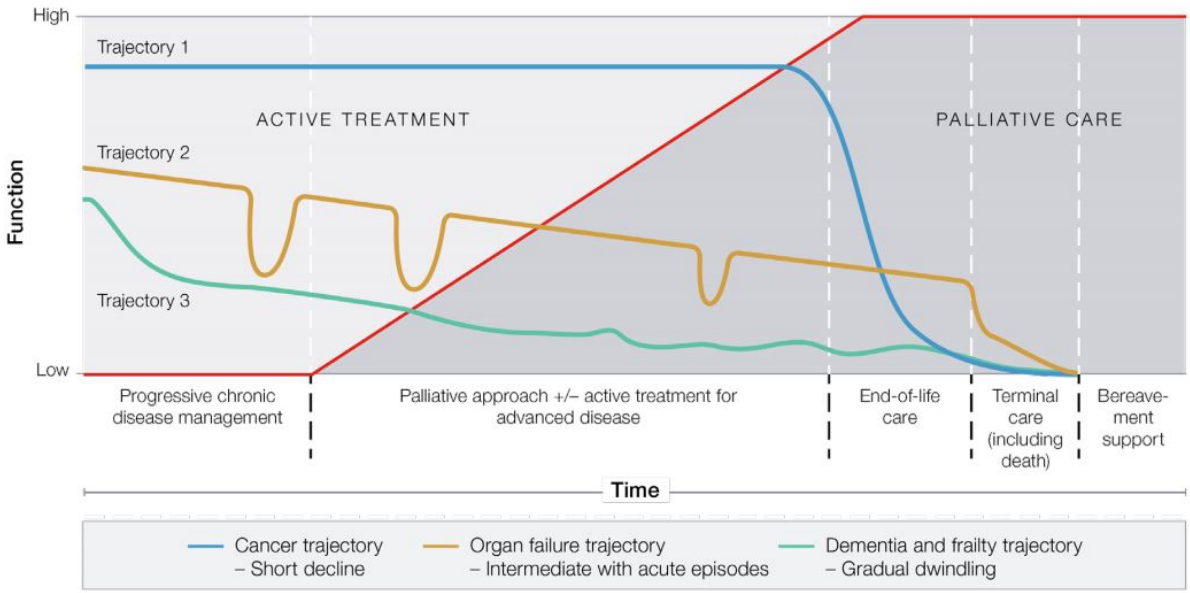

Figure 3. Disease trajectory of advanced lung cancer[27]

The four most essential considerations in end-of-life care are: (1) Recognizing the final time of life. It is the first and most crucial phase because it enables the beginning of a discussion about the wishes of patients and families. The aim is to avoid pointless interventions, educate family members to comprehend the dying process and prioritize care to provide patients with comfort and dignity in their final moments. The patient typically displays the symptoms included in the "Syndrome of Imminent Death", which are as follows: excessive lethargy, decreased cognition and consciousness, inadequate oral intake, variations in respiration, terminal secretions, and reduced vital signs.[2,24] Alsuhail, *et al*. (2020) revealed that 89.3% of patients with imminent death died within 14 days of diagnosis.[28] (2) Communicating with the patient and any family members. Two prospective cohort studies found that fewer than ⅓ of oncologists engage in end-of-life conversations with their patients. As a result, patient satisfaction, psychological morbidity, and QoL were all negatively affected. Communication requires an engaging opening statement, familiarity with the topic at hand, and the capacity to pay attention. Patients expect to be handled with dignity and respect rather than as a disease. Giving families precise information about physical care and comfort measures will also improve the patient's care.[29,30] (3) On the last day of treatment, provide care for treating symptoms. Most patients with advanced lung cancer have discomfort, dyspnea, cough, restlessness, delirium, and fatal respiratory secretions in the later stages of their illness. The primary focus of treatment should be on providing patients with adequate relief from their symptoms. (4) Ethical considerations regarding care provided toward the end of life. Particular issues arising near the end of life, including withholding and discontinuing life-sustaining therapy, such as ventilator support, cardiac resuscitation, artificial hydration, and feeding, may give clinicians pause. When a patient has been denied therapy, it is not in their best interest to continue treatment. Hence, either of these activities is ethically acceptable. Both autonomy and beneficence can be considered to be guiding principles in this scenario.[26,29,31]

Many patients who require palliative care are unable to receive it for various reasons, despite the significant progress that has been made in palliative medicine around the world. Access to palliative care, geographical location, socioeconomic or ethnic background, and awareness can impede patients from receiving adequate EOLC care. Patients, families, and doctors may have limited acceptability of lung cancer palliative care beyond end-of-life care. Furthermore, there needs to be more evidence of palliative care, although Temel, *et al*. (2017) and others have conducted pioneer research.[20]

SUMMARY

WHO identifies palliative care as a holistic, lifelong treatment for patients. Palliative treatment can be initiated as soon as the patient develops symptoms (even in the early stage) or is diagnosed with a late stage. All healthcare personnel who care for patients with serious illnesses, such as advanced lung cancer, should be equipped with the information and skills essential to optimizing end-of-life care. However, inadequate facilities and inadequately trained human resources can become major challenges in developing

nations such as Indonesia. Therefore, health workers should have a greater understanding of the needs of lung cancer patients and gain the necessary abilities to care for patients who have reached this stage of their illness. Even if there is no longer any chance of finding a cure, there is still HOPE: hope for comfort, closure, dignity, and further development of end-of-life care.

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Conflict of Interest
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Authors' Contributions
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