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Contemporary Issues in Cancer Rehabilitation

An Evolving Role for Cancer Rehabilitation in the Era of Low-Dose Lung Computed Tomography Screening

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Abstract

Lung cancer is the number one cause of cancer-related death worldwide, and is often detected in the later stages. Use of low-dose chest computed tomography in at-risk patients provides earlier detection and is being adopted as the standard screening tool, replacing less precise methods of radiography and sputum cytology. In the past, late detection of disease meant that rehabilitation interventions attempted to salvage function and to improve aerobic capacity to the point where patients could tolerate the sometimes-extensive oncologic treatment, including lobectomy or pneumonectomy. Earlier detection may shift this toward more often addressing specific neuromusculoskeletal impairments, such as postthoracotomy pain or peripheral neuropathy, as patients with early-stage disease may not be as debilitated by chronic disease or metastases as those with late-stage lung cancer. Patients with advanced disease, however, will still require rehabilitation interventions, and this fragile population creates unique challenges. Rehabilitation professionals should look for ways to expand care to lung cancer patients, as both the number of those treated and the 5-year survival rate are expected to increase.

Introduction

Lung cancer is one of the most common cancer diagnoses worldwide, and remains the number one cause of cancer-related death in both men and women [1,2]. During 2016, the incidence of new cases in the United States was estimated to be 224,400, representing about 14% of all cancer diagnoses [3]. Approximately 415,000 Americans have a diagnosis of lung cancer, 82% of whom are age 60 years or older, with the average age at diagnosis at 70 (less than 2% are younger than 45 years) [4]. Smoking remains the primary risk factor for developing disease, and nonsmokers who are exposed to second-hand smoke by living with a smoker have a 20%-30% increased risk of developing lung cancer over that of the general population. About 10% of cases arise from toxic exposure, such as to radon or asbestos [3]. The risk of developing lung cancer without any of these factors is unclear. Of note, the majority of people with a history of lung cancer have had their diagnoses made within the past 5 years.

Primary lung carcinoma is a heterogeneous group of tumor subtypes, with the most important distinction being between small-cell and non—small-cell lung cancer (NSCLC). Treatment of NSCLC often involves a combination of surgery, chemotherapy, and/or radiation, whereas small-cell lung cancer often does not involve surgery unless there are focal, large areas of tumor burden in a location amenable to resection [5]. In those with early-stage lung cancer, surgical resection of the tumor is typically the first aspect of oncologic management [6].

The diagnosis of lung cancer is, unfortunately, often late, as patients may be asymptomatic with early-stage lung cancer, and up to two-thirds of patients have metastases at the time of diagnosis [7]. Furthermore, the stage at diagnosis is closely associated with survival, with a 5-year survival of only 6% for patients with metastases present on initial diagnosis, compared with 85% for patients with stage IA disease [8]. Only about 15% of patients are diagnosed with stage I disease [9,10].

Recommendations for lung screening vary by organization, but most generally agree that testing should be administered in individuals 55-74 years of age with a smoking history of $\geq$30 pack-years (defined as "heavy smoking") and who either continue to smoke or have quit within the past 15 years. Additional recommendations include screening patients with a smoking history

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of ≥20 pack-years who have additional risk factors, such as environmental exposure to hazardous chemicals (other than second-hand smoke) [11]. Screening has generally consisted of radiography and/or sputum cytology, with computed tomography (CT) reserved for patients with suspicious but inconclusive findings on these modalities [12].

Due to technological advances and the low rate of early disease detection, in 2014 the US Preventative Services Task Force recommended annual screening for lung cancer with low-dose computed tomography (LDCT) in adults 55 to 80 years of age who have a smoking history of 30 pack-years and currently smoke or have quit within the past 15 years [13]. LDCT uses approximately 20% less radiation than traditional CT screening, making this protocol safer for patients who may need serial imaging [14]. These guidelines have resulted in Medicare coverage of LDCT for patients meeting the aforementioned criteria.

The largest trial looking at the benefits of lung screening, the National Lung Screening Trial (NLST), showed a reduction in lung cancer mortality of 16% and a reduction in all-cause mortality of 6.7% [14]. The use of alternative and more aggressive screening criteria using LDCT are being investigated, potentially preventing another 16,000 additional deaths because of improved identification of at-risk patients [15,16]. Multiple studies continue to evaluate the efficacy of LDCT screening in an effort to improve specificity, to improve detection, to save costs, and reduce mortality [9].

Earlier detection through LDCT has the potential to increase the cure rate of lung cancer through earlier detection and to reduce treatment-associated morbidity due to a smaller tumor burden at the time of diagnosis [9]. It also may change the approach to rehabilitation of lung cancer patients. Rehabilitation interventions often help to optimize a patient for oncologic treatment including surgery, and to manage symptoms such as pain and weakness. With earlier detection, rehabilitation programs may have more opportunities to prevent and to manage symptoms and functional deficits throughout a longer timeframe, and perhaps more often into long-term survivorship.

Symptoms and Rehabilitation Needs of Lung Cancer Patients

Lung cancer and its treatment have the potential to cause significant symptom burden due to worsening pain, dyspnea, fatigue, cognitive deficits, impaired balance, depression, and other symptoms that contribute to a decrease in health-related quality of life (HRQoL) [17,18]. When combined with potential debility from chronic illness such as chronic obstructive pulmonary disease (COPD), diabetes, and peripheral vascular disease, these symptoms can have a negative impact on function and social role [19]. Physical activity and quality of life are lower in patients with NSCLC compared to healthy controls [20], and low physical activity [21] and HRQoL [22] are negative prognostic factors for survival. In advanced stages, metastases to bones [23] and the central nervous system [24] may cause functional decline due to neurologic deficits and pain, necessitating rehabilitation intervention to reduce symptom burden.

The surgical treatment for lung cancer can be deleterious to patients' function, with surgery typically consisting of lobectomy or pneumonectomy for NSCLC patients with locoregional disease. Although both modalities lead to increased dyspnea and short-term worsening of pain and physical function, patients who undergo lobectomy have a reduced burden and duration of symptoms compared to pneumonectomy patients. Those undergoing pneumonectomy may never return to preoperative baseline in physical function, and also frequently experience dyspnea and/or shoulder pain [25,26]. In addition, exercise capacity is decreased in lung cancer patients in general and further by surgery [21]. The larger the resected disease, the more impact that surgery appears to have on HRQoL, and more than 20% of patients report having 3 or more severe symptoms after surgery [27,28]. This suggests that earlier detection of smaller disease with LDCT may reduce the negative impact of surgery.

Extensive disease and/or premorbid chronic illness may also increase the risk of negative outcomes after surgery, including prolonged hospital stays and unanticipated readmissions. In a survey of 11,500 patients undergoing tumor resection, Hu et al found that approximately 13% of lung cancer patients were readmitted to the hospital within 90 days for complications from surgery. Of those who were readmitted, there was a 6-fold increase in 90-day mortality. The most common readmitting diagnoses were respiratory insufficiency, pneumonia, pneumothorax, and cardiac complications [29]. This again highlights the potential benefits of early diagnosis, as chronic comorbidities may be less severe in patients with early-stage disease.

Chemotherapy, which often follows surgery and consists of platinum-containing antineoplastic agents, can contribute to peripheral neuropathy, causing pain and gait abnormalities as well as cognitive deficits. Patients who receive chemotherapy have worse HRQoL at 3-months postoperatively compared to those without [30], and symptoms of neuropathy often did not abate over 2.5 years of follow-up in one longitudinal study [31].

Furthermore, radiation also has potentially negative effects, with pneumonitis and dyspnea being the most common short- and long-term complication, and extensive fibrosis of the lung parenchyma and surrounding neuromusculoskeletal structures being a possible late effect [32]. It is unclear whether the incidence of radiation fibrosis would decrease with