

Increasing Physical Activity and Exercise in Lung Cancer

Reviewing Safety, Benefits, and Application

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Abstract: Lung cancer continues to be a difficult disease frequently diagnosed in late stages with a high mortality and symptom burden. In part because of frequent lung comorbidity, even lung cancer survivors often remain symptomatic and functionally limited. Though targeted therapy continues to increase treatment options for advanced-stage disease, symptom burden remains high with few therapeutic options. In the last several decades, exercise and physical activity have arisen as therapeutic options for obstructive lung disease and lung cancer. To date, exercise has been shown to reduce symptoms, increase exercise tolerance, improve quality of life, and potentially reduce length of stay and postoperative complications. Multiple small trials have been performed in perioperative non-small-cell lung cancer patients, although fewer studies are available for patients with advanced-stage disease. Despite the increased interest in this subject over the last few years, a validated exercise regimen has not been established for perioperative or advanced-stage disease. Clinicians underutilize exercise and pulmonary rehabilitation as a therapy, in part because of the lack of evidence-based consensus as to how and when to implement increasing physical activity. This review summarizes the existing evidence on exercise in lung cancer patients.

Key Words: Exercise, Physical activity, Non-small-cell lung cancer, Small-cell lung cancer, Quality of life.

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Lung cancer is the second most common cancer type, is the leading cause of cancer death, and is expected to comprise 13% of new cancer diagnoses (224,210 new cases) with 159,260 deaths in 2014.¹ Though improved understanding of cancer biology and targeted therapies is improving outcomes, 1-year and 5-year survival rates remain low at 43% and 17%, respectively.¹ Furthermore, lung cancer patients have high symptom burden including dyspnea, cough, fatigue, anxiety, depression, insomnia, and pain.^{2,3} Even lung cancer survivors more than 5 years from diagnosis experience quality of life (QoL) impairment in 35% of cases⁴ and report lower physical and health scores compared with

healthy patients.⁵ Interestingly, the patients who experience QoL improvement after therapy (15%) have no change in symptom burden, suggesting an adaptation to chronic symptoms.⁴

Lung cancer patients are in a uniquely difficult situation in that their disease, their comorbidities, and their treatment may all lead to worsened symptomatology.⁶ Chronic obstructive pulmonary disease (COPD) is present concomitantly in 73% of men and 53% of women with newly diagnosed primary lung cancer.⁷ The diverse causes of activity limitation are listed by the 2013 American Thoracic Society/European Respiratory Society (ATS/ERS) statement on pulmonary rehabilitation (PR) and include ventilatory or gas exchange limitations, cardiac limitation, lower limb or respiratory muscle dysfunction, anxiety, depression, and poor motivation.⁸ Chemotherapy-induced anemia, radiation-induced pneumonitis, and lung resection-related impairment are frequently seen and likely contribute to dyspnea and fatigue.^{6,9,10} With significant cancer burden and rising cancer costs (estimated \$86.6 billion in 2009),¹ an inexpensive cancer therapy to relieve symptoms and improve QoL is appealing.

Inactivity and low-exercise tolerance are increasingly recognized in chronically ill patients. Multiple studies show lower activity and daily step counts in COPD, peripheral vascular disease, and non-small-cell lung cancer (NSCLC).^{11–15} In COPD, for example, physical inactivity is often seen during exacerbation and a predictor of poor outcome.^{16,17} The same pattern is seen in pulmonary hypertension, interstitial lung disease, and lung cancer.^{3,18}

Adding to their burden, functional capacity significantly declines after lung cancer diagnosis.^{19,20} In a recent longitudinal trial, 36% of lung cancer patients (all stages) were noted to reduce or stop walking exercise over the course of 6 months.²¹ The term “dyspnea spiral” has been utilized to describe the development of dyspnea, activity avoidance to prevent further dyspnea, and resultant further loss of function. Some estimates suggest up to 1 of 3 of loss in functional capacity in cancer patients is because of prolonged physical inactivity.¹⁹ Historically, providers and caring family members have contributed to physical inactivity by recommending rest to reduce symptom burden, leading to further deconditioning.²² Lung cancer patients with lower exercise tolerance have worse surgical outcomes, chemotherapy response and tolerance, and survival.³

In the last 20 years, increasing physical activity has shown great promise for cancer and chronic lung disease therapy. Because of the significant overlap between lung cancer and chronic lung disease (namely COPD), lung cancer patients may benefit from physical activity more than other cancer patients. Indeed, exercise therapy represents a low-cost way to improve

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symptoms and potentially outcomes in lung cancer. Given the potential benefit of exercise in this population coupled with the lack of clear recommendations for clinicians providing care, we will review the literature to date on exercise, physical activity, and lung cancer.

Before summarizing the literature, a distinction between “physical activity” and “exercise” should be made. Caspersen et al.²³ defined and distinguished these terms previously. They described physical activity as “a bodily movement by skeletal muscles that results in energy expenditure.” Exercise is physical activity that is planned, structured, and repetitive with the goal to obtain or maintain physical fitness.²³ This review’s goal is to summarize the effect of increased physical activity on lung cancer outcomes. As such, studies utilizing increased physical activity, exercise regimens, or PR are often compared side-by-side. Although the methods differ in application, lung cancer patients likely benefit through increased overall physical activity rather than the regimen itself. As the reader will see, compliance is an often cited challenge in patients with chronic lung disease, and the regimen that maximizes compliance may be the most effective. Indeed, utilizing an exercise regimen or rehabilitation may have more or less benefit than simply increasing physical activity. However, these two regimens have not yet been directly compared. As such, this review will consider physical activity, exercise regimens, and PR as methods to increase physical fitness that may improve cancer outcomes.

The existing literature lacks a review that includes the progression of exercise’s benefit in cancer and lung disease, evaluation of both medically and surgically treated lung cancer patients, and the growing interest of pedometer/accelerometer studies in patients with exercise limitation. To address these issues cohesively, PubMed was searched for the terms “physical activity,” “exercise,” “lung cancer,” “pedometer,” and “step counts.” Resulting articles were individually reviewed by B.C.B. for their applicability to the topic and included as referenced to create this narrative review. Additional articles outside the searched terms were included to appropriately summarize the existing literature or provide sufficient topical background.

REDUCED CANCER INCIDENCE, MORTALITY, AND SYMPTOM BURDEN

Growing evidence supports activity’s benefit in primary and secondary cancer prevention. Much of this work has been done in colon and breast cancer. In 2009–2010, several large trials showed that cardiorespiratory fitness was associated with reduced breast cancer mortality, reduced risk of colon (and overall) cancer development, and reduced mortality with gastrointestinal cancers.^{24–26} Reduced lung cancer incidence with higher activity was confirmed in a 2013 review.²⁷ In fact, physical activity reduces risk of cancer development in multiple cancer types (colon, breast, prostate, pancreatic, endometrial, ovarian, and lung).²⁸

In many cancer types, increased physical activity is also associated with reduced cancer-associated mortality. Large trials in Taiwan (n = 416,175 patients followed for ~8 years) and by the National Institutes of Health (NIH) (n = 293,511)

showed exercise’s association with reduced all-cause mortality,²⁹ and that self-reported moderately vigorous physical activity led to lower risk of all-cause and cancer-specific mortality (colon, liver, and lung), respectively.³⁰

Multiple trials have also shown reduced symptom burden with increased activity. Specifically, exercise can also be used as an adjunctive therapy for cancer-related symptom relief during and after cancer treatment.²⁸ In a randomized, controlled trial (RCT), Segal et al.³¹ showed that breast cancer patients not receiving chemotherapy increased their subjective physical functioning with an exercise regimen. Interestingly, the patients who directed their own regimen appeared to have equal or better improvements. In 2005, Douglas¹⁹ reviewed breast and metastatic tumors, noting that exercise benefited functional capacity, strength, hospital stay, QoL, energy, and fatigue. In hospitalized patients receiving myeloablative chemotherapy, one study found benefit symptom control, cognitive function, and psychosocial function during therapy.³²

A systematic Cochrane review in 2012 focused on exercise intervention and QoL in cancer patients receiving or planning active treatment. Fifty-six trials were included (4826 patients) and concluded that exercise interventions may have beneficial effects on QoL, physical function, social function, and fatigue.³³ The effects were more noticeable with the moderate and vigorous intensity programs.

Is Physical Activity Appropriate?

Some clinicians have recommended limited activity in cancer patients ostensibly to avoid worsening symptoms. To be sure, lung cancer patients limit activity to avoid the “dyspnea spiral.” Similarly, supporting families often limit activity in the cancer patient to prevent acute symptoms. Before advocating more activity, the safety of increasing physical activity in lung cancer patients needs to be established. Research regarding the feasibility and safety of exercise perioperatively (see Table 1),^{34,35} in advanced NSCLC (see Tables 2 and 3),³⁶ and in advanced-stage lung cancer undergoing chemotherapy³⁷ has been performed and is reviewed here.

Several novel studies utilizing a patient-centered approach were recently performed. By surveying NSCLC survivors (average 3.6 years from surgical treatment), Philip et al.³⁸ found that most patients desire physical activity advice before cancer treatment, in a face-to-face fashion, from a physician at a cancer center. Another survey-based study in advanced lung cancer patients revealed that patients preferred activity recommendations from their oncologist, though none had received specific advice.³⁹ These patients also perceived that a lack of recommendation from their physician constituted an acceptance of their exercise regimen. An uncontrolled trial of lung cancer patients (all stages) in 2013 reported ~70% of patients who completed a training program remained physically active.⁴⁰ These data highlight that lung cancer patients (regardless of stage) desire exercise guidance and can increase compliance with a dedicated regimen, yet such discussions are often not held.

BENEFITS IN LUNG CANCER

In 2005, the National Emphysema Treatment Trial (prospective, multicenter trial with 1218 patients) revealed that

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