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Effectiveness and quality of life in lung cancer, pre-, post- and perioperative rehabilitation – A review

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ABSTRACT

Functional conditions like lung function and exercise capacity are important limiting factors of chest surgery in lung cancer with co-morbidities (chronic obstructive pulmonary disease (COPD) and other chronic respiratory diseases). Pulmonary rehabilitation has a favourable effect on the cardiovascular system, metabolism, respiratory and peripheral muscles and lung mechanics. Our aim was to assess the role of pre-, post- and peri-operative pulmonary rehabilitation in lung cancer in this review. We sought to size up the importance of pulmonary rehabilitation in patients undergoing surgery with or without (neo)adjuvant treatment, radiotherapy, chemotherapy, chemoradiotherapy, major physiological impairments and complications. Searches were performed in PubMed and ClinicalTrials.gov databases using the terms "exercise", "rehabilitation", "small cell lung cancer", "non-small cell lung cancer", "exercise capacity", "chest surgery" and "quality of life" from inception to February 7th, 2022. Pulmonary rehabilitation has been

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recognized as an effective intervention to reduce lung cancer related symptoms and improve the pulmonary function, lung mechanics, chest kinematics, respiratory- and peripheral muscle function, physical activity and quality of life (QoL) of the patients. In conclusion, this review shows positive, highly encouraging and effective results of pulmonary rehabilitation in terms of the patients' lung function, functional mobility and quality of life. The tools for complex pulmonary rehabilitation have evolved considerably over the past two decades, thus this research has been conducted on a variety of studies about this subject and serves as a synthesis of the systematic and meta-analytic reviews.

KEYWORDS

lung cancer, small cell lung cancer, non-small cell lung cancer, physiotherapy, exercise, physical activity, pulmonary rehabilitation

INTRODUCTION

Lung cancer is mainly diagnosed in relatively old age: more than 80% of the patients are 60 years old or over [1]. The rate of multimorbidity in this population is considerable due to the high percentage of smokers among individuals with lung cancer. For instance, COPD affects 40%–70% of the patients with lung cancer [2]. Due to the advanced age of the patients, the presence of co-morbidities and the aetiology of lung cancer, this patient group requires complex management.

MEDICAL TREATMENT AND SIDE EFFECTS

Lung cancer is still the leading cause of cancer deaths worldwide, even though medical treatment has improved considerably. While the five-year survival rate for women is about 24%, it is only about 17% for men; the worst rate for small cell lung cancer is approximately 7% for both genders. Surgery, radiotherapy and chemotherapy are the mainstays of treatment, and the choice of drugs used in the treatment depends on the histological type, stage and location of the tumour and the physical condition of the patient. Side effects of the treatment are also important factors, shown in Table 1 [3].

The main symptoms are fatigue, shortness of breath, cough, and chest pain, and the side effects can manifest both during and after of the treatment [4, 5]. Fatigue and physical weakness (asthenia), and in more severe cases exhaustion can develop, which are very common in lung cancer. These symptoms are very important for physiotherapists to be aware of and treat [6].

Cachexia is very common in cancer patients, caused by several factors. On the one hand, it is characterised by physical weakness and a poorer quality of life, and on the other hand, it is associated with a rapid loss of muscle mass, which cannot be compensated by conventional nutrition. This process weakens the effect of the treatment, leads to functional deterioration and increases the mortality of cancer patients [7, 8]. Clinically, cancer cachexia presents due to metabolic alterations, loss of weight, and impaired muscle strength and fatigue [2, 6]. Granger and colleagues [6] described that lung cancer patients had weakened peripheral muscle strength,

Table 1. Common side effects related to lung cancer treatments

Surgery	Chemotherapy	Radiotherapy	Molecular targeted therapies
• Pain • Cough • Fatigue	• Fatigue • Nausea • Infection • Vomiting • Anaemia • Diarrhoea • Constipation • Loss of appetite • Hair loss • Mouth ulcers • Weight loss/gain	• Fatigue • Cough • Oesophagitis • Nausea • Vomiting • Skin erythema • Diarrhoea • Loss of appetite • Hair loss • Rigors • Flu symptoms	• Fatigue • Nausea • Vomiting • Loss of appetite • Diarrhoea • Constipation • Hair, skin changes

particularly in the limbs and leg muscle weakness was more pronounced than the weakness of respiratory muscles and respiratory function in peak exercise.

Preoperative functional capacity measurement is very important and has predictive value. It is crucial for the evaluation of the length of hospital stay, quality of life and survival. The survival of the patient can increase by up to 13%, if the six-minute walking distance (6MWD) improves by 50 m [9, 10]. Given the importance of functional capacity in lung cancer treatment, lung cancer complex cardiopulmonary rehabilitation is crucial.

LUNG CANCER REHABILITATION AND PHYSICAL EXERCISE

Before 1980 lung cancer patients were recommended to rest, recover and save energy, and to keep away from participating in intense physical activity. However, based on Winningham et al.'s study [11], a monumental scientific discovery progressively emerged, reinforcing that physical activity and exercise can produce relevant benefits in oncology. Physical activity also improves strength, flexibility, quality of life and body composition. It has an impact on patients' mental well-being, i.e. self-esteem, vitality, and has been described to reduce anxiety and depression [12–15].

Regular exercise and physical activity are very important for a patient's quality of life. Exercise is essential both before, during and after chemotherapy. A recommendation in the Australian Journal of General Practice details the evidence for regular physical activity in patients' recovery (see Fig. 1) [13].

Sub-intensive aerobic exercise such as walking for half an hour a day is very beneficial and has no side effects for cancer patients. If the patient has metastases, the form of training is determined by a specialist trainer, which can be resistance training with dumbbells, rubber bands or a variety of exercises using gravity, such as squats.

Lung cancer patients are advised to choose exercises, which do not exacerbate symptoms based on the American College of Sports Medicine (ACSM) [14] recommendation. Swimming and hydrotherapy are also very beneficial. If lung cancer is associated with cardiovascular co-morbidities, a cardiopulmonary exercise test - and medical clearance - is recommended before starting an exercise programme.

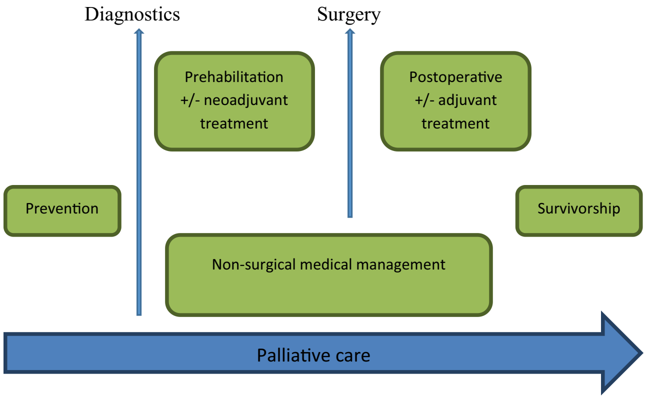

Fig. 1. Timing of exercise delivery across complex management of lung cancer

Very few completed studies deal with the question of how physical activity affects lung cancer outcomes, and the studies are contradictory. Concrete data on the effects of e.g. physiotherapy in the prevention and treatment of lung cancer are notably lacking and may be the subject of the future research.

MATERIALS AND METHODS

This review includes thirty-five studies published between 2009 and 2021, identified by searching PubMed and ClinicalTrials.gov, investigating the effect of exercise and physical activity in lung cancer patients. All original first articles investigating the effect of exercise in lung cancer were scanned. Case reports, non-published abstracts and non-English texts were excluded. The subsequent keywords were the following: lung cancer, rehabilitation, exercise, physical activity, small cell lung cancer, non-small cell lung cancer. Population inclusion criteria were patients encountered with lung cancer, surgically treated, pre- or post-medical therapies. Different physical therapy protocols were used; they are identified as types of interventions supervised or unsupervised, including exercise training delivered to lung cancer patients and carried out for at least two weeks.

OUTCOMES OF LUNG CANCER REHABILITATION

Summary of evidence

A total of 35 rehabilitation studies were included in this review with a total number of 2021 patients with NSCLC and SCLC (see Table 2). This study includes all lung cancer studies in stage I-IV disease at the time of the diagnosis. Lung cancer was treated with either radiation, chemotherapy, surgery or palliative treatment. Sixteen studies from the 35 (46%) were in post-surgery, whereas 16 investigated the effect of rehabilitation during palliative care (46%). Only three studies showed interest in pre-surgery rehabilitation (8%). The rehabilitation studies showed a significant or clinically relevant improvement of the four main assessments: pulmonary function, cardiorespiratory fitness, muscle strength and mass, and quality of life (QoL) (see Table 2).

Table 2. Main studies on outcomes of lung cancer rehabilitation before, during and after treatment

Study	Population and type of study	Duration of the study	Primary outcomes	Secondary outcomes	Main results
2006					
Spruit et al. [16]	10 NSCLC and SCLC Single one arm	Aerobic and muscle strength program for 8 weeks	Cycling peak load and 6MWT	Dyspnoea pulmonary function	6MWT cycling peak load
2008					
Jones et al. [17]	20 NSCLC (IA–IIIB) Single arm	14 weeks of aerobic training	VO_2peak	QoL Fatigue	Peak workload functional well-being fatigue
2009					
Temel et al. [18]	25 NSCLC (IIIB–IV) Single one arm	Aerobic and muscle strength program for 12 weeks	Feasibility	Quality of Life; severity of symptoms 6MWT; Power; survival rate	44% of the patients completed the program extension of elbow strength cancer-related syndromes
2011					
Arbane et al. [19]	53 RCT of NSCLC	Aerobic and strength program vs. usual care for 12 weeks strength	Quality of life	6MWT power duration of stay and postoperative complication	Loss of strength in control group
2012					
Quist et al. [20]	29 NSCLC stage (III–IV) Single one arm	Aerobic power relaxation sessions walking home-based exercises for 6weeks	Feasibility and safety	VO_2peak strength 6MWT FEV_1 QoL	Safe and feasible VO_2peak 6MWT strength emotional well-being
Hwang et al. [21]	24 NSCLC (IIIA–IV) RCT	8 weeks of HIIT vs. usual care	VO_2 peak	Strength insulin resistance inflammatory response	VO_2peak circulation peak exercise dyspnea fatigue QoL
2013					
Granger et al. [22]	15 (LC stage I–IV) RCT	Aerobic and strength training program for 8 weeks vs. usual care	Feasibility and safety	6MWT mobility QoL	Feasible and safe functional mobility 6MWT

(continued)

Table 2. Continued

Study	Population and type of study	Duration of the study	Primary outcomes	Secondary outcomes	Main results
Andersen et al. [23]	59 NSCLC (I–IV) SCLC Pragmatic uncontrolled trial	9 weeks of HIIT and walking	Adherence	FEV_1 VO_2max QoL	44% of patients completed the program 69% of patients stayed active after rehabilitation
Cheville et al. [24]	66 (34 LC stage IV) RCT	Home-based program for 8 weeks of walking and strength vs. usual care	Activity and mobility	QoL pain fatigue ability to carry out daily activities sleep quality	Mobility sleep quality fatigue
Stigt et al. [25]	57 NSCLC RCT	Aerobic program of 12 weeks then follow-up after 3 months and then 6 months vs. usual care	QoL	6MWT pain feasibility after chemotherapy	6MWT after 3 months of intervention Pain
Hoffman et al. [26]	7 NSCLC (I–IIIA) Single one arm	Walking and balance (with Nintendo WII) program for 6 weeks	Feasibility	Self-efficacy fatigue: functional performance (steps/day)	Feasible fatigue walking steps/ day self-efficacy
2014					
Brocki et al. [27]	78 LC RCT	Aerobic and strength program for 10 weeks vs. usual care + follow-up after 12 months	Quality of life	Lung function 6MWT	Pain rate of the body (at 10 weeks)
Henke et al. [28]	46 NSCLC stage (IIIA–IV) SCLC RCT	3 cycles of chemotherapy aerobic, strength training and breathing techniques vs. usual care	Daily living activity (ADL-Bartel Index)	6MWT Quality of life strength dyspnea	ADL 6MWT strength dyspnea QoL
Hoffman et al. [29]	5 NSCLC (IIA–IIIA) Single arm	Walking and balance (with Nintendo WII) for 16 weeks	Tiredness	Cancer-related syndroms quality of life 6MWT	6MWT QoL cancer-related syndroms tiredness

(continued)

Table 2. Continued

Study	Population and type of study	Duration of the study	Primary outcomes	Secondary outcomes	Main results
Chang et al. [30]	65 LC (2 arms) Quasi-experimental	Walking for 12 weeks vs. usual care than 3 months follow-up	Pulmonary function 6MWT quality of life	NA	FEV_1 after 3 and 6 months 6MWT after 3 and 6 months
Kuehr et al. [31]	40 NSCLC (IIA–IV) Single one arm	Aerobic and strength training for 8 weeks, after 8 weeks follow-up	Feasibility	QoL power 6MWT fatigue psychological impairment	Feasible 6MWT strength QoL
Salhi et al. [32]	45 NSCLC (I–III), SCLC RCT	Strength program for 12 weeks vs. usual care	Changes in mass muscle and power	NA	Mass muscle and power after radical treatment complete recovery after rehabilitation
2015					
Tarumi et al. [33]	82 NSCLC (stage IIB–IV) Single arm (retrospective)	8 weeks of respiratory training, lower-extremity exercise	Pulmonary function	NA	FVC FEV_1
Arbane et al. [34]	131 NSCLC stage (I–IV) RCT	Aerobic and strength program for 4 weeks vs. usual care	Level of physical activity	Exercise tolerance power QoL postoperative complication	QoL in patients with airflow obstruction
Edvardsen et al. [35]	61 NSCLC (I–IV) RCT	High-intensity aerobic training program for 20 weeks vs. usual care	VO_2peak	Pulmonary function power mass muscle daily physical functioning quality of life	VO_2peak DLCO strength mass muscle daily physical functioning quality of life
Salhi et al. [36]	70 NSCLC (I–IV), SCLC (LD), mesothelioma (I–III) RCT	12 weeks of CRT vs WBV vs. usual care	6MWT	Exercise capacity changes strength QoL exercise maximal capacity	6MWT quadriceps force in CRT after training program
Quist et al. [37]	114 NSCLC stage (IIIb–IV), and SCLC (ED) Single one arm	Aerobic and strength program for 6 weeks	VO_2peak	6MWT Power FEV_1 cancer-related syndromes	VO_2peak 6MWT strength emotional well-being anxiety

(continued)

Table 2. Continued

Study	Population and type of study	Duration of the study	Primary outcomes	Secondary outcomes	Main results
Chen et al. [38]	116 LC stage (I–IV) RCT	Home-based walking for 12 weeks and weekly training counselling vs. usual care follow-up after 3 months	Depression and anxiety	Cancer-related syndromes	Anxiety and depression
2016					
Zhang et al. [39]	96 NSCLC stage (I–IV), SCLC RCT	Tai Chi for 12 weeks vs. low intensity exercise (control group)	Tiredness	NA	Tiredness
Chen et al. [40]	111 LC stage (I–IV) RCT	Home-based program for 12 weeks and weekly exercise counselling vs. usual care follow up after 3 months	Rest-activity rhythm and quality of sleep	NA	Quality of sleep
Sommer et al. [41]	40 NSCLC stage (I–IIIA) RCT	Preoperative period of 2 weeks + postoperative period of 12 weeks of aerobic and strength training + multidisciplinary intervention	Safety feasibility QoL	Anxiety depression distress perceived social assistance smoking alcohol physical activity VO_2peak 6MWT muscle strength pulmonary activity	Quality of life (some domains) anxiety, depression and distress levels Preoperative interventions not feasible Postoperative interventions safe and feasible 6MWT Strength
2017					
Solheim et al. [42]	64 (26 NSCLC, stage (III–IV) RCT	Multimodal intervention for 6 weeks vs. usual care	Feasibility compliance	Weight, muscle mass physical activity level 6MWT handgrip strength nutritional status, fatigue, safety, survival	Feasible 60% compliance

(continued)

Table 2. Continued

Study	Population and type of study	Duration of the study	Primary outcomes	Secondary outcomes	Main results
Cavalheri et al. [43]	17 NSCLC stage (I–IIIA) RCT	Supervised individual muscle strength and aerobic program for 8 weeks vs. control group	Exercise capacity (VO_2peak and 6MWT)	Physical activity level behaviour muscle strength fatigue depression anxiety quality of life lung function	VO_2peak 6MWT
Dhillon et al. [44]	112 NSCLC stage (III–IV), SCLC RCT	Supervised and unsupervised training program for 2 months then follow up after 4 months and then 6 months	tiredness	ADL, anxiety quality of sleep dyspnoea handgrip strength 6MWT, physical activity sedentary, survival	Physical activity levels at 4 and 6 months
2018					
Sommer et al. [45]	40 NSCLC stage (I–IIIA) RCT	Preoperative program for 2 weeks + postoperative program for 12 weeks of aerobic and strength training + multidisciplinary intervention	Safety feasibility QoL	Anxiety depression distress smoking alcohol VO_2peak 6MWT muscle strength pulmonary function	Quality of life; anxiety; depression; preoperative interventions not feasible postoperative interventions safe and feasible 6MWT strength
Peddle-McIntyre et al. [46]	14 NSCLC (I–IIIB) Single arm	Distance-based program for 12 weeks with printed materials	Feasibility	Level of physical activity quality of life	Eligibility; level of physical activity; Quality of life; Short-term benefits reduced pain
2019					
Messaggi-Sartor et al. [47]	37 NSCLC stage (I–II) RCT	Aerobic program and high-intensity training for 8 weeks vs. UC	VO_2peak	Respiratory muscle strength QoL IGF-1 and IGFBP-3 levels	QoL VO_2peak respiratory muscle strength IGFBP-3 serum level

(continued)

Table 2. Continued

Study	Population and type of study	Duration of the study	Primary outcomes	Secondary outcomes	Main results
2020					
Sommer et al. [48]	119 NSCLC stage (I–IIIA) RCT	Preoperative program for 2 weeks + postoperative of 12 weeks program of aerobic and muscle strength activity + multidisciplinary intervention	NA	QoL measured by both FACT-L and FACT-G	ERL group: QoL decreased after further 26 weeks. LRG group: the first 14 weeks after surgery.
Liu et al. [49]	73 NSCLC, clinical stage (I–III) RCT	2-week multimodal intervention program before surgery, exercises, respiratory training, nutrition counselling	Perioperative functional capacity 6MWD	Lung function disability and psychometric evaluations short-term recovery postoperative complications	6MWD FVC lung function
2021					
Li et al. [50]	80 NSCLC clinical stage (I–III) RCT	2 weeks animation education program (2 sessions/day)	Training-related knowledge and respiratory exercise compliance	PaO_2 $PaCO_2$ FVC FEV_1 FEV_1/FVC	Training-related knowledge respiratory exercise compliance 6MWD

NA: no data available, FEV1: forced expiratory volume in one second, FVC: forced vital capacity, HR-QoL: health-related quality of life, LOS: length of stay, NSCSC: non-small cell lung cancer, PaO2: partial pressure of oxygen, PaCO2: partial pressure of carbon dioxide; QoL: quality of life, RCT: randomized clinical trial, 6MWD: six-minute walking distance, SCLC: small cell lung cancer, VO2: oxygen uptake, WBVT: whole body vibration technique.

PREHABILITATION

The literature includes a few studies delivering exercise prehabilitation in terms of the quality of the cancer care. These studies resulted in an extraordinary reduction in postoperative pulmonary issues (PPCs, 65% reduction), such as duration of intercostal catheter need and hospital length of stay. In the prehabilitation studies, patients did not experience any side effects or adverse events after interval training, even with high intensity exercise, and patients' exercise tolerance improved significantly. However, it is important to underline that the time frame between tumour diagnosis and the planned date of the surgery is very short, usually less than a month. It is a determining factor for the success of the treatment.

POSTOPERATIVE INTERVENTION

The most important principle is early mobilisation - even from the first day after surgery - to get the patient into a chair. Coughing exercises, shoulder girdle mobilisation and chest mobilisation are important and have been shown to reduce post-operative pain and to promote functional improvement for the patient. There is a failure of substantiation to support the use of precautionary targeted respiratory activity interventions for routine causes following lung resection. This is the reason why patient's mobilisation is needed from the first postoperative day, including fresh mobilisation, thoracic expansion exercises, sustained minimal alleviations, active cycle of breathing and non-stop positive airway pressure.

The majority of exercise programmes following oncological treatment include both aerobic (cycle, ground walking) and resistance training factors and in most of the cases the two are combined. They are rarely combined with other components, e.g. breathing exercises, balance exercises, but it is not known whether these contribute to the ultimate success of the treatment. The exercise programmes used usually last two-three months and usually take place in an outpatient setting, but it is also possible or even necessary to continue them at home.

EXERCISE IN ADVANCED DISEASE

Previously published studies have examined physical activity in lung cancer patients who have undergone non-surgical treatment [25, 27, 29, 30, 33, 37, 40–42, 46–49, 51–53]. The Cochrane review, which included six randomised controlled trials (RCT) in severe lung cancer patients, is reported significant improvements in both quality of life and exercise capacity in the intervention group, but no significant differences were found in respiratory function or mood variables. Physiotherapy management of this population includes treatment of breathlessness with breathing retraining, relaxation and neuromuscular electrical stimulation [15].

DISCUSSION

Preoperative rehabilitation outcomes

Sommer et al. [41] investigated the safety and feasibility of a preoperative rehabilitation program. They found it absolutely safe to exercise prior surgery, and none of the patients reported or observed any unexpected reactions, but 70% of patients dropped out due to lack of motivation. The time interval before surgery was only eight days in average. There was no significant difference in exercise adherence prior surgery compared to the existing data. Only one study investigated the same effect: Coats et al. [51] reported a significant difference ($P = 0.05$), patients completed <75% of exercise adherence but the patients were younger in age and with an early stage of lung cancer. In this study, there were four weeks available before surgery, which made the feasibility significant. This study showed that preoperative rehabilitation is completely safe and can lead to promising results, but it is not feasible for patients with advanced stage disease due to the lack of time. Another study investigated the effect of prerehabilitation: Liu et al. [49] conducted the first study to use a multi-model that consisted of aerobic exercises in combination with resistance training plus the possibility of adjusting the intensity, frequency and duration of the program according to the patient's condition. In previous studies, a fixed, not variable model was used for all the patients. Second, one of the innovations introduced in this study was the use of a two-week program as compared to the four-week programs recommended by all previous studies for achieving results [52–55]. There was a significant improvement in the six-minute walk distance by 60.9 m perioperatively in the mixed model compared with the control group, leading to better recovery after preoperative rehabilitation.

REHABILITATION OUTCOMES IN POST-SURGERY

Post-operative interventions reported safety and improved functional capacity, dyspnoea, HRQoL (mainly the physical component) and cancer-related fatigue. Two main studies introduce important changes to the concept of post-operative rehabilitation. Hoffman et al. [29] proved that not only a supervised program but also a home-based low-intensity rehabilitation program led to post-surgical improvements. The 30-min walking distance could increase in the weeks following the operation, and it almost improved to the level of the preoperative value in six weeks. Compared with previous studies, postsurgical interventions were initiated much later in the recovery period (<10 weeks) and supervised programs are only adopted. Since the literature indicates that exercising alone even for a healthy population is difficult to achieve results. Another study (Brocki et al.) [27] made important changes in the domain of post-operative rehabilitation. It was the first study to compare supervised versus unsupervised cancer rehabilitation program in terms of short-term versus long-term effects and found that both programmes resulted in an improvement in the six-minute walk distance and forced expiratory capacity after four months. However, short-term supervised exercises led to faster recovery in functional health domains. SF-36 body pain domain after four months shows that patients in the supervised program experienced less pain compared to the unsupervised group.

REHABILITATION DURING CARE

Exercise in advanced diseases is still hard to perform due to the burden of disease symptoms and side effects of anticancer treatment within the active oncological phase. A limited number of studies support the fact that rehabilitation during this phase may introduce improvements in pulmonary functions, HRQoL and functional capacity of the patients. Quist et al. [20] published the first study to test whether a rehabilitation program during intensive care is safe and beneficial for patients undergoing chemotherapy. There was significant improvement in both functional capacity and VO_2peak in six weeks. In addition, they achieved a cumulative strength improvement of 17%, in contrast to Granger et al. [56] and Jones et al. [57] who did not describe significant improvements in aerobic capacity and muscle strength.

Spirometry as a pulmonary function test to analyse respiratory function is critical to outline therapeutic approaches in lung cancer. More specifically, the predicted postoperative

FEV_1 (% pred.) value and the diffusion capacity of carbon monoxide (DLCO) are the most used variables to evaluate the risk of surgery. We found a significant improvement in spirometry values in the intervention group compared with controls groups in response to training. During induction chemoradiotherapy, pulmonary rehabilitation for lung cancer improves pulmonary function [58, 59].

Cardiorespiratory fitness is a measure of how well the circulatory and respiratory systems are capable of transferring oxygen to skeletal muscles during a continuous physical activity. The tumour mass and clinical operation together affect the respiratory system by decreasing the capacity of diffusion, also in advanced stage cases (lll; lV), and the oxidative capacity of skeletal muscles is damaged with a depletion in mitochondrial density and in capillarization. Furthermore, radiotherapy and chemotherapeutic agents can damage the cardiac pump, vascular function and blood cell populations [60] The 6-min walking test and peak oxygen consumption are the most solicited tests for cardiorespiratory fitness. To date, 27 studies out of 35 (77%) applied these two tests as crucial assessments. Globally considered, all these studies reported a significant improvement in cardiorespiratory fitness following a training period and the potential beneficial effect of exercise in lung cancer patients [30, 33, 41–50, 52–55, 57, 58, 61–67].

Strength and muscle mass are critical determinants of physical function and daily living activities. In the case of lung cancer, patients suffer from lower muscle mass (sarcopenia) or muscle mass alterations defined as pathological conditions, such as cachexia. Both are major contributors to increased mortality. The majority of outpatients affected by advanced disease confronts cachexia (69%) or sarcopenia (47%) [68]. Studies that included muscles strength assessment in their secondary outcomes found a significant improvement in strength and muscle mass [30, 33, 43–46, 49, 53, 58, 61–65], except for Cheville et al. who reported no significant difference in this term before or after the training program [24]. Cheville et al. argue that no improvements in the assessments are due to the end-stage disease (lV) of the patients [24]. Stigt et al. also reported no difference for strength and muscle mass between the two groups, moreover, the experimental group reported more pain after three months [25]. It is recommended that complex pulmonary rehabilitation should start at least three months after hospital discharge [25].

Quality of life is the standard parameter to measure the healthy, comfortable condition, or enjoyable life events [69]. Patients with lung cancer have a critical decrease in quality of life, regarding the domains of physical health score, the degree of quality of life depletion, which can depend on cancer stage, tumour localization and prognosis [61]. The concept of Quality of life is highly questionable in lung cancer rehabilitation and management due to the positive and negative results of the literature; quality of life did improve after rehabilitation in the following studies [54, 57, 65–67]. Patients had improved physical function, strength, resilience, emotional well-being, mental health, and global quality of life because of complex pulmonary rehabilitation. Exercise improves wellbeing and reduces anxiety and depression, which are very common in lung cancer. Furthermore, if psychological parameters are improved, the patient can cope with the disease more easily and prevent complications of lung cancer or other diseases. The effects of physical exercise after lung cancer surgery are scientifically proven: an RCT showed that in forty cases with stage I–IIIA NSCLC global quality of life had improved significantly ($P = 0.0032$) in mental health component ($P = 0.0004$), emotional well-being ($P < 0.0001$). A decrease in anxiety and depression after a multidisciplinary intervention program for 12 weeks was detected based on physical activity, social counselling options. On the other hand, focusing only on lung cancer patients, no direct influence is evident in terms of quality of life after the rehabilitation program. Further investigation with a valid module design and a sufficient sample size are essential to clarify this matter.

LIMITATIONS OF THE STUDY

Our research was a review and not a systematic review of the literature, therefore studies may have been omitted. We focused primarily on studies in English, so publications in other languages were omitted from the review. Due to manuscript length, limitations conference abstracts and meta-analyses were not included in this review. There is a lot of variation in the research descriptions of the rehabilitation programs, as well as what is measured afterwards and when, thus an exact comparison of studies is not possible. There is probably a selection bias because of the different physical condition of the patients.

CONCLUSION

In conclusion, this review communicated positive and encouraging results of rehabilitation on pulmonary function, functional mobility and quality of life of the patients. Research shows that combining endurance and resistance training, as well as personalization are necessary to enhance adherence, treatment tolerance, physical fitness and recovery. Although there is a growing number of studies each year for this particular subject, the clinical effects of rehabilitation on physiological parameters such as blood composition (e.g. uric acid, creatinine, creatine phosphokinase content), immune function system and hormone secretions have still not been investigated.

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