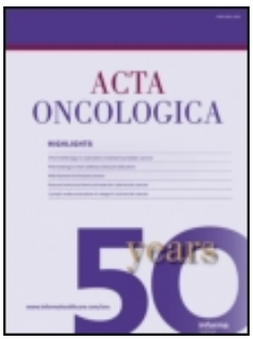

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ORIGINAL ARTICLE

Do patients with lung cancer benefit from physical exercise?

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Abstract

Background. Patients with lung cancer are often burdened by dyspnoea, fatigue, decreased physical ability and loss of weight. Earlier studies of physical exercise of patients with COPD have shown promising results. The aim of this study was to investigate, if a well-documented COPD rehabilitation protocol can improve physical fitness and quality of life (QoL) in patients with lung cancer. *Material and methods*. Forty-five patients, with a minimum walking distance of 50 meters, absence of cognitive deficits or severe heart disease and motivated for physical training were invited to an exercise intervention. The intervention consisted of seven weeks of twice weekly training, focusing on walking training, circuit training, handling of dyspnoea and instructions in daily diary-based training at home. Prior to, and after the intervention, Incremental- and Endurance Shuttle Walk Test (ISWT and ESWT) were performed, and pulmonary function as well as self-reported QoL (EORTC-QLQ-C30 and LC13) were measured. *Results*. Fourteen subjects dropped out before commencement of the intervention. Seven were excluded after physiotherapeutic evaluation. Of the remaining 24, three were excluded because of insufficient attendance (<65% of scheduled exercise sessions) thus 21 patients completed the intervention. For 17 patients with complete pre- and post intervention data, ISWT increased 9% (−77 to 39%) (median and range) ($p = 0.021$), while ESWT increased 109% (−70 to 432%) ($p = 0.002$). Twelve of 17 improved in ISWT, while 15 improved in ESWT. No changes in pulmonary function and improvements in QoL were observed. *Conclusion*. Patients with pulmonary cancer can achieve significant improvements in physical fitness measured with ISWT and ESWT after completion of the intervention program. No changes in pulmonary function and QoL were observed. In addition, we found that a large number of patients dropped out before intervention and that the patients, who succeeded, often discontinued training at home.

Over the last decade studies have shown that physical exercise can play an important role for individuals living with a cancer diagnosis [1,2].

In cancer patients in general, exercise improves cardio-vascular fitness both for patients in treatment and for patients who have completed treatment. Exercise may also diminish side-effects of chemotherapy or radiation therapy [2].

Compared to the increasing amount of evidence supporting exercise as an important component of cancer rehabilitation, relatively few studies regarding lung cancer have been published and most investigate the effect of exercise only in patients eligible for surgery [3–5].

Lung cancer is divided in Small Cell Lung Cancer (SCLC) and Non-Small Cell Lung Cancer (NSCLC). Approximately 80% of all cases of lung cancer are NSCLC, and of those only less than 20% qualify for surgery. The 5-year relative survival rate is around 10% for lung cancer [6]. For patients eligible for surgery the prognosis is significantly better showing a 5-year relative survival rate of approximately 40% [6].

Despite advancements of overall treatment, living with lung cancer is frequently associated with many symptoms. This is caused by the disease itself, and side-effects of the anticancer therapy. Symptoms include dyspnoea, fatigue, reduced physical empowerment, depression, inability to sleep and weight loss [7].

Chronic obstructive pulmonary disorder (COPD) patients experience airway symptoms comparable to lung cancer patients, and COPD is a well known comorbidity to lung cancer. Several studies have shown that an exercise protocol can help improving the lives of COPD patients [8].

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The main objective of the present study was to investigate the feasibility and effect on fitness level of a well-documented COPD-rehabilitation exercise program in patients with lung cancer. The secondary aim was to investigate if the exercise program could affect the quality of life and lead to continued exercise after completion of the intervention program. This was investigated in a prospective single-group intervention study.

Material and methods

Patients diagnosed with lung cancer were recruited from the outpatient clinic at Herlev University Hospital by oncology specialists. Patients in treatment as well as patients in post treatment surveillance were invited to participate in the study. Patients were included on the basis of ability and motivation to exercise. Included patients had to meet the following criteria; 1) walking distance of at least 50 meters; 2) no severe heart disease (NYHA class IV); 3) no cognitive or balance deficits compromising performance of exercise.

Both patients who had pulmonary surgery and patients who were not eligible for surgery were included in the study. All patients gave informed consent. The study was approved by the regional ethics committee.

Overall description of intervention

The exercise protocol from a conventional COPD rehabilitation approach was used [8,9] including seven weeks of supervised exercise twice a week and unsupervised home training sessions the remaining days of the week. The supervised training was performed as group sessions – seven patients at a time with a new patient starting and another patient completing the training intervention every week. In addition to exercise, the protocol also comprised instruction in coping strategies for management of dyspnoea during exercise and introduction to a training diary. Walking distance and Borg breathlessness score [10] were recorded at each training session.

In this COPD-exercise protocol, walking is the key element. In order to achieve optimal improvement in maximal walking distance in COPD patients, an exercise intensity of 85% of maximal oxygen uptake (VO_2max) during training is recommended [11]. Incremental Shuttle Walk Test (ISWT) [12] is used to estimate the VO_2max and Endurance Shuttle Walk Test (ESWT) is used to measure walking time at 85% VO_2max. The overall aim of this approach is to increase functional capacity and encourage continued unsupervised exercise after the intervention period.

Exercise program

At the first appointment in the physiotherapy department, the patient was introduced to respiratory physical therapy focusing on respiratory exercises, pursed lip breathing, resting positions and dyspnoea coping. At this time the final decision regarding participation in the exercise program was made by the physical therapist (PT) based on the current mental and physical condition of patient.

The exercise sessions, each lasting 90 minutes included a 15 minute group session, where patients could share experiences and ask questions related to their current condition followed by a warm-up, walking-training and dyspnoea-coping. Warm-up consisted of seated exercises for upper and lower limbs at a low to moderate intensity to ensure readiness for exercise without inducing fatigue. The key component of the exercise protocol was walking. Consequently, walking-training was performed immediately after the warm-up and was supervised by the PT with a stopwatch to maintain correct walking speed throughout the training session. The dyspnoea-coping consisted of three different dyspnoea provoking exercises – stationary bike riding, step training and chair-to-stand exercise, each exercise was performed twice for two minutes at near maximal exercise intensity. Respiratory techniques were used to regain habitual respiratory comfort and frequency.

Throughout the intervention period, patients were encouraged to continue unsupervised exercise after the intervention. The respiratory physical therapy, the dyspnoea coping strategies, the diary based training and the group session also aimed at providing patients with tools to continue exercise at home.

Assessment of walking performance

At the first and the last supervised training session the patients were tested with Incremental Shuttle Walk Test (ISWT) and Endurance Shuttle Walk Test (ESWT). The ISWT is a valid and reliable test designed to estimate VO_2max for patients with COPD [12,13]. The ISWT has also been validated for patients with lung cancer [14], although these patients were not identical to the present study population regarding stage of disease. In brief, the ISWT is carried out as follows: The patient walks between two cones, nine meters apart (10 including turning), following bleeps played from a CD-player. The patient turns the cone at the sound of the bleep. Each minute the interval between bleeps is shortened, increasing the walking speed. The PT is to measure how many meters, using the number of shuttles performed, the patients can complete before having to discontinue the test due to exhaustion. The test result is used to estimate the

VO_2max. The walking speed corresponding to an exercise intensity of 85% of VO_2max was calculated based on the result of the ISWT. This pace was used for the ESWT according to the COPD protocol.

The ESWT is structured the same way as the ISWT, however the walking speed stays the same throughout the entire test and the measurement of performance is time in minutes/seconds. Learning the ESWT speed at the hospital, the patients had an instrument for training at home.

Assessment of pulmonary function

Pulmonary function was assessed by spirometry (MIR Spirobank II, MIR SRL, Rome, Italy) at the first and last training session. Forced Expiratory Volume during the first second (FEV1) and percentage of predicted FEV1 (FEV1%) was recorded.

Assessment of quality of life

Cancer related quality of life was assessed at baseline and immediately after the exercise intervention using the self report questionnaire EORTC QLQ-30 including the lung cancer specific questionnaire QLQ-LC13 [15]. The questionnaire includes five functional scales, nine symptom scales/items and a global health status / quality of life scale. All questions are answered on a 1–4 scale (except global health and quality of life: 1–7 scale) and a 0–100 score is calculated for each scale. A high score generally indicates a better function and health status except for the symptom scales where a higher score indicates more symptoms and consequently a poorer condition. The QLQ-LC13 questionnaire comprises 13 questions regarding lung cancer specific symptoms such as dyspnoea and symptoms related to adverse effects of treatment such as pain and hair loss. The QLQ-LC 13 is analysed in 10 scales/items and 0–100 scores are calculated. A high score consistently indicates a higher level of symptoms.

The follow-up

Approximately three to four weeks after completing the intervention a nurse from the outpatient clinic contacted the patients by telephone. Based on a fixed interview guide, the patients were asked questions regarding satisfaction with the intervention and follow-up on current exercising habits. The questions were as follows:

1. *Was the information in the outpatient clinic about the intervention sufficient? Yes/No*
2. *Was the respiratory therapy introduction sufficient? Yes/No*
3. *Did you benefit from the forum/discussion part of the intervention? Yes/No*
4. *Do you still train according to the principles you have been introduced to through the intervention? Yes/No*
5. *Was the intensity of the exercise intervention – A: Strenuous, B: Adequate, C: Easy?*

Statistics

Data are presented as median and range and main outcomes (ISWT and ESWT) were evaluated using the Wilcoxon signed ranks test for paired observations. The level of significance was set to $p < 0.05$. The results of the self reported QLQ-C30 and -LC13 questionnaires are presented (according to the questionnaire manual) in 25 scales/items using descriptive statistics.

Results

Flow of patients (Figure 1)

Forty-five patients were recruited from the outpatient clinic. Between time of recruitment and time of intervention 14 patients decided not to participate. From the 31 remaining patients the physical therapist excluded an additional seven patients due to a decline in physical status since referral from outpatient clinic. Twenty-four patients (14 with inoperable non small cell lung cancer, four with inoperable small cell lung cancer, one inoperable of mixed histology (primarily SCLC), five with surgically treated non small cell lung cancer) initiated the intervention (Table I). Three patients did not complete a minimum of 65% attendance, and were therefore excluded from the analysis. Twenty-one patients completed full intervention and for 17 patients full ISWT and

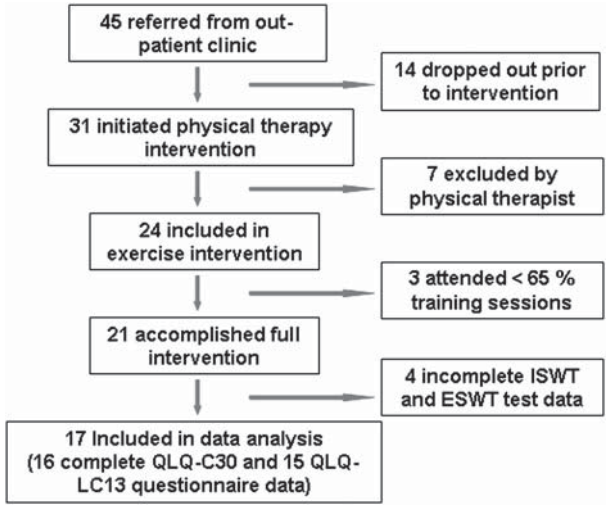

Figure 1. Flowchart of subject.

Table I. Demographic characteristics of the 24 patients initiating exercise at baseline. Data presented as median and range unless otherwise stated.

Demographic characteristics	Women (n = 10)	Men (n = 14)
Age (years)	67 (48–76)	64 (55–77)
Height (cm)	160 (158–169)	177 (166–194)
Weight (kg)	67 (52–120)	82 (68–100)
BMI (kg/m^2)	25 (19–48)	26 (21–36)
FEV1 (liters)	1.3* (0.8–2.0)	1.9* (1.3–3.0)
FEV1/pred. (%)	63* (38–80)	51* (39–85)
Smoking status (number) Current Former Never	181	4100
Previously surgically treated (number)	2	3
NSCLC (number)	8	11
SCLC + Mixed (number)	2	3
Chemo before intervention	8	11
Radiation before intervention	3	5
TKI before intervention	1	0
Chemo during intervention (number)	1	2
Radiation during intervention (number)	1	3
TKI during intervention (number)	1	2

FEV1: Forced Expiratory Volume during the first second. FEV1 pred.: Percent of FEV1 predicted from height, weight, gender, age and ethnicity. TKI: tyrosin kinase inhibitor (erlotinib)
*Pulmonary function was not measured in two patients: One woman and one man, consequently n = 9 for women and n = 13 for men.

ESWT data was obtained. Of the 17 patients, 16 completed the QLQ-C30 questionnaire both prior to and after the exercise intervention and 15 completed the QLQ-LC13 at both occasions. Only the 17 patients with complete ISWT and ESWT data sets were included in the analysis. The three patients with low compliance and the four patients with incomplete data were not different from the remaining patients regarding physical characteristics, cancer histology or type of treatment. Reasons for dropping out were: falling incident (N = 1), insufficient mental or physical energy (N = 2), co morbidity (N = 3) and resuming employment (N = 1).

Walking performance

The results of the ISWT testing showed improvement in maximum aerobic capacity (i.e. ability to reach a higher walking speed during the incremental test procedure) in 12 of 17 patients (p = 0.021) (Figure 2). Median improvement was 9% (-77 to 39%). For the ESWT test 15 of 17 patients improved in performance (Figure 3). The median of improvement was 109% (-70 to 432%) (p = 0.002). Due to a ceiling effect in the ESWT test (the CD has a maximum walking time of approximately 20 minutes) some patients may potentially have been able to improve even further.

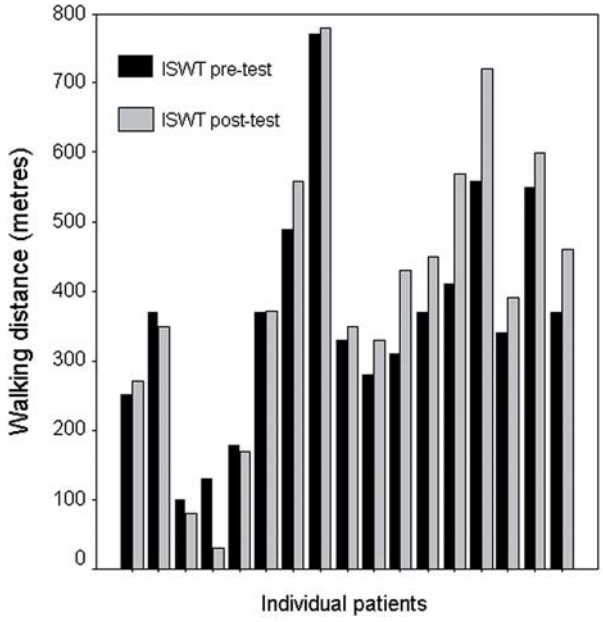

Figure 2. Incremental Shuttle Walk Test results pre- and post intervention.

Pulmonary function

No change was observed in FEV1 and FEV1% (Median change = 0 (−0.3 to +0.6)) in 15 patients where both pre- and post intervention measurements are available.

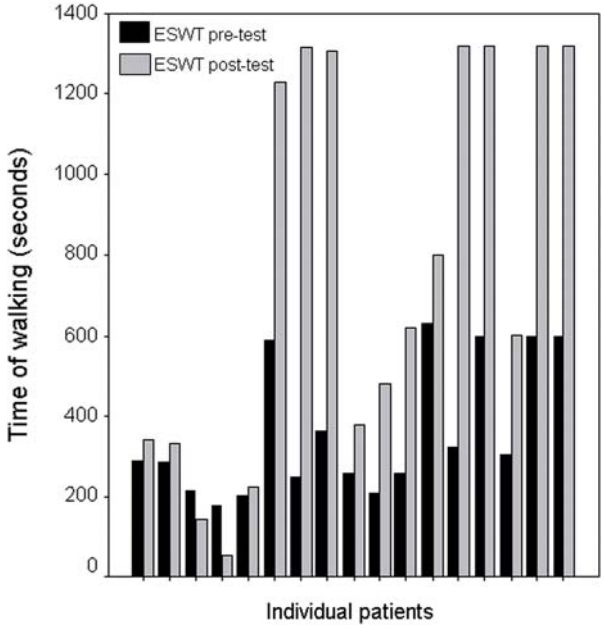

Figure 3. Endurance Shuttle Walk Test results pre- and post intervention.

Quality of life

Median scores at base-line and after the exercise intervention of the scales/items of the QLQ-C30 and QLQ-LC13 is presented in Table II. Generally no changes in the median scale scores were observed. The data available for analysis had insufficient power for statistical conclusions. However, inspection of individual items revealed that in the item regarding global health only one patient scored more than five on the 1–7 scale (7 indicating perfect health) while this was the case for six patients after the intervention (data not shown). A similar tendency was observed for the item regarding quality of life where four patients scored more than 5 at baseline compared to 7 after the intervention. In both items nine patients scored more than 4 both prior to and after the intervention and consequently the median combined global health/quality of life scale score of 5 ≈ 67 remained unchanged despite a progress of at least one point for 11 patients (global health) and six patients (quality of life), respectively.

Adherence to exercise during follow-up

Of the 16 of 24 patients available for telephone follow-up all found the information from the outpatient clinic sufficient, 15 found the introduction to respiratory therapy sufficient, 13 found the forum/discussion part beneficial (one did not, two did not participate) and two continued exercising following the principles of the intervention. Seven patients indicated that they continued to be physically active although not complying with exercise principles of the intervention. Ten found the intensity of the intervention adequate, five found it strenuous and one found it easy.

Table II. Patient reported quality of life: EORTC QLQ-C30 and QLQ-LC13

QLQ-C30 Subscale (n = 16)	Base line	Post intervention
Global health status/Qol.	67 (25–83)	67 (17–92)
Physical functioning	70 (33–87)	73 (33–93)
Role functioning	67 (0–100)	67 (0–100)
Emotional functioning	88 (17–100)	92 (58–100)
Cognitive functioning	92 (17–100)	100 (33–100)
Social functioning	92 (33–100)	100 (50–100)
Fatigue	22 (11–89)	33 (11–100)
Nausea and vomiting	0 (0–67)	0 (0–33)
Pain	8 (0–67)	17 (0–100)
Dyspnoea	50 (33–100)	33 (33–100)
Insomnia	17 (0–67)	0 (0–67)
appetite loss	33 (0–100)	0 (0–67)
Constipation	0 (0–67)	0 (0–67)
Diarrhea	0 (0–100)	0 (0–33)
Financial difficulties	0 (0–67)	0 (0–33)
QLQ–LC13 Subscale (n = 15)		
Dyspnoea	33 (11–89)	33 (11–100)
Coughing	33 (0–67)	33 (0–67)
Haemoptysis	0 (0–0)	0 (0–33)
Sore mouth	0 (0–67)	0 (0–100)
Dysphagia	0 (0–33)	0 (0–33)
Peripheral neuropathy	0 (0–100)	0 (0–100)
Alopecia	0 (0–100)	0 (0–100)
Pain in chest	0 (0–67)	33 (0–100)
Pain in arm or shoulder	33 (0–67)	0 (0–100)
Pain in other parts	33 (0–67)	0 (0–100)

Discussion

The lung cancer patients in the present study showed improved physical fitness after the exercise intervention. This study found an overall improvement in both maximum aerobic capacity (ISWT) and walking distance (ESWT). Compliance with the supervised training sessions for the group who initiated exercise was high indicating a relatively high feasibility of the intervention, however, adherence to the exercise after intervention was low.

In a study by Temel et al. including 25 patients with advanced NSCLC who underwent a structured exercise programme, the authors found a significant reduction in lung cancer symptoms and no deterioration in performing the six minute walk test. However, only 11 of 25 patients completed the exercise programme. The exercise programme described by Temel et al., was more strenuous than the present study and this could explain the higher number of patients unable to complete [16].

Spruit et al. found that lung cancer patients with mixed histology and treatment all benefited from exercise. Multidisciplinary exercise significantly improved six minute walk test and peak load cycling test. The study was a pilot study and only included ten patients [17].

To our knowledge no earlier studies have applied a well documented COPD exercise protocol in lung cancer patients. The tests (ISWT and ESWT, EORTC-QLQ-C30 and LC13) used in the present study have all been used to evaluate physical fitness and quality of life among cancer patients in previous studies [14,15,18], although the patients of these studies do not match the present patients regarding diagnosis and stage of disease. Using this method our study measured both subjective and objective effects of the intervention. Several previous studies have examined the role of physical exercise in relation to surgery for lung cancer. In contrast, the present study examines a group consisting mainly of patients not eligible for surgery who in general have more advanced disease and a poorer prognosis.

Lung cancer patients are often characterised by pulmonary symptoms such as dyspnoea, secretion

and coughing. Exercising is often associated with discomfort and fear. Dimeo et al. described "a vicious circle" or "dyspnoea spiral". The patients avoid dyspnoea, and become increasingly sedentary. This leads to diminished exercise tolerance, and aggravation of dyspnoea [19].

The fact, that the patients who completed the present intervention increased their physical performance as measured by the shuttle walk tests, indicated that the introduction to a well-coordinated exercise program enabled them to break the "vicious circle" and increase exercise tolerance. In addition, exercise in a group of patients with the same diagnoses also provided an opportunity to share experiences.

The limitations of this study include the lack of a control group and the relatively small number of patients investigated.

The tests used in this study have limitations, which should be taken into consideration.

QoL questionnaires have a relatively poor sensitivity, which makes it possible that differences in quality of life could be overlooked. Secondly the ESWT test had a ceiling effect when measuring the best performing patients. A closer look at the results of the present study, may also give the impression that the best performing patients in ISWT also had the best potential for improvement in the ESWT. Consequently, future studies should assure adequate testing methods that oblige both poor- and well performing patients.

A number of patients who were offered the physical exercise programme did not participate in the intervention. This could be caused by at variety of psychological (e.g. anxiety, depression) as well as physical (e.g. fatigue, discomfort) barriers. However, our study showed that patients who enrolled in the exercise intervention had a high rate of completion and the participating patients expressed satisfaction and gratitude with the intervention program.

Our study showed low adherence to exercise after intervention. Some patients found sessions monotonous and at times unexciting, which should be addressed when planning future studies.

In conclusion, a seven-week COPD exercise program applied in mainly inoperable lung cancer patients increased physical function in patients completing the program, while pulmonary function and self reported QoL remained unchanged. The poor prognosis for lung cancer patients considered, this could be interpreted as a positive result. However, the low adherence to the exercise program and the relatively high drop-out prior to exercise initiation indicated that the intervention could be improved. Future studies may elucidate if strategic changes in the recruitment of patients and the exercise program itself can increase the number of patients participating in and continuing the exercise program.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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