Support Care Cancer (2013) 21:2247–2253
DOI 10.1007/s00520-013-1781-z

ORIGINAL ARTICLE

A modified exercise protocol may promote continuance of exercise after the intervention in lung cancer patients—a pragmatic uncontrolled trial

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Received: 10 July 2012 / Accepted: 4 March 2013 / Published online: 20 March 2013

Abstract
Purpose A previous study investigated the effects of a well-documented COPD exercise protocol in lung cancer patients. The study showed improvements in physical fitness, but poor adherence to continued exercise after intervention. The aim of the present study was to investigate the effect of a modified exercise intervention on post-intervention adherence, and physical fitness in a broad group of lung cancer patients.
Methods Fifty-nine patients enrolled in a 9-week exercise program. Eligibility criteria were limited to presence of motivation, and absence of comorbidities that could jeopardize safety. The intervention included three times 3 weeks of exercise (3 weeks supervised, 3 weeks home-based and 3 weeks supervised). The patient's activities were structured by logbooks during the 3 weeks at home. VO_2 max was estimated at baseline and at the end of intervention. Self-reported quality of life was recorded before and after the exercise program. Post-intervention exercise activity was assessed by telephone interviews 4 weeks after intervention.
Results Fifty-one patients initiated the exercise intervention and 29 patients successfully completed the exercise program. Full data were available for 25 patients regarding estimated VO_2 max. Twenty-six of the 29 were available for follow-up with respect to continuance of physical activity.

Among the 26 who completed the 9-week training program, 18 (69 %) continued to be physically active on a daily basis. No change in estimated VO_2 max was observed. A trend towards increased quality of life and better symptom control was noted.
Conclusions The present study showed an increased level of continuance of physical activity compared to the previous study. The present study could, however, not repeat the significant improvements in estimated VO_2 max from the previous study.

Keywords Lung cancer · Physical exercise · Adherence · Rehabilitation

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Introduction

A growing body of evidence documents that exercise is both feasible and safe in patients with lung cancer [1]. For a significant part of lung cancer patients, physical activity can improve muscular and cardiovascular strength and endurance, as well as symptoms from both the cancer disease and treatment leading to an overall improvement in quality of life [1]. Lung cancer patients represent a subgroup of cancer patients characterized by specific symptoms such as dyspnoea and loss of empowerment [2]. However, lung cancer patients are quite heterogeneous with respect to stage, performance, comorbidity and symptoms. It is therefore challenging to design a physical exercise programme that fits most patients. Most previous studies have been conducted on specific sub-groups of lung cancer patients, for example patients eligible for surgery [3–5], patients undergoing chemotherapy [6, 7] or patients with advanced disease [8]. Consequently, it is difficult to create a standardized program for physical rehabilitation for a broader group of lung cancer patients.

The present knowledge on exercise interventions and lung cancer often focuses on effect, measured as exercise capacity or quality of life. However, another problem is to

what extent the patients follow the physical rehabilitation program (compliance), and whether patients actually continue the daily training once the intervention program has ended (adherence). To improve adherence, motivational interviewing has been conducted in cancer survivors, predominantly breast cancer, with positive results [9]. To our knowledge, no studies have investigated the adherence to continued physical exercise after physical rehabilitation in lung cancer.

We recently published a study [10] showing that a well-documented COPD exercise protocol [11, 12] improved the estimated exercise capacity as measured by Incremental Shuttle Walk Test (ISWT) in a mixed group of lung cancer patients. Furthermore, physical exercise and dyspnoea coping techniques also improved walking distance measured with Endurance Shuttle Walk Test (ESWT).

However, patients found that the exercise program was monotonous, and that the intervention period of 7 weeks was too short. From the physical therapist's point of view, the setup was difficult because the ESWT test was time-consuming and had a ceiling effect when testing the best-performing patients. Only few patients continued to follow the exercise programme as instructed, indicating that although patients experienced improved exercise capacity, there was low adherence to continued exercise after the intervention [10].

Consequently, it appears to be challenging to construct an exercise protocol for a broad group of lung cancer patients that not only improves exercise capacity and quality of life but also provides the patients with sufficient motivation for continued physical activity. The aim of the present study was to investigate the impact of a modified exercise intervention on adherence.

Material and methods

Patients were recruited from the outpatient clinic at the Department of Oncology at Herlev University Hospital (HUH). HUH is a regional multidisciplinary hospital covering a part of the Greater Copenhagen Area. Annually, more than 500 new lung cancer cases are referred for treatment. Most patients live less than 50 km from the hospital. All patients were offered transportation if needed. The intervention was free of charge. All lung cancer patients, regardless of histology, stage and treatment, were included. The only eligibility criteria were that the patients should be motivated for the intervention and not have symptomatic brain metastasis or heart failure (NYHA class IV). All patients gave informed consent. The study was approved by the regional ethics committee.

Overall description of intervention

Patients were to attend supervised physical exercise for 1.5 h twice a week for 3 weeks then perform 3 weeks of daily unsupervised physical exercise at home according to instructions, and then return to the hospital for another 3 weeks of supervised physical exercise. The purpose of the 3-week period of training at home was to give the patients some experience with training on their own before returning for another period of supervised training.

Directions for the exercise intervention

The supervised exercise was performed in groups of 8–12 patients, commencing and finishing the intervention at the same time. All supervised physical exercise took place at HUH, and was conducted by two physical therapists. No specific training equipment was used for the intervention.

A modified version of a conventional COPD exercise protocol [11, 12] was applied. At the first exercise session, the patients were introduced to dyspnoea coping strategies, such as "pursed lip breathing technique" and respiratory resting positions. If indicated, the patients were introduced to a positive expiratory pressure breathing device.

Each 90-min session began with a 10–15-min warm-up. The warm-up focused on major muscle groups in both upper and lower extremities and was adjusted to an intensity of low to moderate.

As part of each exercise session, the patients performed either a walking test (ISWT) or a running (the Yo-Yo endurance (continuous) test) [13] depending on physical ability. Estimated VO_2 max was calculated from these tests.

The testing was followed by endurance training. The endurance training was performed as interval training, and would change from session to session always aiming for a level of training intensity equivalent to 16–18 on rate of perceived exertion (RPE) [14]. Typically, the interval training was performed using stationary bikes, stairs, rowing machines, ball games, et cetera. The intervals would last from 2 to approximately 10 min depending on the choice of activity. However, for the longer lasting games or activities patients could not sustain the level of intensity projected. Degree of exertion was self-rated, and therapist would verbally motivate patients to reach the projected degree of exertion during activity. During breaks, patients would use respiratory techniques to regain normal respiratory frequency and comfort. Each session would end with 15 min of either stretching or relaxation.

Directions for home-based exercise

The logbook instructed the patients to be physically active at least once a day, and included a table where patients could note choice of exercise, time spent and RPE. Patients were free to choose any type of physical activity that could elicit the prescribed RPE used during the supervised exercise sessions.

In addition, the logbook consisted of practical information regarding the intervention, information about the exercise

intervention at the hospital, the home-based exercise and advice concerning dyspnoea coping, respiratory physical therapy, as well as advice on food intake in relation to exercise. In addition, the logbook also suggested websites or local activity centres that could help the patients stay active after the intervention.

Assessment of walking performance

At all supervised exercise sessions, patients either performed an ISWT or a Yo-Yo endurance test. ISWT is a valid and reliable test designed to estimate VO_2 max in COPD patients [15, 16] and validated in lung cancer patients [17].

The ISWT was performed as follows: The patient was instructed to walk between two cones, 9 m apart (10 m including turning). The walking would follow pre-recorded beeps from a CD player, instructing the patient to turn a cone with each beep. Each minute the interval between each turn would shorten, forcing the patient to increase walking speed. The physical therapist measured how many metres the patient could keep the pace of the CD player, using the amount of shuttles performed, before discontinuing due to exhaustion. The distance covered by the patient was used to calculate the estimated VO_2 max.

The Yo-Yo endurance test was performed like the ISWT, but the patients were running instead of walking. The patient ran between two cones 20 m apart. A computer programme controlled the pace of the patients and estimated the patients VO_2 max [18]. As with the ISWT test, the test finished when the patient could no longer keep the pace of the pre-recorded beeps.

Assessment of pulmonary function

Pulmonary function was measured with spirometry using the MIR Spirobank II (MIR SRL, Rome, Italy) at the first and the last training session. FEV1 (forced expiratory volume within the first second) and FEV1% (percentage of predicted FEV1) were recorded.

Assessment of quality of life

Patients completed the self-reported quality-of-life (QOL) questionnaire EORTC QLQ-30 and the lung cancer-specific questionnaire QLQ-LC13 at baseline and at the end of the exercise intervention [19].

The follow-up

Patients were contacted by a nurse from the outpatient clinic approximately 4 weeks after the end of the intervention. Patients were interviewed about continuance of physical exercise. Staying physically active was defined as a planned daily activity that would cause the patient to experience a level of exercise intensity equivalent to 16–18 on rate of perceived exertion (RPE).

Statistics

Baseline characteristics, pre/post-intervention VO_2 max, FEV1 and QOL scores are presented as mean±SD. As female and male participants exhibited very similar baseline values, and responses to the intervention for the main outcomes, they were analysed together. End points were chosen: (1) the proportion of patients who continued to perform daily physical exercise at 4 weeks after the intervention, (2) pre/post-intervention estimated VO_2 max, (3) global health status/QoL score, (4) fatigue score and (5) dyspnoea score. Paired *t* tests were used to analyse the change in end points 2–5, while Fischer's exact test was used to test for gender difference in the number of patients reporting continued physical activity. The level of significance was set to $p<0.05$. All results of the self-reported QLQ-C30 and -LC13 questionnaires were presented (according to the questionnaire manual) in 25 scales/items (Table 2).

Results

Flow of patients

Fifty-nine lung cancer patients agreed to participate in the intervention (Fig. 1). Between time of inclusion and time of intervention, eight patients dropped out. Consequently, 51 patients initiated the exercise intervention. Demographic characteristics are presented in Table 1. Twenty-two patients did not complete a minimum of eight supervised exercise sessions, leaving 29 patients with full compliance. Full pre- and post-intervention data on estimated VO_2 max were available for 25 of these patients, while 27 patients completed the QoL questionnaires both pre- and post-intervention. Not all patients answered all items resulting in less than 27 responses for some items (Table 2). At follow-up, 18 reported to be continuing physical activity on a daily basis at home, 8 did not continue and 3 were lost to follow-up (due to hospitalization and severe illness). No differences in baseline characteristics between those with full compliance and those who did not successfully complete the intervention were observed (data not shown). Reasons for dropping out were not systematically collected, although decline in performance status and/or increasing level of fatigue were often mentioned.

Primary outcomes

Mean pre- and post-intervention values for FEV1, VO2 max and QOL are presented in Table 2. No gender differences were observed regarding the response to the exercise

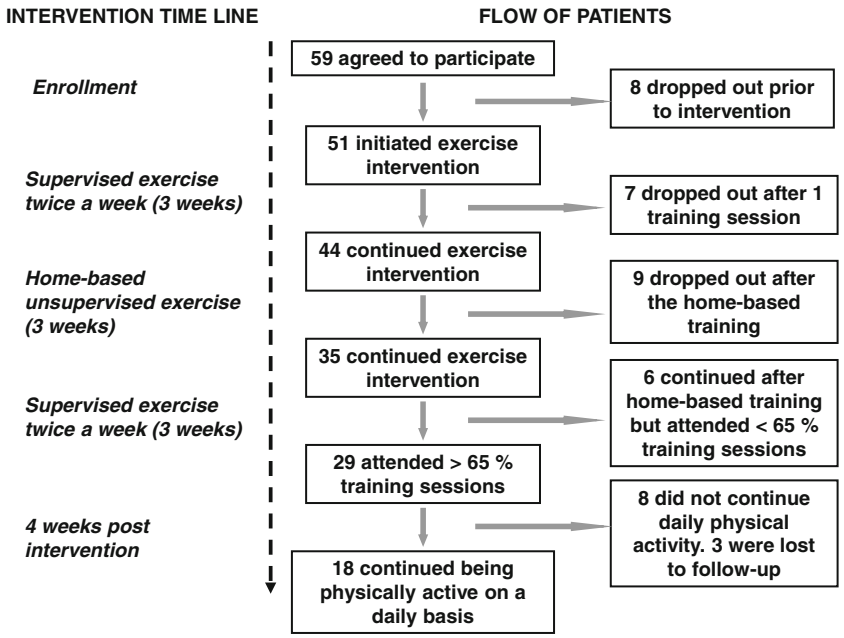

Fig. 1 Flowchart of patients agreeing to participate in intervention. Time line illustrating the different phases of the intervention and follow-up

intervention for the following primary outcomes: VO_2 max, global health status/QoL, fatigue and dyspnoea. Consequently, men and women were analysed together.

No change from pre- to post-intervention was observed regarding mean estimated VO_2 max: pre-test, 14±3 ml O_2/kg/min and post-test, 14±3 ml O_2/kg/min (p=0.763). FEV1 remained unchanged during the intervention from baseline. Although not statistically significant, the Global Health Status (QOL) increased from 59 to 65 during the intervention. (p=0.204). Fatigue score decreased from 40 to 33 (p=0.290). Dyspnoea score increased from 44 to 48 (p=0.212).

A total of 18 out of the 26 patients (69 %) who successfully completed the physical rehabilitation program, and who was not lost to follow-up, reported that they continued with some form of daily physical activity. A trend for a gender difference was observed for continuance of exercise among the compliant patients as 10 of 11 (90 %) women continued, whereas only 8 of 15 (53 %) men continued being physically active (p=0.084).

Discussion

The main results of the present study are that almost 70 % of the patients with good compliance during the exercise program continued exercising 4 weeks after completing the

Table 1 Demographic characteristics of the 51 patients initiating exercise at baseline

Demographic characteristics	Women (n=20[a])	Men (n=31[a])
Age (years)	65±7	65±8
Height (cm)	166±6	179±6
Weight (kg)	71±11	86±20
BMI (kg/m^2)	26±4	27±6
FEV1 (liters)	1.60±0.42	2.17±0.67
FEV1 pred. (%)	66±16	62±17
Smoking status (number)[b]		
Current	1	3
Former	16	25
Never	1	2
Previously surgically treated (number)	6	4
NSCLC (number)	14	25
SCLC+mixed (number)	5	5
Chemo during intervention (number)	9	17
Radiation during intervention (number)	1	2
TKI during intervention (number)	1	1

Data presented as mean and SD unless otherwise stated

FEV1 forced expiratory volume during the first second, *FEV1 pred* percent of FEV1 predicted from height, weight, gender, age and ethnicity, *TKI* tyrosine kinase inhibitor (erlotinib)

[a]Missing data for one female and one male patient in all fields except age

[b]Missing data for a second female patient

Table 2 Estimated VO_2 max, pulmonary function (FEV1) and patient reported quality of life: EORTC QLQ-C30 and QLQ-LC13

	Baseline			Post-intervention	
	(*n*)	Mean±SD		Mean±SD	
Estimated VO_2 max	(25)	14±3		14±3	
FEV1	(28)	2.0±0.6		2.0±0.5	
QLQ-C30 subscale					
		Mean±SD	(%≥80)	Mean±SD	(%≥80)
Global health status/QoL	(26)	59±21	(26 %)	65±19	(19 %)
Physical functioning	(27)	73±20	(56 %)	76±20	(63 %)
Role functioning	(26)	63±34	(46 %)	66±25	(42 %)
Emotional functioning	(24)	79±20	(67 %)	92±13	(88 %)
Cognitive functioning	(27)	84±16	(78 %)	86±17	(81 %)
Social functioning	(26)	81±23	(62 %)	85±18	(69 %)
		Mean±SD	(% no symptoms)	Mean±SD	(% no symptoms)
Fatigue	(23)	40±29	(4 %)	33±25	(9 %)
Nausea and vomiting	(26)	9±14	(62 %)	5±10	(77 %)
Pain	(26)	22±26	(42 %)	15±21	(62 %)
Dyspnoea	(27)	44±33	(19 %)	48±32	(19 %)
Insomnia	(27)	25±31	(52 %)	20±32	(67 %)
Appetite loss	(27)	21±34	(63 %)	11±21	(74 %)
Constipation	(27)	7±17	(81 %)	7±17	(81 %)
Diarrhoea	(26)	23±29	(54 %)	14±25	(69 %)
Financial difficulties	(27)	11±23	(74 %)	7±21	(89 %)
QLQ-LC13 subscale					
Dyspnoea	(25)	40±24	(4 %)	35±25	(12 %)
Coughing	(25)	39±28	(24 %)	37±29	(24 %)
Haemoptysis	(26)	0±0	(100 %)	1±7	(96 %)
Sore mouth	(26)	4±14	(96 %)	5±15	(88 %)
Dysphagia	(26)	10±25	(81 %)	9±29	(85 %)
Peripheral neuropathy	(26)	13±23	(73 %)	18±30	(65 %)
Alopecia	(26)	15±32	(77 %)	8±24	(88 %)
Pain in chest	(26)	21±28	(58 %)	19±25	(54 %)
Pain in arm or shoulder	(26)	14±29	(77 %)	13±21	(69 %)
Pain in other parts	(21)	22±29	(52 %)	13±25	(76 %)

No statistically significant changes were observed for the primary endpoints (highlighted) while statistical significance was not formally tested for the remaining scores. The EORTC QLQ-C30 and QLQ-LC13 are scored on 0–100 scale. 0 indicates the lowest level of function (worst score) and 100 the highest level of function (best score) in the top six items. In the remaining items, 0 indicates the lowest level of symptoms (best score) and 100 the highest level of symptoms (worst score). In addition to the mean score±SD, the percentage of the patients scoring 80 points or more in the items regarding function and percentage of the patients reporting no symptoms in the remaining items are provided

intervention. No significant changes in walking/running VO_2max performance estimated with ISWT or Yo-Yo endurance (continuous) test or pulmonary function was found. We found no significant changes in QoL.

The present study is limited by the lack of a control group, and the relatively small sample size. The study is furthermore limited because of the application of two estimated VO_2max tests instead of a directly measured VO_2 max test. The Yo-Yo endurance (continuous) test has, to our knowledge, not previously been used for cancer patients and is not validated for the present group of patients. However, the test was used because of the practical similarity to the ISWT and the fact that both tests estimated VO_2 max in millilitres O_2 per kilogram per minute.

The 3-week break in the middle of the intervention intended to give patients the opportunity to exercise on their own. However, compliance data showed that a relatively large group (9 of 44) did not return for the second part of the intervention.

As inclusion in study was only restricted by very few exclusion criteria, and as patients were offered transportation, and as the intervention was free of charge, we believe that the participants are representative to the general lung cancer population treated in a clinical setting. The revised intervention used in this study was modified from a previous intervention by changes in the testing procedure, to make it less time-consuming, and by designing the intervention not to require any specific material/equipment. These changes were made with the intention of developing an intervention program that was easy to implement anywhere.

A concern regarding interpretation of results were that anticancer treatment could have an impact on pulmonary function

and thus exercise capacity. We therefore measured pulmonary function pre- and post-intervention but found no changes

The pragmatic approach with broad eligibility criteria, simple testing procedure and the lack of a control group affected the internal validity negatively. On the other hand, this approach increased the generalizability and applicability of the results to a broad spectrum of clinical settings and patients. These methodological considerations need to be taken into account when interpreting the present findings.

Compared to a previous study conducted at our facility on a similar group of patients [10], two main differences regarding the effect of the intervention were observed: (1) no changes in estimate VO_2 max were observed in the present study compared to significant improvements in the previous study and (2) the percentage of patients reporting that they continued with some form of regular physical activity was higher in the present study (69 %) compared to the previous study (56 %). This may be explained by the changes made in the revised intervention. In the present study, emphasis was placed on variation, rather than repetition of one type of exercise exclusively focusing on exercise intensity. It is likely that a more individual approach to training increased the likelihood of patients being motivated for exercise after the intervention, but at the same time reduced the exercise intensity.

The supervised exercise was delivered in two periods separated by a 3-week period of unsupervised training. This approach was intended as a way to allow patients to experience training on their own before continuing the supervised program.

The split up exercise intervention of the present study may have led to the lack of effect on estimated VO_2 max compared to the previous study since compliance to home-based unsupervised exercise may be low in lung cancer patients [6, 7]. Moreover, nine patients dropped out of the program during the 3 weeks of unsupervised exercise. The potential advantage in terms of increased adherence to physical activity of the split-delivery seems to come at price of decreased physiological adaptation to physical exercise, and an increased risk of patient dropout. This knowledge is important when designing future exercise interventions for lung cancer patients.

The present study introduces two adherence promoting initiatives in comparison to the previous study. First of all, the exercise intervention was changed to focus on motivation and joy of being physically active. The second was, due to the split-up design, to enable patients to experience incorporating physical exercise in their everyday lives while still being under supervision. The observed tendency to a difference between men and women in adherence to continued physical exercise at 4 weeks was unexpected but may provide an important clue to how to overcome the problem of adherence. It is possible that intervention programs should be designed differently for men and women.

Further improvement in adherence may come from motivational interviewing, with the aim of clarifying patient resources and balancing expectations and multidisciplinary interventions. This could also enable counselling about not only exercise capacity but also nutrition, smoking cessation and psychological support. Access to a physical therapist by phone during and after the intervention is another possible way of increasing adherence, and thus benefit for lung cancer patients.

In summary, the present study has shown that it is possible to design a physical exercise intervention to a broad group of lung cancer patients. The present study indicates that a varied exercise program designed to motivate the patients has a positive influence on adherence to continuance of exercise after the intervention. The study could not show the same improvements on physical fitness, as found in the previous study performed at our facility. This could indicate that a varied choice of exercise modalities and a split-up treatment program may attenuate the improvements in physical fitness. However, maintaining quality of life and physical fitness in addition to providing the patients with tools to continue being physically active may represent a rather positive outcome.

Conflict of interest The present study has been read and approved by all authors. The contents of this manuscript are our original work and have not been published, in whole or in part, prior to or simultaneous with our submission of the manuscript to Supportive Care in Cancer. The authors state that they have full control of all primary data, and that they agree to allow the journal to review data if requested. There are no financial conflicts of interest.

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