ORIGINAL ARTICLE

High-intensity training following lung cancer surgery: a randomised controlled trial

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ABSTRACT

Background Many patients with lung cancer are deconditioned with poor physical fitness. Lung resection reduces physical fitness further, impairing the patient's ability to function in daily life.

Methods We conducted a single-blind randomised controlled trial of high-intensity endurance and strength training (60 min, three times a week, 20 weeks), starting 5–7 weeks after surgery. The control group received standard postoperative care. The primary outcome was the change in peak oxygen uptake measured directly during walking until exhaustion. Other outcomes included changes in pulmonary function, muscular strength by one-repetition maximum (1RM), total muscle mass measured by dual energy X-ray absorptiometry, daily physical functioning and quality of life (QoL).

Results The intention-to-treat analysis of the 61 randomised patients showed that the exercise group had a greater increase in peak oxygen uptake (3.4 mL/kg/min between-group difference, p=0.002), carbon monoxide transfer factor (Tlco) (5.2% predicted, p=0.007), 1RM leg press (29.5 kg, p<0.001), chair stand (2.1 times p<0.001), stair run (4.3 steps, p=0.002) and total muscle mass (1.36 kg, p=0.012) compared with the controls. The mean±SD QoL (SF-36) physical component summary score was 51.8±5.5 and 43.3±11.3 (p=0.006), and the mental component summary score was 55.5±5.3 and 46.6±14.0 (p=0.015) in the exercise and control groups, respectively.

Conclusions In patients recently operated for lung cancer, high-intensity endurance and strength training was well tolerated and induced clinically significant improvements in peak oxygen uptake, Tlco, muscular strength, total muscle mass, functional fitness and QoL. This study may provide a basis for exercise therapy after lung cancer surgery.

Trial registration number NCT01748981.

Key messages

What is the key question?

- What are the effects of high-intensity endurance and strength training after lung cancer surgery?

What is the bottom line?

- Compared with standard postoperative care, high-intensity endurance and strength training is well tolerated and improves cardiorespiratory fitness, carbon monoxide transfer factor, muscular strength, daily physical functioning, total muscle mass and quality of life.

Why read on?

- Because it is not possible to compensate for the loss of lung tissue after lung resection, clinicians should encourage patients to improve cardiorespiratory fitness and skeletal muscle strength to increase their physical fitness after lung resection.

INTRODUCTION

Patients with non-small-cell lung cancer (NSCLC) are often deconditioned and may have a poor cardiorespiratory fitness (CRF).[1] This probably reflects cardiopulmonary comorbidities and a sedentary lifestyle with subsequent loss of muscle mass.[2] Lung resection surgery reduces the CRF further,[3] leading to persistent dyspnoea and lower functional outcome.[4] Chemotherapy and/or radiation therapy are associated with additional impairment which affects all pathways involved in oxygen transport from the lungs to the working muscles.[5] Taken together, these aspects may markedly reduce the patient's ability to function in daily life.

The gold standard for measurement of CRF is a direct measure of the maximal or peak oxygen uptake.[6] In general, a minimum peak oxygen uptake of 12–15 mL/kg/min is the threshold for the ability to perform activities of daily independent living.[7] Unfortunately, a number of patients with lung cancer do not achieve this threshold, especially after surgery.[3] Furthermore, a low peak oxygen uptake is associated with increased morbidity and mortality,[8 9] also in patients with lung cancer undergoing surgery.[1] An increase in peak oxygen uptake may increase the survival[10] as well as the functional ability and quality of life (QoL).[11]

A few studies have previously examined the effects of exercise in patients after lung resection.[12] To our knowledge, only a small number of studies used a randomised design,[13–16] and the results have been conflicting.[12] In addition, the duration of the intervention in these studies has been short.[13 14 16] Given the clinical importance of CRF,[10] none of these studies measured peak oxygen uptake directly.

We conducted a single-blind randomised controlled trial to evaluate the effects of high-intensity endurance and strength training shortly after lung cancer surgery. Our primary hypothesis was that patients who perform endurance and strength

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training after lung cancer surgery would show improvements in peak oxygen uptake compared with controls receiving standard postoperative care. Changes in pulmonary function, muscular strength, total muscle mass, daily physical functioning and QoL were also studied.

METHODS

Study design

From November 2010 to September 2012 we enrolled newly diagnosed patients with resectable NSCLC to a single-blind single-centre randomised controlled trial of a high-intensity endurance and strength training programme compared with standard oncological care. The study was conducted at Oslo University Hospital in Norway and follow-up was completed by May 2013. Eligible patients were ≤80 years of age, had newly diagnosed or suspected NSCLC and had been accepted for surgery. Patients were not eligible if they were unable to perform a maximal exercise test (eg, unable to cope with equipment or high risk for comorbidities), lived too far from a training centre or were not able to understand Norwegian. After signing an informed consent form, the patients were enrolled in the study and underwent lung cancer surgery through a muscle-sparing lateral thoracotomy or by video-assisted thoracoscopic surgery (VATS).

Four to 6 weeks after surgery, patients were randomised into an exercise or a control group that was stratified for receiving chemotherapy and for having chronic obstructive pulmonary disease (COPD). The randomisation was done in blocks with varying block size (4–6 subjects) and put into sealed opaque envelopes generated by an external statistician.

The study was conducted in accordance with the CONSORT statement for non-pharmacological interventions and was approved by the Regional Committee for Medical Ethics.

Measurements

Measurements were performed by exercise physiologists before surgery, 4–6 weeks after surgery and immediately after the 20-week intervention.

Spirometry, maximum voluntary ventilation and carbon monoxide transfer factor (Tlco) were conducted (SensorMedics, Yorba Linda, California, USA) according to guidelines.[17]

CRF was evaluated through a direct peak oxygen uptake test (SensorMedics) using a continuous graded exercise protocol involving walking uphill on a treadmill (Woodway, Würzburg, Germany) until exhaustion within 6–12 min. The rating of perceived exertion (RPE) was obtained by the Borg scale_{6-20}.

Concentric leg strength was assessed by the sum of the maximum weight that could be lifted once (one-repetition maximum, 1RM) using a horizontal hip and knee extension movement with a starting angle of 90° flexion. Maximum hand strength was measured by a grip strength dynamometer and the best of three attempts was recorded. Measures of daily physical functioning included the chair stand test,[18] maximum stair steps for 15 s and a modified one-foot static balance test on soft ground for a maximum of 60 s.[19] Total muscle mass was measured by dual energy X-ray absorptiometry (DXA; GE Lunar Prodigy, GE Healthcare, Madison, Wisconsin, USA).

The Medical Outcomes 36-Item Short Form Health Survey (SF-36) was used to evaluate QoL.[20] A dyspnoea score was calculated using the European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QOL-C30).[21]

Exercise intervention

The exercise programme was undertaken at fitness centres near the patients' home, starting 1 week after randomisation. Each session lasted 60 min and exercise was performed three times per week for 20 weeks; 1 h per week exercising in groups if possible. Highly qualified personal trainers and physiotherapists supervised each training session. Because of somewhat reduced availability of local physiotherapists, the total number of training hours was 55. The exercise programme was individualised and included a cardiovascular warm-up, interval training, progressive resistance training (PRT) and daily inspiratory muscle training. The intervention focused on high-intensity training, mainly by walking uphill on a treadmill at 80–95% of the maximum heart rate and by PRT in three series of 6–12 RM of the leg press, leg extension, back extension, seat row, bicep curls and chest-and-shoulder press. During the first 4 weeks the programme focused on safety, technique and becoming familiar with the exercises. The intensity and duration of each interval was then individually increased continuously based on the patient's improvement, ability to cope with dyspnoea and feelings of well-being or fatigue on each exercise day. For patients undergoing chemotherapy, the training continued as usual if the patient was able to exercise. If not, the time away from training was added after the completion of chemotherapy. Hence, all patients in the intervention group fulfilled the total amount of 20 weeks of training, regardless of whether or not they received chemotherapy. All training sessions were documented in an exercise log for each patient, where the patient logged the RPE and the personal trainer logged the intensity and degree of feasibility. Patients in the control group were not given any advice about exercise beyond general information from the hospital.

Outcomes

The primary outcome was the change in peak oxygen uptake from baseline to after intervention. Secondary outcomes included changes in pulmonary function, muscular strength, total muscle mass, daily physical functioning, and QoL.

Statistical analysis

Sample size calculations were based on the primary outcome of a change in peak oxygen uptake of 4 mL/kg/min, assuming a SD of 4.6 mL/kg/min (estimated from Kushibe *et al*[22]). A sample size of 21 per group for 80% power was required to detect the assumed difference between means with a 5% significant level. However, it was not certain how many would be excluded before randomisation because of complications after surgery. We expected a large number of dropouts (45% of those randomised) during the intervention because of morbidity or mortality after surgery and adverse events after chemotherapy and radiation. We thus planned to recruit 80 patients to obtain the required number of patients.

Demographic data are presented as mean and SD for continuous variables, median and range for not normally distributed data and proportions for binary variables. Binary outcomes were compared between the two study groups using the Fisher exact test.

p Values were calculated using the χ^2 test for categorical variables and the analysis of covariance for continuous variables. Effects were evaluated on an intention-to-treat basis. Missing values were imputed using a multiple imputation model for all of the 61 randomised patients. Because dropping out was not expected to be related to treatment allocation, we assumed that missing patient data at the end were grossly at random.

Per-protocol analyses were also evaluated for the primary outcome where the analysis included a comparison between exercising and non-exercising patients.

Because there were too many missing values for QoL variables, only post-intervention values were included when testing for differences between treatment groups. Statistical analyses were performed using SPSS software V.21.0.

RESULTS

Study population and characteristics

A total of 106 patients were screened for participation and 69 patients were enrolled before surgery. After surgery, eight patients were not randomised because of postoperative mortality (n=3) or unexpected events. Five patients in the exercise group and two patients in the control group did not complete the intervention (figure 1).

Eighteen of the patients (30%) had COPD, 17 (28%) had a history of arrhythmia and/or cardiovascular disease and seven (11%) had diabetes. Ten patients underwent pneumonectomy, two underwent bilobectomy and 51 underwent single lobectomy. VATS was used in 10 patients (table 1).

Adherence and training intensity

The adherence rate during the 20 weeks of exercise was 88 ±29% (technically, some could exceed 100% of the 55 h available). The exercise intensity during the interval training was 90.8±6.0% of the maximum heart rate.

Of the patients receiving chemotherapy, none were able to exercise during the last course of treatment, but seven of nine patients continued successfully thereafter (figure 1). One serious adverse event, a hip fracture during balance training, was recorded. Otherwise, the intense training was well tolerated. In the control group, five patients reported that they had performed supervised exercise training on a regular basis for 2 h a week.

Cardiorespiratory fitness

Intention-to-treat analyses for peak oxygen uptake are presented in table 2. Per-protocol analysis showed an increase of 4.5 ±3.4 mL/kg/min compared with –0.6±2.7 mL/kg/min, giving a between-group difference of 5.0 mL/kg/min (30.3%) (95% CI 3.3 to 6.7; p<0.001). Sixteen patients (53%) in the exercise group and four patients (13%) in the control group had the same or a higher peak oxygen uptake following the intervention compared with the peak oxygen uptake measured before surgery (p<0.001; figure 2). Of the patients receiving chemotherapy, the median increase in peak oxygen uptake was 2.6 mL/kg/min (range –0.9 to 3.9) in the exercise group (n=5) and –0.4 mL/kg/min (range –7.9 to 10.2) in the control group (n=8).

There were no differences between the groups in the typical end criteria for peak oxygen uptake such as respiratory exchange ratio, blood lactate concentration or Borg RPE before and after the intervention. For measures of pulmonary limitation after surgery, the breathing reserve was high in both groups but was significantly lower in the exercise group after the intervention (p=0.02; table 3).

Pulmonary function

In contrast to the spirometric variables, there was a significant increase in Tlco after the intervention, giving a between-group difference of 5.2% predicted (p=0.007).

Muscular strength, physical functioning and total muscle mass

The 1RM in the leg press increased by 27.4±26.2 kg in the exercise group but decreased by 2.1±25.0 kg in the control group (p<0.001; table 2). Of the patients receiving chemotherapy, the median increase in leg press was 20 kg (range 10–40 kg) in the exercise group (n=4) and a decrease of 15 kg (range –50 to 30 kg) in the control group (n=8). Total muscle mass increased by 1.35 kg more in the training group than in

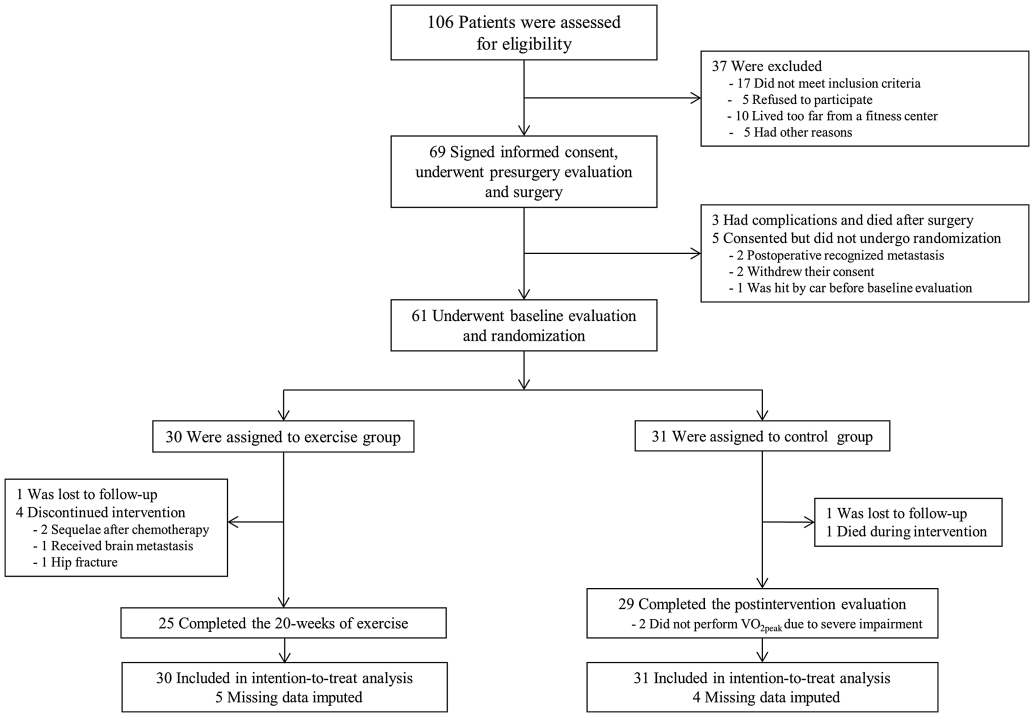

Figure 1 Eligibility, preoperative evaluation, randomisation and follow-up of the study population. VO_{2peak}, peak oxygen uptake.

Table 1 Characteristics of the study population before and after surgery

Variables	Training (N=30)	Control (N=31)
Age, years	64.4±9.3	65.9±8.5
Female sex, n (%)	17 (57)	16 (52)
Body mass index, kg/m^2	25.4±5.1	25.1±5.2
University degree or more, n	3	9
Smoking history (pack-years)	25.5 (0–87.5)	20.0 (0–50.0)
Presence of COPD, n (%)	10 (33)	8 (26)
Thoracoscore	1.64±1.26	2.19±1.83
Pneumonectomy, n (%)	4 (13)	6 (19)
Quality of life before surgery		
SF-36 score: Physical-component*	48.3±9.0	48.3±11.9
SF-36 score: Mental component*	46.4±11.1	45.4±12.1
EORTC QOL-C30: dyspnoea score†	33.3 (0–100)	33.3 (0–100)
Mean pulmonary function and cardiorespiratory fitness before surgery‡		
FEV_1, % of predicted value	88.6±20.7	91.7±23.5
FVC, % of predicted value	115.1±20.9	111.6±22.9
Tlco, % of predicted value	81.4±18.1	83.9±24.2
Peak oxygen uptake, mL/kg/min	24.1±6.5	23.6±5.6
Peak oxygen uptake, % of predicted value	80.6±17.2	79.2±16.8
Histological features at surgery		
Adenocarcinoma, n (%)	14 (47)	16 (52)
Squamous cell carcinoma, n (%)	11 (37)	10 (33)
Large cell carcinoma, n (%)	1 (3)	0 (0)
Other, n (%)	4 (13)	5 (15)
TNM stage[L2]		
Stage I, n (%)	18 (60)	15 (48)
Stage II, n (%)	7 (23)	12 (39)
Stage III, n (%)	5 (17)	5 (7)
Stage IV, n (%)	0	1 (3)
Additional treatment after surgery		
Chemotherapy, n (%)	9 (30)	9 (29)
Radiotherapy, n (%)	3 (10)	4 (13)

Data are presented as mean±SD, median (range) or n (%).
*Higher scores indicate better functioning (scaled from 0–100).
†Lower scores indicate less dyspnoea (scaled from 0–100).
‡Pulmonary function was calculated from equations from the European Community for Steel and Coal[23] and peak oxygen uptake from the equations of Edvardsen and coworkers.[24]
COPD, chronic obstructive pulmonary disease defined as FEV_1/FVC <70% and FEV_1 <80% of predicted; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; MVV, maximal voluntary ventilation; Thoracoscore, the Thoracic Surgery Scoring System, which is a risk model for in-hospital events; Tlco, carbon monoxide transfer factor.

Table 2 Between-group differences between baseline and after intervention for peak oxygen uptake, pulmonary function, muscular strength, body composition and functional capacity

Outcome variable	Baseline		After intervention		Between-group difference	
	Exercise group	Control	Exercise group	Control	Difference (95% CI)	p Value
Peak oxygen uptake (L/min)	1.38±0.37	1.28±0.46	1.76±0.49	1.39±0.51	0.26 (0.11 to 0.42)	0.005
Peak oxygen uptake (mL/kg/min)	19.2±5.1	18.1±5.5	23.3±5.5	19.0±6.0	3.4 (1.3 to 5.5)	0.002
FEV_1 (% of predicted value)	71.1±16.3	72.3±18.5	77.9±16.2	78.4±22.8	0.6 (−4.2 to 5.4)	0.738
MVV (% of predicted value)	78.6±22.0	78.9±22.1	83.2±22.4	79.8±21.8	3.7 (−2.6 to 10.1)	0.064
Tlco (% of predicted value)	67.8±19.2	63.4±16.8	73.7±16.5	64.9±18.2	5.2 (0.0 to 10.4)	0.007
Leg press, maximum (kg)*	131.9±45.7	131.6±48.5	159.3±48.4	129.5±39.5	29.5 (15.2 to 43.7)	<0.001
Hand grip, maximum (kg)*	34.2±11.5	32.9±8.4	36.6±11.4	33.3±8.6	2.1 (0.0 to 4.1)	0.056
BMI	24.9±4.9	24.4±5.3	25.6±4.8	24.9±4.7	0.2 (−0.6 to 1.1)	0.034
Total muscle mass (kg)	46.43±11.63	46.32±10.34	47.91±13.75	46.45±10.10	1.36 (0.32 to 2.40)	0.012
Chair stand (times)	11.4±2.1	11.4±3.5	14.3±2.8	12.2±3.0	2.1 (0.8 to 3.3)	<0.001
Stair run (number of steps)	30.5±8.3	28.3±9.9	37.0±9.5	30.8±9.3	4.3 (1.6 to 7.1)	0.002

Data are presented as mean±SD.
*To convert leg and hand press values to lb, divide by 0.45359.
1RM, one-repetition maximum; BMI, body mass index; FEV_1, forced expiratory volume in 1 s. FVC, forced vital capacity; MVV, maximal voluntary ventilation; Tlco, carbon monoxide transfer factor.

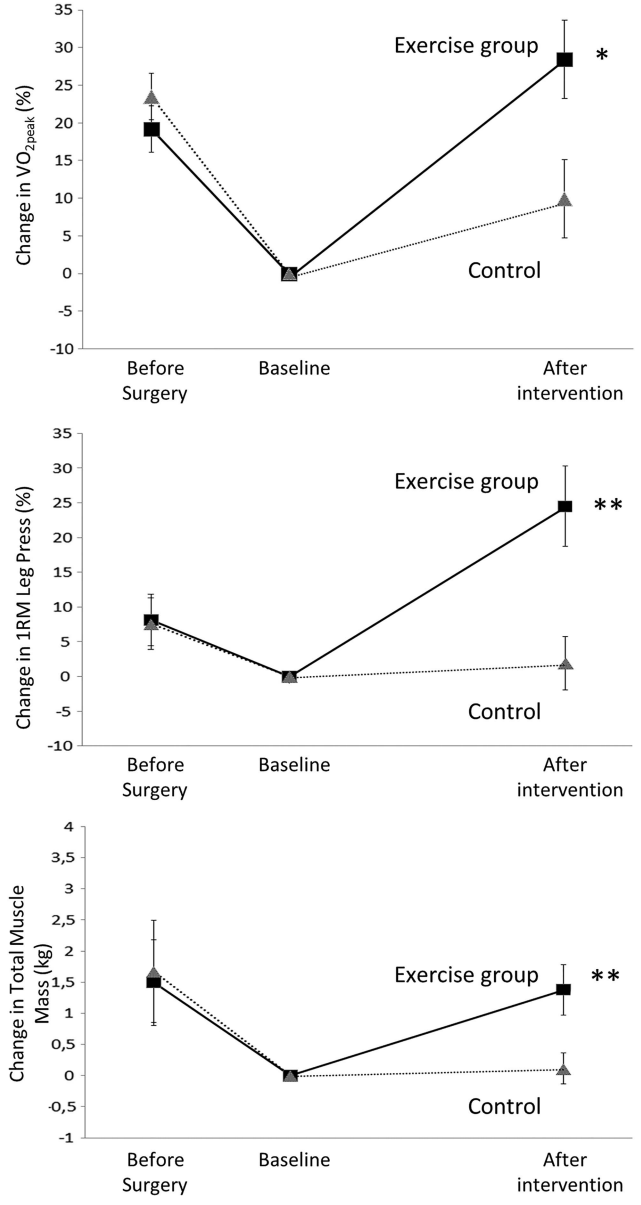

Figure 2 Changes in objective measures of (A) peak oxygen uptake, (B) leg press (1RM) and (C) total muscle mass from before surgery to after the intervention according to intervention group. Error bars indicate SDs of the mean. In (C), measurement of total muscle mass before surgery was missing in 48% of the patients because of the short time before surgery. Data were imputed only at baseline and after the intervention. Between-group level of significance after intervention: (A) p=0.002, (B) p<0.001, (C) p=0.012. Vo_{2peak}, peak oxygen uptake; 1RM, 1 repetition maximum.

the controls (p=0.012; figure 2). Balance testing of the patients did not reveal significant differences between the groups (p=0.33).

Quality of life

Before surgery, QoL did not differ significantly between the groups (table 1). After the intervention the physical component summary score of the SF-36 QoL scale was 51.8±5.5 in the exercise group and 43.3±11.3 in the control group (p=0.006). The mental component summary score was 55.5±5.3 and 46.6 ±14.0 in the exercise and control groups, respectively (p=0.02). The dyspnoea score in the EORTC QOL-C30 was 37.0±25.3 and 58.0±32.1 in the exercise and control groups, respectively (p=0.03).

Table 3 Ventilation, breathing reserve, typical end criteria for maximum effort and reason for termination during the cardiopulmonary exercise test at baseline and after intervention

Variables	Exercise	Control	p Value
Mean baseline, after surgery			
Peak ventilation, L/min	48.5±13.2	46.1±14.8	0.517
Breathing reserve*, %	39.2±13.6	44.4±12.3	0.122
Respiratory exchange ratio	1.05±0.08	1.08±0.09	0.132
Blood lactate concentration†, mmol/L	3.9±1.1	4.6±1.9	0.159
Maximum heart rate, beats/min	140±18.2	132±23.5	0.154
6–20 Borg scale, rating number	17.5±0.8	17.3±1.2	0.937
Reason for test termination			
Leg fatigue, n (%)	5 (17)	5 (16)	
Dyspnoea, n (%)	15 (50)	15 (48)	
General fatigue, n (%)	5 (17)	8 (26)	
After intervention			
Peak ventilation, L/min	60.3±16.9	49.8±15.8	0.025
Breathing reserve*, %	29.1±17.3	39.7±13.3	0.017
Respiratory exchange ratio	1.09±0.08	1.12±0.09	0.220
Blood lactate concentration†, mmol/L	4.9±1.7	5.1±2.2	0.730
Maximum heart rate, beats/min	148±19.9	136±21.8	0.045
6–20 Borg scale, rating number	17.7±1.4	17.6±0.9	0.652
Reason for test termination			
Leg fatigue, n (%)	4 (56)	7 (26)	
Dyspnoea, n (%)	14 (56)	11 (41)	
General fatigue, n (%)	5 (20)	7 (26)	

Data are presented as mean±SD or n (%).
*Breathing reserve (%) was calculated using the following equation: ([MVV–VE_{max}]/MVV)×100.
†Blood lactate concentration was taken 60 sec after termination as an indicator of high effort.[25]
MVV, maximum voluntary ventilation; VE_{max}, maximum minute ventilation

DISCUSSION

This randomised controlled trial showed that supervised endurance and strength training increased CRF, maximum strength and physical functioning following lung resection in patients with NSCLC. The observed effects exceeded the thresholds for clinically significant improvement in peak oxygen uptake for men[9] and women,[8] as did the measures of maximum leg press strength.[26] Total muscle mass increased significantly after the exercise intervention, and QoL was significantly higher in the exercise group compared with the controls. High-intensity endurance and strength training was well tolerated shortly after surgery in these patients. However, patients receiving the last courses of chemotherapy had to postpone their training sessions until they had completed the treatment.

We have demonstrated that patients with NSCLC were able to perform high-intensity training shortly after major lung cancer surgery. The net increase in peak oxygen uptake of 18.9% is higher than that reported previously in cancer patients in general,[11] in patients with COPD,[27] in patients with coronary heart disease[28] and in older healthy individuals.[29] The per-protocol analysis revealed a net increase in peak oxygen uptake of 30.3%. Even though peak oxygen uptake was reduced by nearly 20% from before to after surgery, in addition to a prolonged impairment in leg strength and muscle mass (figure 2), more than half of the patients in the exercise group increased their peak oxygen uptake above the preoperative level.

Surgically treated NSCLC patients are reported to suffer from persistent physical functional impairment lasting up to 24 months after surgery.[4] This study shows that high-intensity training seems to counteract this loss of physical capacity and even improves functional ability beyond the preoperative level. In addition, all patients in the exercise group surpassed the threshold for peak oxygen uptake of 12–15 mL/kg/min for daily independent living,[7] while five patients in the control group did not. An increase in peak oxygen uptake of 3.5 mL/kg/min (1 MET) corresponds to a 12–17% improvement in survival rate in general,[8 9] and peak oxygen uptake is a strong independent predictor of survival in patients with NSCLC.[10] In addition, studies in young and older populations have shown that the health benefits associated with improved fitness are in general likely to endure for some years.[30] Thus, high-intensity endurance and strength training may hold considerable promise for maintaining the ability of daily independent living after surgery and for improving prognosis in patients with NSCLC. Further studies are required to address these questions fully.

Comparison with other studies

To our knowledge, only one published exercise intervention study has measured peak oxygen uptake after lung resection in patients with NSCLC. In an uncontrolled study, Jones and coworkers assessed the effect of an individually tailored training programme on peak oxygen uptake.[31] Despite excellent adherence (85%), peak oxygen uptake increased non-significantly by 1.1 mL/kg/min. The authors stated that the lack of improvement in peak oxygen uptake was related mainly to chemotherapy.[31] We note, however, that the use of chemotherapy was the same in our study and the study by Jones and coworkers. The reason for the different findings may be explained by the longer intervention period and higher exercise intensity in the current study. In patients with COPD, short periods at a higher intensity have shown a reduction in the ventilatory response and dyspnoea,[32] which is an important factor for choosing high-intensity interval training in patients with lung cancer. In addition, it is less time consuming and the rating of perceived enjoyment has been reported to be higher that for moderate intensity continuous training.[33] In addition, we included PRT, which may also have contributed to a greater increase in peak oxygen uptake. It is known that resistance training can increase peak oxygen uptake, especially in severely deconditioned adults.[34] A recent meta-analysis by Strasser and coworkers showed that cancer patients regained muscle mass, improved their performance of daily life activities, reduced cancer-related fatigue and improved QoL after whole-body resistance training.[26] The net increases of 29.5 kg (23%) in the 1RM in leg press and the overall increase in total muscle mass of 1.36 kg in our study are high compared with the results from other resistance training studies in cancer survivors.[26] This is important because muscular strength is independently and inversely associated with death from all causes, even after adjusting for CRF.[35]

There were no associations between the improvement in peak oxygen uptake and pulmonary function, number of lung segments removed or cardiopulmonary comorbidities. In fact, those patients with the poorest peak oxygen uptake tended to improve the most ($r=-0.49$, $p=0.01$). We note that peak oxygen uptake increased by 6.7% in the control group during the intervention period. However, exclusion of the five controls who reported exercising regularly eliminated this increase.

After lung cancer surgery, QoL is related mainly to symptoms such as weakness, tiredness, dyspnoea and changes in post-operative physical functioning.[4] The present study demonstrates that exercise may positively influence QoL and components such as physical health, mental health and dyspnoea. These findings are particularly important as it is known that NSCLC survivors report inferior QoL compared with patients with other forms of cancer, and also that their cancer-related symptoms persist for a long time.[4]

Strengths and limitations of the study

The strength of this study was the use of high-intensity endurance and strength training that had been tailored individually to each patient's condition. In addition, we succeeded in achieving exhaustion in the vast majority of patients by choosing uphill treadmill walking during the cardiopulmonary exercise test; this was confirmed by the higher maximum heart rate compared with others.[31] This suggests strong validity of the primary outcome. Finally, our dropout rate was low compared with the expected rate in both groups, which emphasises the importance of follow-up after surgery.

A methodological limitation to the study was a low response rate to the QoL questionnaires. Furthermore, we cannot rule out the possibility that the technicians were not blinded during the last data collection. However, the end criteria for maximal effort confirmed no difference in effort between the groups (table 3).

CONCLUSION

This is the first randomised controlled trial to investigate the effects of high-intensity endurance and strength training in patients with lung cancer shortly after surgery. We have demonstrated clinically significant effects on peak oxygen uptake, Tlco, muscular strength, total muscle mass, daily physical functioning and QoL. The high-intensity training was well tolerated. Given the favourable prognostic effects of CRF and muscular strength in general,[8 9 35] our results should stimulate clinicians and healthcare workers to encourage physical training of patients with lung cancer following surgery. However, in view of the absence of training effects using short moderate-intensity training,[13 14 16] a more intensive and close follow-up training programme is needed in routine clinical practice.

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Contributors EE, OHS, FB and SAA were responsible for the design and conduct of the study. EE was responsible for data collection, laboratory instruments and training sessions, and LN was responsible for the DXA scan. IH and EE were responsible for the statistical analysis. All authors contributed to the interpretation of data. EE drafted the manuscript which was critically reviewed and approved by all authors.

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Competing interests None.

Patient consent Obtained.

Ethics approval Ethics approval was obtained from the Regional Committee for Medical Ethics (REK Sør-Øst B).

Provenance and peer review Not commissioned; externally peer reviewed.

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