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## SHORT COMMUNICATION

# Exercise capacity before and after an 8-week multidisciplinary inpatient rehabilitation program in lung cancer patients: A pilot study

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### KEYWORDS

Lung cancer;  
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distance;  
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**Summary** Although lung cancer is a highly prevalent type of cancer, the effects of an inpatient multidisciplinary rehabilitation program on pulmonary function and exercise capacity have never been studied in these patients.

Pulmonary function, 6-min walking distance and peak exercise capacity of 10 patients with a severely impaired pulmonary function following treatment of lung cancer were assessed in this pilot study before and after an 8-week inpatient multidisciplinary rehabilitation program. At baseline, patients had a restrictive pulmonary function and an apparent exercise intolerance (median 6-min walking distance: 63.6% predicted; median peak cycling load: 58.5% predicted). Despite the lack of change in median pulmonary function [FEV1:  $-0.01$  L,  $p=0.5469$ ], functional exercise capacity [145 m; 43.2% of the initial values,  $p=0.0020$ ] and peak exercise capacity [26 W; 34.4% of the initial values,  $p=0.0078$ ] improved significantly compared to baseline.

Future trials have to corroborate the present findings. Nevertheless, patients with lung cancer have a clear indication to start a comprehensive rehabilitation program following intensive treatment of their disease. In fact, based on the results of the present pilot study it appears that these patients are good candidates for pulmonary rehabilitation programs.

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## 1. Introduction

Improved physical fitness and psychological well-being have been reported following an exercise training program in survivors of mostly breast cancer [1–3]. The effects of a multidisciplinary inpatient rehabilitation program on func-

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tional and peak exercise intolerance has never been studied in a group of consecutive lung cancer patients who have had a severely impaired pulmonary function following active treatment of their disease (i.e. lobectomy, pneumonectomy, chemotherapy and/or radiotherapy). Nevertheless, lung cancer is one of the most prevalent types of cancer in the western population [4] and its treatment has been shown to affect patients' exercise tolerance [5]. Moreover, 4–12-week exercise training programs have shown to improve exercise tolerance in patients with moderate to severe chronic obstructive [6,7] or restrictive pulmonary disease [8,9] without changes in pulmonary function. The present authors therefore hypothesized a priori that an 8-week inpatient exercise training program as part of multidisciplinary rehabilitation program would result in significant improvements in functional and peak exercise capacity without changes in the impaired pulmonary function in patients who had recently undergone lung cancer treatment.

## 2. Methods

A non-randomised, clinical pilot trial was designed to study the effects of a multidisciplinary inpatient rehabilitation program on pulmonary function, 6-min walking distance and peak cycling load. Patients were recruited by their chest

physician at the outpatient clinic a median of 3.0 months (IQR: 2.5–9.3) after completing intensive lung cancer treatment. Volunteering patients [median age: 65.5 years (IQR: 59.5–70.0)] were diagnosed with and treated for different types of epithelial tumours (Table 1). A majority of the patients had one additional earlier diagnosed comorbidity (chronic obstructive pulmonary disease ( $n=5$ ), arterial hypertension ( $n=1$ ), transient ischemic attack ( $n=1$ )) or had undergone previously an invasive medical treatment (percutaneous transluminal coronary angioplasty ( $n=1$ ), hysterectomy ( $n=1$ )). None of the patients were experienced with any form of exercise training in the 6-month period before initiating the rehabilitation program.

Methodology concerning assessment of pulmonary function, 6-min walking distance and symptom-limited incremental peak cycling test has been described in detail elsewhere [6,10]. Exercise training, consisting of daily ergometry cycling, treadmill walking, weight training and gymnastics, was the cornerstone of the multidisciplinary rehabilitation program. Initially, cycle ergometry was performed for 20 min non-stop at 60% of baseline peak cycling load and treadmill walking was performed for 20 min non-stop at 80% of baseline mean walking speed (expressed in kilometres per hour; calculated by dividing the amount of metres walked in 6 min by 100). Weight training for muscle groups of the upper (chest press, lat pulley and ver-

**Table 1** Diagnosis, status, treatment and current treatment

No.	Sex	Age	Diagnosis	Treatment LC	Status	Pharmacological treatment during rehabilitation
1	F	69	Squamous CC	Bilobectomy	T2N0M0	Combination of ipratropiumbromide monohydrate and salbutamol sulphate, combination of budesonide and formoterolfumaratedihydrate, pantoprazol-sodium-sesquihydrate, lactulose, metoclopramide, tramadolhydrochloride, sodiualendronate, rofibanhydrochloridemonohydrate
2	M	60	Squamous CC	Pneumon + RT	T2N2M0	Paracetamol, rofibanhydrochloridemonohydrate, salbutamolhemisulfate, <i>N</i> -acetylcystein, salbutamol sulfate, metoprololtartrate
3	M	59	Squamous CC	Lobectomy	T2N0M0	Insulin, hydrochlorothiazide, combination of budesonide and formoterolfumaratedihydrate, tiotropium, theophylline, <i>N</i> -acetylcystein, esomeprazol
4	M	69	Squamous CC	Lobectomy	T1N0M0	Ipratropium, <i>N</i> -acetylcystein, fenprocoumon, bisoprolol, enalaprilatdihydrate, tamsulosine hydrochloride, eprosartanmesylate, paracetamol
5	M	60	Adenocarcinoma	RT + CT <sup>1</sup>	T4N0M0	Pantoprazol-sodium-sesquihydrate, citalopramhydrobromide
6	M	66	Squamous CC	Pneumon	T2N0M0	Fluticasonpropionate, salbutamol sulfate, flecainid-acetate, verapamilhydrochloride, paracetamol
7	M	71	Adenocarcinoma	Lobectomy	T2N0M0	Prednisolon, ipratropium, <i>N</i> -acetylcystein, tamsulosine hydrochloride.
8	M	78	Squamous CC	Lobectomy	T2N0M0	Combination of salmeterol and fluticason-propionate, tiotropium, paroxetinehydrochloride, alfuzosinehydrochloride
9	M	57	Squamous CC	Pneumon + CT <sup>2</sup>	T1N1M0	Pravastatinesodium, bisoprololfumarate
10	F	65	Small CC	Pneumon + RT + CT <sup>3</sup>	N.A.	Metoclopramide, Ferrosi gluconas, tamsulosine hydrochloride, tramadolhydrochloride, paracetamol

Female (F); male (M); cell carcinoma (CC); primary tumour (T); regional lymph nodes (N); distant metastasis (M); lung cancer (LC); pneumonectomy (pneumon); radiotherapy (RT); chemotherapy (CT); gemcytabin and cisplatinum (<sup>1</sup>); vinorelbine and cisplatinum (<sup>2</sup>); carboplatin and etoposide (<sup>3</sup>); not applicable (N.A.).

tical traction) and lower extremities (leg press, leg curl, hip adductors, hip abductors and leg extension) was performed  $3 \times 15$  repetitions at 60% of the one-repetition maximum. Moreover, all patients participated in 30 min of gymnastics which focused on general mobilization and flexibility [11]. Intensity of ergometry cycling, treadmill walking and weight training was adapted over time based on Borg symptom scores for dyspnoea and/or fatigue (target scores: 4–6 on a 10-point scale) to maintain the same relative training load during the intervention period of 8 weeks [12,13]. Exercise training was executed under close supervision of a physiotherapist in a rehabilitation group of inpatients with severe chronic obstructive pulmonary disease.

An occupational therapist, dietician, behavioral scientist and a respiratory nurse specialist could be consulted if necessary. Tests and treatment were performed in the clinical routine and were in accordance with World Medical Association declaration of Helsinki [14].

Median and interquartile range (IQR) were calculated for baseline values. In addition, Wilcoxon matched pairs test was used to compare baseline pulmonary function and exercise capacity with those obtained 8 weeks after baseline. A priori, the level of significance was set at 0.05. All statistics were done using GraphPad Prism 4.03.

### 3. Results

At baseline, patients generally had a normal median body mass index [ $23.9 \text{ kg/m}^2$  (21.3–28.3)], a restrictive pulmonary function [median forced expiratory volume in the first second (FEV1): 55.0% predicted (IQR: 49.5–68.5); median FEV1/forced vital capacity: 70.0% (IQR: 52.1–75.9); total lung capacity: 74.5% predicted (IQR: 59.5–91.5)] and an impaired diffusion capacity [lung transfer factor for carbon monoxide: 45.0% predicted (IQR: 31.5–48.4); carbon monoxide transfer coefficient: 57.4% predicted (IQR: 54.0–87.0)].

Patients had an apparent exercise intolerance [median 6-min walking distance: 351 m (IQR: 240–436); 63.6% predicted (IQR: 44.3–75.6); median peak cycling load: 82.0 W (IQR: 54.5–91.0); 58.5% predicted (IQR: 31.0–78.0)] accompanied with moderate to severe median Borg symptom scores for dyspnoea [6-min walking distance: 3.0 points (IQR: 1.5–7.4); peak cycling load: 6.0 points (IQR: 3.5–7.0)] and fatigue [6-min walking distance: 2.0 points (IQR: 0.3–8.3); peak cycling load: 6.0 points (IQR: 3.5–7.0)] at the end of both exercise tests.

Eight weeks after baseline, pulmonary function did not change [median change in FEV1 [–0.01 L (IQR: –0.19 to 0.08),  $p=0.5469$ ]. In contrast, significant improvements were found in 6-min walking distance [median change: 145 m (IQR: 65–245); 43.2% of the baseline values (IQR: 17.3–73.8),  $p=0.0020$ ] (Fig. 1), without significant changes in Borg symptom scores for dyspnoea [median change: –0.3 points (IQR: –2.4 to 0.5),  $p=0.2969$ ] and fatigue [median change: –0.3 points (IQR: –3.4 to 1.5),  $p=0.4922$ ]. In addition, peak cycling load increased with a median of 26 W [IQR: 16–39] or 34.4% of the baseline values [IQR: 24.6–36.5,  $p=0.0078$ ]. Also after this test, Borg symptom scores for dyspnoea [median change: 0.0 points (IQR:

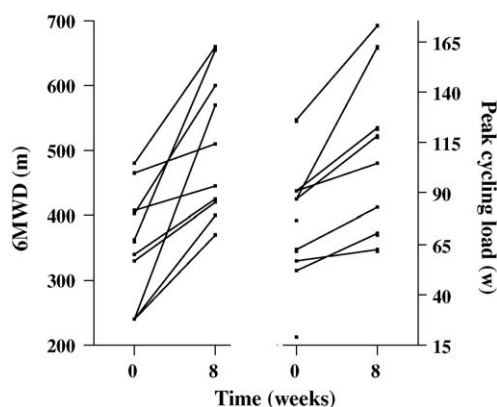


Fig. 1 Walking distance in 6 min (6MWD, expressed in meters) and peak cycling load (expressed in watts) at baseline and following an 8-week inpatient multidisciplinary rehabilitation program in lung cancer patients.

0.0–2.0),  $p=0.2500$ ] and fatigue [median change: 0.0 points (IQR: –3.0 to 3.0),  $p=0.9999$ ] did not change significantly.

### 4. Discussion

The present study has two important clinical findings: (1) lung cancer patients have a clear functional and peak exercise intolerance following intensive treatment of their disease, accompanied by a severely impaired pulmonary function and; (2) 6-min walking distance and peak cycling load increased significantly in lung cancer patients following an intensive 8-week multidisciplinary inpatient rehabilitation program without changes in pulmonary function.

Significant improvements in functional and peak exercise capacity in lung cancer patients together with no change in pulmonary function may be surprising at first sight, but are in line with previous findings in patients with chronic obstructive [6,7] or restrictive pulmonary disorders [8,9]. Indeed, Bobbio and colleagues reported a worsening of the peak exercise capacity in patients with chronic obstructive pulmonary disease following a (bi)lobectomy, which could not entirely be explained by changes in pulmonary function [5]. Improved skeletal muscle function may, at least in part, explain the improvements in 6-min walking distance and peak cycling load in the present patients. Indeed, skeletal muscle dysfunction has shown to be related to exercise intolerance in patients chronic obstructive pulmonary disease or chronic heart failure, irrespective the impaired pulmonary or cardiac function, respectively [15–17]. Moreover, skeletal muscle function improves significantly following a rehabilitation program in patients with moderate to severe chronic obstructive pulmonary disease without changes in pulmonary function [18].

Although muscle function has not been studied in the present study, the present exercise training program was in accordance with the recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility [11].

A potential learning effect cannot be ruled out as a possible explanation of the changes observed in exercise capacity. Nevertheless, both exercise tests were highly standardized (for example time of the day, patient instructions,

patient inducement, testing procedures, testing equipment and equipment calibration were identical before and after the rehabilitation program). Moreover, the probability that the observed change in 6-min walking distance and peak cycle load occurred by chance was 0.20 and 0.78%, respectively.

Although a control group was lacking in the present design, the improved exercise capacity may be of clinical relevance. In fact, present patients had a substantially greater improvement in 6-min walking distance (median change: 145 m; 43.2% of the baseline values) and peak cycling load (median change: 26 W; 34.4% of the baseline values) than values obtained previously in patients with chronic obstructive pulmonary disease (mean change in 6-min walking distance: 49 m [19]; mean change in peak cycling load: 8 W [20]) or various restrictive pulmonary disease (mean change in 6-min walking distance: ~50 m; ~15% of the baseline values) [8,9]. In fact, the change in 6-min walking distance clearly exceeded the upper limit of the 95% confidence interval of the minimal clinically important difference in 6-min walking distance: 72 m [19].

Future well-designed randomised controlled clinical trials have to corroborate the present findings in a larger sample size. At least 28 patients have to be included in each group (control or rehabilitation) to detect a significant difference in change of 100 m in functional exercise capacity with a power of 0.90 and a level of significance of 0.05.

Future trials may consider additional primary or secondary outcomes. For example, disease-specific quality of life questionnaires [21], body composition [22], fatigue and skeletal muscle function [23]. But perhaps also less obvious outcomes such as behavioral performance [24].

In conclusion, patients with lung cancer have a clear indication to start a comprehensive rehabilitation program following intensive treatment of their disease. In fact, based on the present result it appears that these patients are good candidates for pulmonary rehabilitation programs.

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