Preoperative pulmonary rehabilitation in patients undergoing lung resection for non-small cell lung cancer

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Received 21 June 2007; received in revised form 28 September 2007; accepted 3 October 2007; Available online 19 November 2007

Abstract

Background: The impact of short-term preoperative pulmonary rehabilitation on exercise capacity of patients with chronic obstructive pulmonary disease undergoing lobectomy for non-small cell lung cancer is evaluated. Methods: A prospective observational study was designed. Inclusion criteria consisted of an indication to lung resection because of a clinical stage I or II non-small cell lung cancer and a chronic obstructive disease on preoperative pulmonary function test. In such conditions, maximal oxygen consumption by a cardio-pulmonary exercise test was evaluated; when this resulted as being <15 ml/kg/min a pulmonary rehabilitation programme lasting 4 weeks was considered. Twelve patients fulfilled inclusion criteria, completed the preoperative rehabilitation programme and underwent a new functional evaluation prior to surgery. The postoperative record of these patients was collected. Results: On completion of pulmonary rehabilitation, the resting pulmonary function test and diffuse lung capacity of patients was unchanged, whereas the exercise performance was found to have significantly improved; the mean increase in maximal oxygen consumption proved to be at 2.8 ml/kg/min (p < 0.01). Eleven patients underwent lobectomy; no postoperative mortality was noted and mean hospital stay was 17 days. Postoperative pulmonary complication was recorded in 8 patients. Conclusions: Short-term preoperative pulmonary rehabilitation could improve the exercise capacity of patients with chronic obstructive pulmonary disease who are candidates for lung resection for non-small cell lung cancer.

Keywords: Lung cancer surgery; Preoperative care; Surgery; Complications

1. Introduction

A comprehensive pulmonary rehabilitation (PR) programme is always considered for patients presenting with chronic pulmonary disease. Chronic obstructive pulmonary disease (COPD) patients are those most often referred to PR and, regardless of the severity of the disease, PR has been shown to be effective in reducing symptoms, increasing daily activity and minimizing exacerbation of the disease [1–3].

The role of PR in a preoperative setting has been largely explored in patients with pulmonary emphysema enlisted for lung volume resection surgery. In the NETT trial, PR was considered an inclusion criterion before randomization to undergo surgery [4]; its value in patient screening, exercise testing and individualized exercise prescription has been stated, and preoperative PR has been shown to lead to a significant improvement in exercise capacity, dyspnoea and health-related quality of life [5–7]. In the case of lung volume resection surgery, however, PR plays an essential part in the treatment of the disease and is always delivered in long-term courses. Interestingly, its impact on postoperative morbidity and mortality is yet to be established [8,9].

On the other hand, a preoperative PR in COPD patients who are candidates for lung resection for NSCLC with the aim of optimizing preoperative lung function and global conditioning, although frequently advocated, has seldom been explored and its value is still to be assessed [9–15].

In view of the lack of data on the value of preoperative PR in COPD patients who are candidates for lung resection for NSCLC, we have designed a pilot observational study to investigate the effect on pulmonary function and exercise performance of a 4-week PR programme; PR was scheduled for those patients in whom an impairment of exercise capacity was found during a preoperative maximal incremental cycle ergometer cardio-pulmonary exercise test (C-PET), and the effects of PR were evaluated by means of a new resting and dynamic functional evaluation programmed at the end of PR.

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2. Patients and methods

2.1. Study design and population

Between April 2004 and March 2006 a prospective observational study was conducted on patients who had preoperative functional evaluation in the Respiratory Disease Division of the Department of Clinical Science of the University of Parma and on whom surgery was performed at the Unit of Thoracic Surgery of the University of Parma. Informed consent was obtained from all patients. The research was conducted according to recommendations outlined in the Helsinki Declaration.

During the study period, in all patients with a diagnosis of NSCLC, clinical staging protocol consisted of chest radiography, fiberoptic bronchoscopy, and thoracic, upper-abdominal, and cerebral CT scan. In the presence of enlarged (>1.5 cm) mediastinal nodes a biopsy was always obtained before considering lung resection. Preoperative functional evaluation consisted of spirometric and plethysmographic tests, diffuse lung capacity (DLCO) and arterial blood gas measurement. In the case of a diagnosis of COPD defined by the presence of a FEV1/FVC ratio lower than 0.7 and a FEV1 lower than 70%, a C-PET was undertaken. In the face of a maximal peak of oxygen consumption (VO2max) ≤ 15 ml/kg/min, such patients were enlisted to undergo a preoperative PR programme. Only patients with clinical Stage I or II NSCLC were considered and no facilities for transport or accommodation were granted to the participants. Patients who could not completely adhere to the PR programme were excluded.

A new functional evaluation by resting pulmonary function test (PFT), DLCO and C-PET measurement was obtained during the last daily session of the PR programme. Surgery was scheduled within the two weeks after completion of PR. Of the patients examined during the study period, 12 fulfilled the inclusion criteria and all completed the PR programme. Eleven patients underwent surgery; 1 refused surgical intervention. Lung resection was performed in accordance with standard techniques, and hilar and mediastinal lymph node dissection was always performed.

2.2. PR programme

Preparation for intervention for all patients included the cessation of smoking and optimization of pharmacological treatment. Bronchodilators were prescribed whereas steroids were not introduced. The PR programme consisted of a daily one and a half hour hospital appointment, 5 days a week for 4 weeks. During the first session physical modality therapy, including controlled breathing and cough techniques, was taught; the patients were instructed in incentive spirometry exercises by a coaching device (Coach II; Kendall, Tyco Healthcare) and they were asked to repeat the exercises twice daily at home. The peripheral muscle exercise training programme consisted of aerobic work on a leg cycle ergometer; each training session consisted of a 5-min warm-up at 30% of maximal work rate, followed by 30 min at 50% of maximal work rate, ending with a 5-min cool-down. Workloads were calculated from the work rate obtained during the C-PET examination and were then progressively increased weekly up to 80% of maximal work rate. At the end of cycling, patients underwent muscle stretching for 10 min and the session was then completed with upper extremity and trunk muscle conditioning free weight exercises. Trained medical and physical therapist staff supervised patients during the whole session.

2.3. Statistical analysis

Computation were performed using the SPSS for Windows statistical software package (SPSS Inc., version 12.0, Chicago, IL). Data are expressed as mean ± standard deviation (SD). In all continuous variables, the distribution was assessed by means of the Kolmogorov–Smirnov test. Normally distributed variables were compared by paired t-test and non-normally distributed variables by Wilcoxon’s signed rank test. A p value of less than 0.05 was considered significant.

3. Results

During the study period, 12 patients fulfilled the inclusion criteria and all completed the four-week preoperative PR programme. There were 10 men and 2 women, with a mean age of 71 ± 4 years and with a mean body mass Index (BMI) of 27 ± 5. The PFT and C-PET records of these patients prior to and after PR are shown in Table 1. A statistically significant mean improvement of 2.8 ml/kg/min of VO2max was found (13.5 ± 1.3 vs 16.3 ± 1.9 ml/kg/min; p < 0.001), and the individuals gaining in VO2x/max are shown in Fig. 1. VO2max at anaerobic threshold (p < 0.016 vs baseline) workload capacity (p < 0.001 vs baseline) and oxygen pulse (p < 0.007 vs baseline) also resulted as having significantly improved at the end of PR.

Table 1

<table>
<thead>
<tr>
<th>Pre PR data</th>
<th>Post PR data</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1 (l)</td>
<td>1.23 (±0.4)</td>
<td>1.29 (±0.4)</td>
</tr>
<tr>
<td>FEV1 (% pred)</td>
<td>47 (±10)</td>
<td>49 (±12)</td>
</tr>
<tr>
<td>VO2max/FVC</td>
<td>53 (±9)</td>
<td>52 (±12)</td>
</tr>
<tr>
<td>TLC (% pred)</td>
<td>114 (±28)</td>
<td>113 (±28)</td>
</tr>
<tr>
<td>DLCO (% pred)</td>
<td>68 (±19)</td>
<td>65 (±21)</td>
</tr>
<tr>
<td>C-PET</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO2max (ml/kg/min)</td>
<td>13.5 (±1.3)</td>
<td>16.3 (±1.9)</td>
</tr>
<tr>
<td>VO2max (l)</td>
<td>1.05 (±0.21)</td>
<td>1.26 (±0.26)</td>
</tr>
<tr>
<td>VO2AT (l)</td>
<td>0.85 (±0.13)</td>
<td>1.05 (±0.27)</td>
</tr>
<tr>
<td>VO2AT (ml/kg/min)</td>
<td>10.1 (±1.9)</td>
<td>13.4 (±3.3)</td>
</tr>
<tr>
<td>Workload (W)</td>
<td>65 (±14)</td>
<td>79 (±19)</td>
</tr>
<tr>
<td>Oxygen pulse (ml/bpm)</td>
<td>9.3 (±2.9)</td>
<td>11.2 (±4.1)</td>
</tr>
<tr>
<td>VE/max (l)</td>
<td>39 (±8)</td>
<td>44 (±9)</td>
</tr>
<tr>
<td>BR (%)</td>
<td>19 (±19)</td>
<td>13 (±12)</td>
</tr>
<tr>
<td>VE/VCO2</td>
<td>38 (±7)</td>
<td>35 (±6)</td>
</tr>
</tbody>
</table>

Data are expressed as mean values with standard deviation. FEV1: forced inspiratory volume at 1st second; FVC: forced vital capacity; TLC: total lung capacity; DLCO: diffusion lung capacity of CO; VO2: oxygen uptake; VO2AT: oxygen uptake at anaerobic threshold; VE: minute ventilation; Oxygen pulse: oxygen uptake/heart rate; BR: breathing reserve; VE/VCO2: ventilatory equivalent for CO2.
In those 11 patients who underwent surgery, there were 4 upper right, 3 upper left, 2 lower left and 2 lower right lobectomies. Final pathological examination showed a diagnosis of squamous cell carcinoma in 6 patients, adenocarcinoma in 4 and large-cell carcinoma in 1, respectively; definitive pathological staging yielded two la cases, five Ib cases, three IIb cases and one IIIa case.

No mortality was recorded; median hospital stay resulted as being 17.5 ± 14.8 days. Eight patients (73%) underwent a complicated postoperative course. In all of these cases, a pulmonary complication was recorded: 2 patients had atelectasis that regressed after chest physiotherapy, whereas the other 6 patients underwent a fiberoptic bronchoscopy for aspiration and bacteriological sampling. In 4 of these patients, a cricothyroid minitracheostomy was positioned 24 h after bronchoscopy; among these latter patients 1 had acute respiratory insufficiency and, after being admitted to the ICU for oro-tracheal intubation, was subsequently referred to the Respiratory Disease Unit (with an overall hospital stay of 56 days). A final diagnosis of pneumonia was made in 5 of these 8 patients. Concomitant atrial fibrillation occurred in 3 out of the 8 patients who had a pulmonary complication. Prolonged air leaks were observed in 3 cases.

4. Discussion

The indications for enrolling patients in PR are increasing; its use in a preoperative setting has recently been focused on by various reports. In 1998, Chumillas showed that preoperative breathing exercise could reduce postoperative pulmonary complications in patients undergoing upper abdominal surgery [13] and, in the setting of thoracic surgery, Weiner in 1997 showed that preoperative incentive spirometry and inspiratory muscle training could improve preoperative lung function [14]; Sekine has recently explored the efficacy of aggressive pulmonary exercise for 2 weeks preoperatively in the outcome of patients undergoing lung resection [15]. In these studies, however, preoperative PR did not include peripheral muscle training, which is known to play an essential role in reconditioning COPD patients. In this light, Cesario has very recently reported the results of inpatient preoperative PR including symptom-limited exercise and muscle electric stimulation in patients with NSCLC and with a very limited lung function; interestingly, PR led to improvement in the resting pulmonary function test and 6-min walking exercise, and some of these patients were able to undergo surgery with excellent results in terms of postoperative outcome [16].

The most frequently advocated limitation to the scheduling of a preoperative PR when there is a diagnosis of NSCLC is the necessity to carry out prompt surgical therapy of the malignancy; however, in a non-operative setting an intensive short-term PR programme of one month has demonstrated to be effective in ameliorating the conditioning of COPD patients and as such, the delay in the surgical treatment of NSCLC has not been found to affect its long-term prognosis [16,17].

Based on the stated point that the optimization of the respiratory function, lifestyle behaviour and global conditioning is the crucial goal during the preoperative evaluation of patients who are candidates for lung resection, and on the evidence that maximum oxygen capacity uptake is a strong predictor of postoperative outcome, we referred for preoperative PR those COPD patients who presented with a preoperative degree of exercise capacity impairment carrying a high risk of surgical morbidity and mortality according to Smith. The latter, by correcting the oxygen uptake for body weight, found 100% of patients with preoperative VO2max values lower than 15 ml/kg/min to have a postoperative cardio-pulmonary complication; further studies have indicated a threshold of VO2max greater than 15 ml/kg/min as a safe cut-off point for performing pulmonary resection [18–20].

Thanks to our comprehensive PR intervention in these high-risk surgical patients, we were able to obtain an improvement in the integrative response to exercise despite the absence of changes in resting PFT; doubtless because of the very small number of patients enrolled in the study and because of the absence of a control group, no conclusion could be drawn as to the clinical impact that the improvement in the conditioning status might have on postoperative outcome. Nonetheless, the demonstration of the possibility to obtain an amelioration in exercise capacity would seem to be an important starting point for the extensive exploration of the role played by preoperative maximization of conditioning status in the postoperative course of lung resection and in the time taken to return to full exercise performance after surgical trauma and loss of lung volume [21]. Finally, as exercise intolerance still remains a main factor limiting surgical therapy in COPD patients with NSCLC [22], preoperative PR could be employed in order to select possible surgical candidates.

References
