Exercise capacity assessment in patients undergoing lung resection

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Abstract

Background: The value is examined of preoperative functional assessment, including exercise capacity measurement by a cycloergometric maximal exercise test, in the prediction of postoperative cardio-pulmonary complication after lobar resection. Methods: In a prospective study over a 3-year period, all patients who were candidates for lung resection underwent preoperative functional evaluation by means of resting pulmonary function tests, measurement of the lung diffusing capacity for carbon monoxide and cardio-pulmonary exercise test. Patients who had had pneumonectomy or less than anatomical segmentectomy were excluded. The study population consisted of 73 patients. The postoperative morbidity and mortality record was collected. Results: Sixty-four patients underwent lobectomy, five bilobectomy and four segmentectomy. Indication for surgery was NSCLC in 71 cases. Two postoperative deaths were recorded (2.7%). A pulmonary (n = 19) and/or cardiac (n = 17) complication was scored in 30 patients (41%). Mean preoperative FEV1 and VO2max of patients who developed pulmonary complications were significantly lower (p = 0.013 and p = 0.043 respectively) than those of patients without pulmonary complications. Logistic regression analysis found FEV1 to be an independent factor in pulmonary complication (p = 0.002). With regard to pulmonary complication occurrence, the receiver operating characteristic curve showed an area of 0.69 with VO2max expressed in ml/kg min and of 0.62 when VO2max was expressed as a percentage of the predicted value. The widest point of the curve was found at a VO2max value of 18.7 ml/kg min. Six out of the 14 patients (43%) with a preoperative VO2max equal to or lower than 15 ml/kg min had a pulmonary complication. No functional preoperative identifiers were found for the 16 patients who presented with postoperative new onset atrial fibrillation. The mean preoperative value of carbon monoxide lung diffusing capacity was significantly lower (p = 0.037) in the 30 patients who had postoperative cardio-pulmonary complications than in the complication-free population. Conclusions: Preoperative exercise capacity assessment helps in stratifying patients at risk for postoperative pulmonary complication. However, it does not appear to be an independent prognostic factor for postoperative outcome.

1. Introduction

Since the historical study of Gaensler et al. in 1955 [1], on the value of spirometric preoperative functional assessment of patients undergoing surgery for pulmonary tuberculosis, various methods have been devised for the preoperative identification of the subset of patients with an increased risk of postoperative complications after lung resection [2]. Reichel is held to be the first author to have examined, in 1972, the value of exercise test before lung surgery [3], although it was only about 10 years later that the value of preoperative exercise capacity in predicting the postoperative outcome of lung resection was extensively investigated [4,5]. In 2007, a meta-analysis concluded that a lower exercise capacity is found in patients with complicated postoperative outcome [6]. However, the interpretation of the data of these previous studies is difficult because of the different protocols employed, the heterogeneity of the populations enrolled and the type of postoperative outcome indicators examined [7–9]. Moreover, a relatively limited experience is available from large clinical series on the subject [10,11].

The aim of this study is to report our experience with a cohort of consecutive patients undergoing lung resection who were prospectively included in a preoperative functional evaluation protocol including an exercise capacity assessment by cycloergometric exercise test. Because the extension of the resection is known to represent an independent risk factor of postoperative complicated outcome, we
excluded from the analysis patients who had had a pneumonectomy, a lung wedge excision or an explorative thoracotomy, and thus the study population consists of 73 patients operated on for a lobar, bilobar or anatomical segmental resection [12].

Demographic and preoperative functional exploration data, as well as surgical records, were collected and matched to postoperative outcome, and in particular to the onset of postoperative cardiac and/or pulmonary complications.

2. Methods

2.1. Study design and population

This prospective study took place from January 2004 to December 2006 at the Unit of Pulmonary Diseases and at the Unit of Thoracic Surgery of the University of Parma. During this period all patients who were candidates for lung resection underwent a thorough preoperative functional evaluation including spirometry, plethysmography, lung diffusing capacity for carbon monoxide (DLCO) measurement and cycloergometer maximal incremental cardio-pulmonary exercise test. The study received local committee approval and a signed informed consent was obtained from all participants.

During the study period the functional limit to undergo a lobar resection was established as being a predicted postoperative FEV\textsubscript{1} greater than 35%; patients under this threshold were excluded from surgery if preoperative VO\textsubscript{2}\text{max} was lower than 10 ml/min kg, whereas surgery was undertaken in the case of a VO\textsubscript{2}\text{max} greater than 15 ml/min kg. In those patients with a VO\textsubscript{2}\text{max} ranging between 10 and 15 ml/min kg, surgery was performed after the completion of a 4-week program of pulmonary rehabilitation, as previously reported [13].

Those patients who had undergone a pneumonectomy or less than an anatomical segmental lung resection were excluded and 73 patients were ultimately included in the study analysis. Recorded data included: demographic information, medical comorbidities, results of preoperative functional evaluation, type of operation, pathological diagnosis and staging in the case of NSCLC. All patients had surgery through a posterolateral muscle-sparing thoracotomy and, in the case of NSCLC, pulmonary resection was associated with a mediastinal lymph node dissection. During the first three postoperative days, postoperative analgesia was assured with a continuous infusion of bupivicaine through a peridural indwelling catheter.

Operative mortality and morbidity were considered for all events occurring within 30 days of surgery. Cardiac and pulmonary complications were defined in line with previous publications [14,15]; a pulmonary complication was recorded in the presence of pulmonary atelectasis requiring bronchoscopy, in the case of pneumonia (defined as a progressive radiological infiltrate with fever and/or leukocytosis) and in the case of respiratory failure. A cardiac complication was scored in the case of myocardial infarction or in the case of a new onset of arrhythmia.

Results are expressed as mean ± standard deviations. Continuous variables were compared by nonparametric test (Mann–Whitney) and categorical variables by chi-square test or Fisher’s exact test as appropriate. A value of p lower than 0.05 was assumed as significant. The parameters of preoperative functional evaluation were analyzed for correlation by Spearman’s test and those significantly associated with morbidity were analyzed by receiver operating characteristic (ROC) curves. Data processing and analysis were performed with the statistical software system SEM (Silex Development, Mirefleurs, France).

3. Results

3.1. Preoperative data

The study population included 61 men and 12 women, with a mean age of 66.7 ± 8.7 years. The mean preoperative body mass index was 25.8 ± 5.2. The mean preoperative FEV\textsubscript{1} was 1.85 ± 0.7 l and 66.7 ± 22.8% of the predicted value. Mean DLCO expressed as a percentage of the predicted value resulted as being 71 ± 24.9%. The mean preoperative VO\textsubscript{2}\text{max} was 1.38 ± 0.37 l, 18.7 ± 5.4 ml/kg/min when corrected for body weight, and 69 ± 17.8% when the value corrected for body weight was expressed as a percentage of the predicted value. Mean workload resulted as being 90.4 ± 30.6 W.

On preoperative functional evaluation 14 patients had a postoperative predicted value of FEV\textsubscript{1} lower than 35%; of these patients, 9 had a preoperative VO\textsubscript{2}\text{max} ranging between 10 and 15 ml/min kg and underwent preoperative pulmonary rehabilitation, whereas the other 5 had a VO\textsubscript{2}\text{max} greater than 15 ml/kg min and were promptly operated on.

Sixty-four patients underwent a lobectomy (22 upper right, 18 upper left, 12 lower right, 11 lower left and 1 medium), 5 patients had a bi-lobectomy (2 upper-medium and 3 medium-lower) and 4 patients had a segmentectomy (2 apical left tri-segmentectomy, 1 right apico-dorsal bi-segmentectomy and 1 right lower apico-posterior bisegmentectomy). Histological examination showed non-small cell lung cancer in 71 cases, while the remaining 2 cases were a solitary pulmonary metastasis of colon cancer and a pulmonary aspergiloma.

3.2. Postoperative outcome

Postoperative mortality was 2.7% (n = 2); postoperative pneumonia and subsequently acute respiratory distress was responsible for one death; the second was caused by acute myocardial infarction followed by intractable cardiogenic shock. Median hospital stay was 9 days (range: 6–56). A cardiac or pulmonary complication was recorded in 30 patients (41%). A diagnostic or therapeutic fiber optic bronchoscopy was performed in 15 out of the 19 (26%) patients in whom a pulmonary complication was diagnosed, while 7 underwent a percutaneous crico-thyroidal mini-tracheostomy. Two patients had acute respiratory failure and underwent tracheal intubation. A diagnosis of pneumonia was ultimately established in 12 cases.

Cardiac complications occurred in 17 cases: 16 (22%) had atrial fibrillation and one a myocardial infarction. Other complications consisted of prolonged air leaks, observed in
yielded a significant correlation between FEV1 and VO2max. Preoperative VO2max was higher than 20 ml/kg min, and in 2 out of the 22 patients (9.1%) in whom the pulmonary complication (FEV1: forced expiratory volume at first second; DLCO: diffusion lung capacity for CO; VE: minute ventilation; VEVCO2 ventilatory equivalent for CO) was observed, the mean DLCO value resulted as being lower but not statistically significant (95%CI = 0.48—0.80) when corrected for body weight and (95%CI = 0.49—0.78) when expressed in liters and 0.62 (95%CI = 0.57—0.85) (Fig. 1), 0.63 (95%CI = 0.57—0.85) versus pulmonary complication with respect to the mean value of DLCO (95%CI = 4.6—27.9, respectively); among this group of patients the mean DLCO value resulted as being lower but not statistically significant (p = 0.068; 95%CI = −0.99 to 26.7). The Spearman rank test yielded a significant correlation between FEV1 and VO2max (r = 0.596; p < 0.0005), as well as between VO2max and DLCO (r = 0.291; p = 0.038). In univariate analysis neither demographic factors (age, sex, BMI) nor surgical (type of lobectomy and number of segments resected) ones were found to be correlated with pulmonary complication occurrence and, because of the correlation of functional parameters found by Spearman's rank test. Logistic regression analysis including clinical, functional and surgical data found FEV1 to be an independent factor of postoperative pulmonary complication (p = 0.005).

In ROC curves, the area below the curve of VO2max expressed in ml/kg min resulted as being 0.69 with respect to pulmonary complication (95%CI = 0.57—0.85) (Fig. 1), 0.63 (95%CI = 0.49—0.78) when expressed in liters and 0.62 (95%CI = 0.48—0.80) when corrected for body weight and calculated as a percentage of the predicted value.

A pulmonary complication was observed in 6 out of 14 patients (43%) with a preoperative VO2max lower than 15 ml/kg min, and in 2 out of the 22 patients (9.1%) in whom the preoperative VO2max was higher than 20 ml/kg min.

In the ROC curve the VO2max value farthest from the diagonal was at 18.7 ml/kg min (index of de Youden Se/Sp-1 at 0.370), with a 52.8% sensitivity and 84.2% specificity for pulmonary complications. At a VO2max value of 15 ml/kg min, the sensitivity versus pulmonary complication was 84.9% and the specificity 31.6%, while at 20 ml/kg min the sensitivity was 35.8% and the specificity 89.5%. The area below the ROC curve of FEV1 expressed as a percentage of the predicted value resulted as being 0.706 (95%CI = 0.57—0.85).

Univariate analysis of demographic, functional and surgical data of the 16 patients who had a postoperative new onset atrial fibrillation compared with those without cardiac complications failed to highlight any statistically significant parameters.

When considering the group of 30 patients in whom a cardiac and/or pulmonary complication occurred, at univariate analysis the mean DLCO value resulted as being significantly lower than that of the rest of the population (76.5% vs 63.1%; p = 0.037).

4. Discussion

In the present study we report evidence that preoperative exercise capacity assessment is a valuable test to identify patients at risk of postoperative pulmonary complications after lung lobar resection.

In the last 25 years, there has been a considerable rise in interest in the preoperative evaluation of exercise capacity in patients who are candidates for lung resection. A recent meta-analysis concluded that a low preoperative exercise capacity is associated with a postoperative complicated outcome. It is interesting to note that this meta-analysis concluded that FEV1 and DLCO are also lower in patients with postoperative complicated outcomes. This figure, which is in

<table>
<thead>
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<th>No pulmonary complication (n = 54)</th>
<th>Pulmonary complication (n = 19)</th>
<th>p</th>
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<tr>
<td>Age</td>
<td>66.2 ± 8.1</td>
<td>68.3 ± 10.2</td>
<td>0.35</td>
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<td>Body mass index</td>
<td>26.1 ± 4.5</td>
<td>26.1 ± 3.3</td>
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<td>FEV1%</td>
<td>70.9 ± 22.2</td>
<td>54.6 ± 20.4</td>
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<tr>
<td>DLCO%</td>
<td>74.0 ± 25.2</td>
<td>61.1 ± 19.4</td>
<td>0.06</td>
</tr>
<tr>
<td>VO2max (ml/kg min)</td>
<td>19.7 ± 5.1</td>
<td>16.9 ± 4.2</td>
<td>0.04</td>
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<tr>
<td>Watts</td>
<td>92 ± 32</td>
<td>84 ± 24</td>
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<td>34.7 ± 6.6</td>
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FEV1: forced expiratory volume at first second; DLCO: diffusion lung capacity for CO; VE: minute ventilation; VEVCO2 ventilatory equivalent for CO.

Table 1
Univariate analysis with regard to pulmonary complication occurrence (data are expressed as mean values with standard deviation).

3.3. Data analysis

At univariate analysis (Table 1), mean preoperative VO2max expressed in ml/kg min and mean FEV1 expressed as percentage of the predicted value were found to be significantly lower in patients who presented a postoperative pulmonary complication with respect to the mean value of patients without pulmonary complications (p = 0.043; 95%CI = 0.8—5.3 and p = 0.013; 95%CI = 4.6—27.9, respectively); among this group of patients the mean DLCO value resulted as being lower but not statistically significant (p = 0.068; 95%CI = −0.99 to 26.7). The Spearman rank test yielded a significant correlation between FEV1 and VO2max (r = 0.596; p < 0.0005), as well as between VO2max and DLCO (r = 0.291; p = 0.038). In univariate analysis neither demographic factors (age, sex, BMI) nor surgical (type of lobectomy and number of segments resected) ones were found to be correlated with pulmonary complication occurrence and, because of the correlation of functional parameters found by Spearman’s rank test. Logistic regression analysis including clinical, functional and surgical data found FEV1 to be an independent factor of postoperative pulmonary complication (p = 0.005).

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agreement with our results, can be explained, at least for the data reported in the present study, by the linear correlation found among the preoperative functional resting and exercise parameters.

In our experience, exercise capacity corrected for body weight resulted as being the best parameter among those deriving from the preoperative cardio-pulmonary exercise test for the prediction of pulmonary complication occurrence. However, in our study protocol a preoperative pulmonary rehabilitation was prescribed in patients with exercise capacity under 15 ml/kg min, and thus a bias could have been introduced when comparing preoperative functional parameters.

The postoperative cardio-pulmonary complication rate of 41% of our cohort might seem relatively high, at least if compared with current literature figures in standard populations, but it should be considered that mean preoperative functional parameters of our study population are lower than those generally reported in larger series (i.e.: VO₂max = 18.7 ml/min/kg; FEV1 = 5.4 ml/kg min; FEV1/FVC = 66.7% ± 22.8; DLCO = 71% ± 24.9).

In conclusion, this study shows that systematic preoperative exercise capacity assessment in patients undergoing lung resection could help in stratifying patients at risk of postoperative pulmonary complication. On the other hand we failed to find a superiority of exercise capacity over resting functional parameters in predicting postoperative outcome after lung resection. The results of our study, in accordance with recently published guidelines on preoperative functional evaluation of lung resection, appear to limit the usefulness of exercise capacity measurement in those patients with preoperative borderline lung function on resting pulmonary function test [16,17].

References


Appendix A. Conference discussion

Dr S. Cassivi (Rochester, MN): My question to you is this. After going through this whole exercise, what have you done differently in your practice?

Dr Bobbio: We have changed. At the beginning we did the exercise test only in patients with a preoperative borderline function on standard pulmonary function tests; in this study we wanted to explore the role of the preoperative cardio-pulmonary exercise test in the whole population undergoing lung resection. Now we will probably go back to doing the preoperative cardio-pulmonary exercise test only in patients with a limited function.

Dr Cassivi: So you are back to where you started from?

Dr Bobbio: Yes, I think so.

Dr Cassivi: One question that I think both of us have up here at the podium was why you excluded patients who were going to undergo a pneumonectomy. These are the patients who you are typically most worried about.

Dr Bobbio: The principle reason is that, in my mind, the postoperative outcome of pneumonectomy is not the same as that of lobectomy. The preoperative functional exploration could also be quite different. Another reason is that we ultimately had a small number of patients who had pneumonectomy.

Dr A. Brunelli (Ancona, Italy): The value of oxygen consumption you used is before or after rehabilitation?

Dr Bobbio: Before.

Dr Brunelli: So, as you stated, there may be some bias?

Dr Bobbio: Certainly.

Dr Brunelli: Because I read some of your studies and you showed that these patients improved after rehabilitation.

Dr Bobbio: Exactly. That is probably why we have a low specificity of the threshold at 15 ml/kg min; under this threshold patients had preoperative pulmonary rehabilitation, and they increased their exercise capacity before surgery.