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Results of a simple exercise test performed routinely to predict postoperative morbidity after anatomical lung resection☆,☆☆

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Abstract

Background and objective: Exercise tests are considered the most reliable ones for the preoperative workup of lung resection candidates but frequently are indicated only in cases with low predicted postoperative forced expiratory volume in 1 s (FEV1) and carbon monoxide diffusing capacity (DLCO). The aim of this investigation is to evaluate if a simple, standardised incremental bicycle exercise test routinely performed in patients considered operable is predictive of postoperative cardio-respiratory complication and if its performance is comparable to a logistic regression model including frequently cited clinical predictive variables. **Methods:** A series of 103 lung resection candidates were included in a prospective observational study. All patients underwent a standardised, incremental exercise test on a bicycle up to exhaustion. The analysed outcome was the occurrence of postoperative cardio-respiratory complications prospectively recorded and codified. The correlation of distance reached at the end of the test and the outcome was estimated by non-parametric tests. A logistic regression model including age, BMI, predicted postoperative (ppoFEV1%) and predicted postoperative DLCO (ppoDLCO) was adjusted and the individual probability of complication calculated and set as a new variable. Finally, two receiver operating characteristic (ROC) curves were constructed and compared: one with distance at the exercise test and the other with logistic regression probability of complication. **Results:** Mortality of the series was nil. Outcome prevalence was 14%. Distance reached at the end of the exercise test was lower in cases with a positive outcome (3498.6 m vs 4543.5 m, $p = 0.001$). On logistic regression analysis, age of the patient ($p = 0.016$) and ppoDLCO ($p = 0.000$) were predictive for the outcome. On ROC analysis, C-indices were 0.77 (distance) and 0.78 (logistic model, $p = 0.95$). **Conclusion:** Reached distance in a simple standardised exercise test is related to postoperative morbidity after lung resection; and the accuracy of prediction using this variable alone is comparable to a logistic regression model including age and ppoDLCO.

Keywords: Lung resection; Exercise tests; Surgical risk

1. Introduction

Exercise capacity, expressed as VO_{2max}, is lower in patients who develop postoperative cardio-respiratory complications after lung resection [1]. In fact, either VO_{2max} direct measurement [2—4] or estimation by stair climbing [5] has shown a good performance to predict postoperative outcome after lung resection. Although in the majority of recently published guidelines [6,7] VO_{2max} is recommended only in selected cases with low predicted postoperative forced expiratory volume in 1 s (ppoFEV1) and/or predicted postoperative carbon monoxide diffusing capacity (ppoDLCO), the European Respiratory Society/European Society of Thoracic Surgeons (ERS/ESTS) guidelines recommend exercise tests in all cases with preoperative FEV1 and/or DLCO under 80% of the predicted value, according to the patient's sex, age and height [8].

Unfortunately, measuring VO_{2max} as a routine is not possible in most centres and it is replaced by several low-technology tests such as 6 min walking, shuttle-walk test or stair climbing. Currently [5], symptom-limited stair climbing can be used as a screening test to select those patients needing high-technology cardiopulmonary function tests to decide on their operability. The main disadvantage of the stair-climbing test is that it must be conducted outside the pulmonary function laboratory and in non-favourable surroundings — it would be unfortunate if an unexpected emergency develops due to coronary or any other kind of cardiac event.

In this study, we have tried to investigate if the patient's performance during a simple exercise test performed on an ergometric bicycle in the laboratory is correlated to cardiopulmonary morbidity after lung resection and if the

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accuracy of prediction is comparable to the accuracy of a regression model constructed with predictive variables frequently cited in the literature.

2. Methods

2.1. Studied population

A total of 103 consecutive patients scheduled for pulmonary anatomical resection between April 2007 and August 2008 have been prospectively included in the study. Patient selection criteria consisted of the absence of major co-morbidity refractory to medical therapy, and estimated postoperative FEV1 and DLCO (calculated according to the number of non-obstructed pulmonary segments to be resected) over 40% of the normal value. In cases with either low ppoFEV1 or low ppoDLCO, VO_{2max} was calculated and the patient was admitted for surgery if VO_{2max} was found to be over 15 ml kg^{-1} min^{-1}. Patients with a known coronary or symptomatic cardiac valve disease or arrhythmia prior to surgery and patients needing resection extended to chest wall were excluded from the study. The surgical approach was muscle-sparing or video-assisted small axillary thoracotomy in all cases.

2.2. Analysed variables

The following independent clinical variables were recorded: age of the patient, body mass index, predicted postoperative FEV1 (ppoFEV1) and DLCO (ppoDLCO) and estimated distance at the end of the test (see below). All variables used in the study were complete.

The dependent variable was the occurrence of post-operative cardio-respiratory complications prospectively defined. Any of the following postoperative events were considered: pulmonary atelectasis or pneumonia, respiratory or ventilatory insufficiency at discharge (PO_2 under 60 mmHg or PCO_2 over 45 mmHg), need of mechanical ventilation at any time after extubation in the operating room, pulmonary thrombo-embolism, brain stroke, arrhythmia, myocardial ischaemia or infarct and clinical cardiac insufficiency.

2.3. Exercise test

Patients were asked to perform an incremental cycle ergometer protocol to exhaustion. Exercise started without charge and the power increased by 30 W every 3 min. Patients were encouraged to maintain a cycling cadence not lower than 50 per min, but the upper limit was not established. The test was interrupted after 12 min or before if the patient presented extreme dyspnoea or fatigue, bradycardia, hypotension, electrocardiography (EKG) ischaemic changes or angina. Finger oximetry (by means of a calibrated Nonin 8600 pulse oximeter) and EKG were continuously monitored during the test. At the end of the test, the estimated distance reached, in metres, was recorded.

2.4. Statistical analysis

A logistic regression model using the resampling technique by bootstrap analysis (1000 replications) was constructed. All previously cited independent variables were introduced in the model. Variables with a 95% confidence interval (CI) regression coefficient including the unit and a p-value over 0.05 were manually withdrawn from the model. After adjusting the final model with the rest of variables, the probability of a positive outcome was calculated for each patient and recorded in the database.

The distance reached at the end of the exercise test was compared in cases with and without cardio-respiratory complications by means of the non-parametric Wilcoxon rank-sum test.

Finally, two receiver operating characteristic (ROC) curves were constructed: the first one using the individual probability of complication calculated by logistic regression analysis, and the second one with the distance reached by each patient during the exercise test. The C-indices of both curves were compared. The statistical package Stata 11.0 (StataCorp, College Station, TX, USA) was used for the analysis.

3. Results

The series consisted of 94 cases of lobectomy and nine pneumonectomies. Descriptive analysis of continuous variables is shown in Table 1. Five cases had ppoFEV1 or ppoDLCO under 40% of calculated theoretical values for sex, age and height and underwent a conventional exercise test with calculation of VO_{2max}. All patients reached 15 ml kg^{-1} min^{-1} or over and were judged operable.

Outcome prevalence was 14% (14 cases) and consisted of atrial fibrillation (six cases), lobar atelectasis, cardiac insufficiency and respiratory insufficiency (two cases each), pulmonary embolism and brain stroke (one case each). Table 2 shows the results of the logistic regression model. BMI and ppoDLCO were excluded from the final model ($p = 0.284$ and 0.901, respectively) while age and ppoDLCO were the best predictors of postoperative cardio-respiratory complications ($p = 0.016$ and 0.000, respectively).

As can be seen in Fig. 1, patients with postoperative complications reached a mean distance of 3498.6 m (SD: 874.7) while patients without postoperative cardio-respira-

Table 1
Descriptive statistics of the continuous variables.

Variable	Mean	SD	Range
Age	62.6	13.5	20–85
BMI	25.6	5.3	15.1–40.3
ppoFEV1	68.3	18.3	38.4–129
ppoDLCO	66.8	18.3	28–118
Distance	4401.4	1091.3	1460–5950

Table 2
Logistic regression model using two different sets of variables (in both models resampling techniques by bootstrap analysis have been used).

Variable	Coefficient	Bootstrap standard error	95% CI	p
Age	0.0406	0.0169	0.0074/0.0738	0.016
ppoDLCO	−0.0733	0.0196	−0.1118/−0.0347	0.000

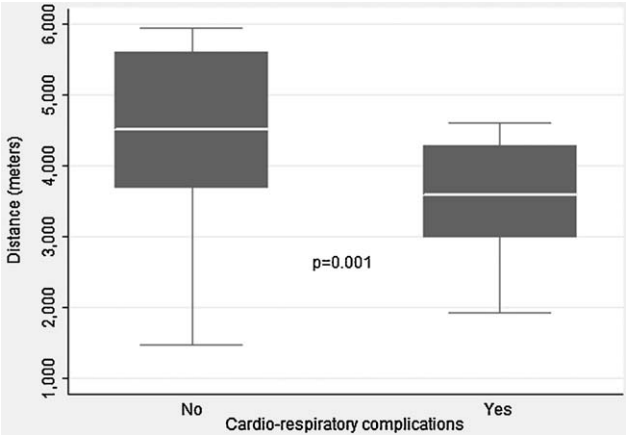

Fig. 1. Box-plot showing that patients without cardio-respiratory complications reached a longer distance at the exercise test.

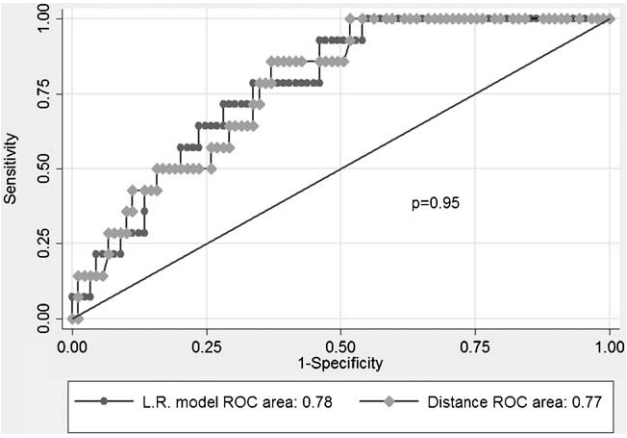

Fig. 2. ROC curves constructed using the individual probability of complication calculated with the logistic regression model and the distance reached at the end of the exercise test.

tory events reached a mean of 4543.5 m (SD 1056.9, $p = 0.001$).

On ROC analysis (Fig. 2), C-indices were 0.777 (95% CI: 0.66997—0.8854, regression model) and 0.774 (95% CI: 0.66559—0.8836, distance at the exercise test, $p = 0.9530$).

4. Discussion

Due to their capacity of integrating cardiac and respiratory evaluation, exercise tests are considered the most reliable ones for the preoperative workup of lung resection candidates. Performance on exercise is well correlated with the immediate postoperative outcome [2] and with long-term functional capacity [9].

Exercise tests have been recommended as a routine during preoperative workup [8] in cases with a preoperative FEV1 and/or DLCO under 80% of theoretical values. VO_{2max} calculation is usually considered the last step of preoperative workup in high-risk patients according to other criteria such as predicted postoperative pulmonary volumes and DLCO [6,7]. In a prospective analysis [3], exercise testing was indicated before split-function calculation and the authors showed a reduced morbidity and mortality; furthermore, no patient was erroneously excluded from surgery. An absolute, or better, percentage over theoretical value of VO_{2max} [2,9] can be fixed as a cut-off value to indicate either lung resection or not. The threshold of VO_{2max} for surgical intervention could be set between 50% and 60% of predicted to avoid excess surgical mortality. Further, $ppoVO_{2max}$ can be calculated [3]. A percentage of predicted value from 35% to 40% can be considered acceptable provided that the absolute VO_{2max} value is $\geq$10 ml kg^{-1} min^{-1}.

Unfortunately, measuring VO_{2max} is expensive and is not available in all centres and this is the reason why several low-technology tests have been considered during the decision-making process before lung resection. Among low-technology studies, 6 and 12 min walking tests were implemented by several authors with non-conclusive results due to the lack of standardisation and reproducibility; they have not been reported again in the recent medical literature. The shuttle-walk test has been reported to be more reproducible and more highly correlated with VO_{2max} and a cut-off value of 25 shuttles was suggested in the functional algorithm proposed by BTS [6]. However, Win et al. [10] did not find any statistically significant difference in shuttle-walk distance between patients with and without complications after lung resection and they do not recommend the shuttle test to predict poor surgical outcome in lung cancer patients [11].

Stair climbing seems to be the most reliable and accurate test to predict postoperative outcome after lung resection. According to recently published articles [12,13], the altitude reached and the occurrence of oxygen desaturation during stair climbing are highly predictive of mortality and morbidity after pulmonary lobectomy. The main problem to indicate a routine stair-climbing test in clinical settings comes from the need of performing the test out of the pulmonary function laboratory and the potential harm to the patient in case a cardiac event happens away from a fully equipped room.

To our knowledge, the distance reached at the end of an ergometric bicycle protocol has never been published as a tool to predict the postoperative outcome after lung resection. Cycling up to exhaustion is used for VO_{2max} calculation not only during preoperative workup before lung resection and transplantation but also for chronic obstructive pulmonary disease (COPD) assessment. In COPD patients, an impairment of striated muscle endurance, not related to pulmonary volumes, has been demonstrated [14]. This finding could be dependent on the decrease of capillary density at the striated muscles [15] and on significant impairment of blood flow to the legs, mainly in ageing people [16]. Cycling tests used for COPD and transplant assessment consist usually in ramp protocols increasing 10 W per min. For technical reasons related to the available equipment, we have implemented a test increasing 30 W every 3 min that could not be acceptable for patients with severe COPD, probably being unable to perform the test. This is not the case in lung resection candidates since patients with severe COPD are not referred for surgical evaluation to our department.

The purpose of our investigation was neither correlating the results of distance and VO_{2max} nor finding a distance cut-off to exclude patients for surgery. We have compared the

predictive capacity of the distance at the end of the test and the performance of a logistic regression model in which clinical predictive variables frequently cited in the literature have been included. The results of our investigation do not confirm the reliability of a simple exercise test on ergometric bicycle to exclude patients from surgery, and future investigations are warranted to correlate distance and VO_{2max} and to find a distance cut-off to either recommend lung resection or not.

Due to the population characteristics, we have included a few numbers of high-risk cases according to frequently used criteria (ppoFEV1 and/or ppoDLCO under 30%). This represents a limitation of our study, since postoperative morbidity in average risk cases is expected to be lower and, therefore, difficult to predict. Only high-risk patients in our series were also referred for VO_{2max} evaluation, since our investigation was designed and started before publication of the ERS/ESTS recommendations on functional assessment before lung resection [8]. Thus, the operability criteria used during the study period are different to the ones currently in use in our centre.

According to our results, we can conclude that a non-invasive standardised exercise test performed on an ergometric bicycle is related to postoperative cardio-respiratory morbidity and the performance of prediction is comparable to obtained by logistic regression using age and ppoDLCO. A larger series of cases and external validation are needed to confirm the use of the distance test as a routine in clinical practice.

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