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Preoperative Exercise Testing Is a Better Predictor of Postoperative Complications than Pulmonary Function Testing for Patients with Lung Cancer

Atsushi Hata[1], Yasuo Sekine[1*], Eitetsu Koh[1], Nobuyuki Yamaguchi[2]

[1]Department of Thoracic Surgery, Tokyo Women's Medical University Yachiyo Medical Center, Yachiyo, Japan
[2]Division of Clinical Physiology, Tokyo Women's Medical University Yachiyo Medical Center, Yachiyo, Japan
Email: *sekine.yasuo@twmu.ac.jp

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Abstract

Objective: The aim of this preliminary study was to evaluate the feasibility of exercise testing (ET) for predicting postoperative complications in patients with impaired pulmonary function. Methods: Thirteen patients were prospectively enrolled. The enrollment criteria were $FEV_{1.0}\% < 70\%$ and emphysema score > 8 by the Goddard classification or interstitial pneumonia on chest computed tomography. Patients underwent testing for pulmonary function, six-minute walking test (6MWT), and stair-climbing test (SCT). Postoperative cardiopulmonary complications (PCPCs) were recorded. Results: Four patients developed PCPCs. There were no significant differences between the patients with PCPCs ($n = 4$) and those without PCPCs ($n = 9$) for background data and PFT. The distances achieved in the 6MWT were 503 ± 72.7 m for patients without PCPCs and 369 ± 50.7 m for patients with PCPCs ($p = 0.011$). The SCT climbing heights were 20.4 ± 5.3 m for patients without PCPCs and 14.9 ± 4.0 m for patients with PCPCs ($P = 0.187$). Cut-off points, including a 6MFT distance of less than 400 m, SCT height lower than 15 m, and SCT climbing speed less than 8.5 m/min, were predictive of CPCP. Conclusions: Exercise testing is more feasible for predicting postoperative cardiopulmonary complications than stationary pulmonary function testing.

Keywords

Lung Cancer, Exercise Testing, Postoperative Complication, Pulmonary Function Testing

*Corresponding author.

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1. Introduction

Pulmonary resection is a standard treatment option for patients with stage I and II non-small cell lung cancer. Preoperative physiologic evaluation is mandatory for resection of one or more pulmonary lobes. The American College of Chest Physicians (ACCP) has proposed evidence-based clinical practice guidelines for preoperative physiologic evaluation of patients with lung cancer [1]. The guidelines present a risk assessment algorithm, which recommends that patients with abnormal results on pulmonary function testing (PFT) undergo additional testing, such as diffusing capacity of the lung for carbon monoxide (DLco) and cardiopulmonary exercise testing (CPET). However, sometimes the predicted postoperative (PPO) pulmonary function is underestimated and the actual postoperative physiologic capacity has no relationship to the predicted capacity [2].

Lung volume reduction surgery has been found to be beneficial for patients with heterogeneous emphysema, and lobectomy has also been shown to be beneficial for patients with a malignant tumor located in an upper emphysematous lobe [3]. These findings suggest that postoperative lung function and exercise capacity may differ based on the physiologic or anatomic pulmonary abnormalities and the volume of lung resected.

Criteria for safe lung resection have been reported, but they may over- or underestimate the risk of postoperative cardiopulmonary complications (PCPCs) in patients who undergo lung surgery [4], because PFT only estimates pulmonary function and does not evaluate cardiac function. Furthermore, since the estimation of PPO PFT is based on the number of segments to be resected, the risk for patients with emphysema could be overestimated if the lung resection benefits the patient because of the reduction in volume of emphysematous lung. On the other hand, CPET can evaluate cardiopulmonary function and oxygen transport [5]. CPET can reveal serious pathophysiologic abnormalities of the oxygen transport system and can predict the risk of postoperative complications [4]. Therefore, PFT and CPET are both indicated for patients with impaired pulmonary function [6].

The aim of this preliminary study was to evaluate the feasibility of exercise testing for predicting postoperative complications in patients with impaired pulmonary function who undergo lung resection.

2. Materials and Methods

The study was approved by the institutional review board of our hospital. This study comprised 13 male patients with impaired pulmonary function who were candidates for lung resection. They were prospectively enrolled from August 2011 through August 2013 after providing informed consent. Impaired pulmonary function was defined as follows: Forced expiratory volume in one second ($FEV_{1.0}$%)/Forced vital capacity (FVC) less than 70% and emphysema score higher than 8 points by the Goddard classification or interstitial pneumonia on chest computed tomography [7]. Preoperative functional evaluation consisted of spirometry, DLco, and exercise testing, as follows: six-minute walking test (6MWT) and stair-climbing test (SCT).

The following spirometric variables were considered: $FEV_{1.0}$; predicted postoperative (ppo) $FEV_{1.0}$ (ppo $FEV_{1.0}$ [preoperative $FEV_{1.0}$ × number of postoperative functioning segments/number of preoperative segments]); predictive postoperative DLco (ppoDLco) [(preoperative DLco × number of postoperative functioning segments/ number of preoperative segments]); and $FEV_{1.0}$/FVC [2].

The 6MWT is a simple, practical test that requires a 100-ft hallway, but no exercise equipment or advanced training for technicians [8]. This test measures the distance that a patient can quickly walk on a hard, flat surface during a 6-min period. The SCT is also a practical test that measures the total height of stairs a patient can climb [4] [9]. Each stair step is 0.17-m high. The study patients were asked to climb, at their own pace, the maximum number of steps before needing to stop because of exhaustion, limiting dyspnea, leg fatigue, or chest pain. The total number of steps climbed and the time taken to complete the test were recorded for each patient. Each patient's climbing pace was calculated from the total height climbed per time taken to complete the test in minutes. Finger pulse oximetry was used to measure oxygen saturation and pulse rate continuously for both tests.

Each patient was accompanied by a physician during his tests and encouraged to complete the test. Moreover, the physician maintained continuous verbal interaction with the patient to assess dyspnea and the occurrence of other signs/symptoms. The 6MWT and SCT evaluate the global and integrated responses of all the systems involved during exercise, including the pulmonary and cardiovascular systems, systemic circulation, peripheral circulation, neuromuscular units, and muscle metabolism.

Every patient with a concomitant cardiac disease underwent extensive cardiac evaluation before performing the 6MWT and SCT. Concomitant cardiac disease was defined as follows: previous cardiac surgery, previous myocardial infarction, history of coronary artery disease, pulmonary hypertension, an arrhythmia such as atrial fibrillation, or cardiac failure. A patient with a concomitant cardiac disease was allowed to undertake the tests after undergoing cardiac evaluation and subsequently considered to be hemodynamically stable. Patients with orthopedic disorders such as herniated intervertebral disks and dysfunction of lower extremities were also excluded from this study because they could not undergo exercise testing.

PCPCs were considered to be cardiopulmonary complications occurring within 30 days after the surgery or those occurring during a longer period if the patient was still in the hospital. According to other reports [10] [11] and for the sake of comparison, the following complications were recorded: respiratory failure requiring mechanical ventilation for 48 h; pneumonia; atelectasis requiring bronchoscopy; pulmonary edema; pulmonary embolism; myocardial infarction; hemodynamically unstable arrhythmia requiring medical treatment; cardiac failure; and death.

3. Statistical Analysis

We compared the results of patients who developed PCPCs with those of the patients without PCPCs. Furthermore, we evaluated cut-off values for 6MWT and SCT for use as predictors of postoperative complications. The Mann-Whitney U test was used to analyze continuous variables, and the Fisher exact test to analyze categorical variables. Continuous variables were calculated as mean ± SD and categorical variables as number of patients (percent). A *P*-Value < 0.05 was considered to be statistically significant. Analysis was performed using JMP11 software (SAS Institute Inc., NY, USA).

4. Results

Table 1 summarizes the characteristics of the 13 patients. Twelve patients had lung cancer and one patient had metastatic lung cancer. The patients underwent 7 lobectomies and 6 wedge/segment ectomies (limited resections). There were no significant differences between patients with and without PCPCs. Four patients developed the following postoperative pulmonary complications: three patients developed pneumonia and one patient developed pulmonary dysfunction that required home oxygen therapy (**Table 2**). Two patients with pulmonary complications died in the hospital.

Table 3 shows the PFT and DLco data. There were no significant differences between the patients with and without PCPCs. **Table 4** shows the 6MWT and SCT data. The patients who developed PCPCs had a significantly shorter mean preoperative 6MWT distance than the patients without PCPCs. The mean maximum SCT pulse rate and climbing pace of the patients with PCPCs were significantly lower than those of the patients without PCPCs.

We evaluated cut-off values for the CMWT and SCT based on previous reports that indicated that patients with a 6MWT less than 400 m or SCT height less than 15 m tended to have postoperative complications [4] [12]. **Table 5** shows that three patients who developed PCPCs walked less than 400 min 6 min and none of the patients without PCPCs walked less than 400 m ($P = 0.014$). Three patients with PCPCs climbed less than 15 m in the SCT and one patient without PCPCs climbed less than 15 m (**Table 5**, $P = 0.052$), and four patients with PCPCs and two patients without PCPCs achieved a climbing paces lower than 8.5 m/min ($P = 0.021$). For the 6MWT, a 6-min walking distance shorter than 400 m had a sensitivity of 75%, specificity of 100%, positive predictive value of 100% and negative predictive value of 90% for the development of PCPC. For the SCT, a climbing pace shorter than 8.5 m/min had a sensitivity of 100%, specificity of 77.8%, positive predictive value of 66.7%, and negative predictive value of 100%. Conversely, there were no significant differences in the numbers of patients with and without PCPCs who satisfied the traditional criteria of %ppoDLco less than 40% and %ppoFEV1 less than 40% (**Table 5**; $P = 0.308$, $P = 0.077$, respectively).

5. Discussion

We found that 6MWT and SCT were more valid assessments than conventional PFT for predicting the development of PCPCs in our study patients with impaired pulmonary function and emphysema. Although the PFT variables, which were regarded to be predictors of postoperative complications, did not predict PCPCs, the walking distance of the 6MWT and height and climbing pace of the SCT were predictive of PCPCs.

The operability of patients with impaired cardiopulmonary function and type of surgical procedure are traditionally decided using the percent predicted $FEV_{1.0}$ and percent predicted DLco [12]. Patients with percent

Table 1. Patient characteristics.

Variables	+PCPC (*n* = 4)	NoPCPC (*n* = 9)	*P*-value
Age	78.5 ± 4.5	74.9 ± 7.7	0.407
BMI	18.7 ± 2.72	22.7 ± 3.23	0.087
Smoking Index (pack-year)	57.0 ± 12.9	40.6 ± 23.2	0.189
Cardiac Disease, *n* (%)	2 (50)	2 (22.2)	0.530
Lobectomy, *n* (%)/Limited resection	3 (75)/1 (25)	4 (44.4)/5 (55.6)	0.559
Blood loss (g)	1336 ± 1059	178 ± 237	0.036
VATS, n (%)	4 (100)	6 (66.7)	0.497

PCPC: postoperative cardiopulmonary complication; BMI: body mass index; VATS: video-assisted thoracic surgery.

Table 2. Type of postoperative complications.

Age (y)	Procedure	Stage-Type	Preoperative disease	Complication
84, Male	Segmentectomy	IA-SCC	COPD	Pneumonia, death
78, Male	Lobectomy	IB-SCC	CPFE	Acute respiratory distress syndrome
79, Male	Lobectomy	IIIA-Ad	COPD	Hepatic failure, pneumonia, death
73, Male	Lobectomy	IIA-SCC	COPD	Respiratory failure

SCC: squamous cell carcinoma; Ad: adenocarcinoma; COPD: chronic obstructive pulmonary disease; CPFE: combined pulmonary fibrosis and emphysema.

Table 3. Pulmonary function data.

Variables	+PCPC	NoPCPC	*P*-value
FVC	2.50 ± 0.72	3.28 ± 0.71	0.189
%FVC	80.9 ± 23.7	101.7 ± 18.2	0.190
FEV1	1.70 ± 0.43	2.12 ± 0.67	0.247
%FEV1	85.0 ± 28.4	97.6 ± 26.8	0.488
% ppoFEV1.0	67.3 ± 27.0	85.9 ± 25.7	0.396
FEV1/FVC%	69.6 ± 13.5	65.5 ± 18.8	0.939
RV/TLC	45.9 ± 18.0	36.9 ± 8.60	0.671
%DLco	77.3 ± 38.7	80.2 ± 22.5	0.671
%DLco/VA	58.9 ± 28.5	70.0 ± 20.3	0.799
PaO_2	83.7 ± 2.33	98.7 ± 31.5	0.552
$PaCO_2$	38.2 ± 6.15	37.0 ± 6.23	1.000
CT evaluation			
Goddard Score	9.75 ± 4.35	4.00 ± 7.16	0.0601
PF, *n* (%)	2 (50)	1 (11)	0.2028

PCPC: postoperative cardiopulmonary complication; ppo: predicted postoperative: DLco: diffusing capacity of the lung for carbon monoxide: VA: alveolar ventilation; PF: pulmonary fibrosis.

Table 4. 6MWT and SCT data.

Variables	+PCPC	NoPCPC	*P*-value
Distance in6MWT (m)	369 ± 50.7	503 ± 72.7	0.011
Minimum SpO_2 in 6MWT (%)	84.3 ± 6.70	89.9 ± 6.03	0.213
Maximum PR in 6MWT	103 ± 6.93	118.9 ± 19.6	0.142
SCT height (m)	14.9 ± 4.00	20.4 ± 5.31	0.187
Minimum SpO_2 in SCT (%)	83.3 ± 7.29	89.3 ± 4.90	0.133
Maximum PR in SCT	109 ± 8.0	132 ± 14.5	0.030
SCT climbing time (min)	2.32 ± 0.91	2.05 ± 1.29	0.480
SCT climbing pace (m/min)	6.8 ± 0.87	11.8 ± 4.11	0.045

PCPC: postoperative cardiopulmonary complication; 6MWT: six-minute walk test; SCT: stair climbing test; SpO_2: oxygen saturation; PR: pulse rate.

Table 5. Cut-off values of selected variables.

Cut-off values	+PCPC (*n*, %)	NoPCPC (*n*, %)	*P*-value
Distance in 6MWT < 400 m	3 (75)	0 (0)	0.014
Heightin SCT < 15 m	3 (75)	1 (11)	0.052
Pacein SCT < 8.5 m/min	4 (100)	2 (22)	0.021
%ppoFEV1.0 < 40%	1 (25)	0 (0)	0.308
%ppoDLco < 40%	2 (50)	0 (0)	0.077

PCPC: postoperative cardiopulmonary complication; ppo: predicted postoperative value.

predicted $FEV_{1.0}$ and percent predicted DLco > 40% are considered to be operable [12]. These standards are meaningful but not always predictive of the development of PCPCs without the addition of other tests [13]. Various tests and scoring systems have been reported [14]-[18]. A modified Thoracoscore, which predicts postoperative outcomes after thoracic surgery, can be calculated based on the following variables: age, gender, priority of the procedure, malignancy, type of procedure, Zubrod score, ASA class, and number of co-morbidities [18]. However, such a scoring system is difficult to use on a daily basis in clinical practice.

The 6MWT and SCT are global exercise tests that can evaluate cardiopulmonary function, particularly for patients with chronic obstructive pulmonary disease (COPD) [8] [13]. These tests consist of the following variables: distance walked, height climbed, change in SpO2, maximum pulse rate, and SCT pace [4] [13].

There were no significant differences in the traditional PFT results for the patients with and without PCPCs. Three of four patients developing PCPCs had percentppo$FEV_{1.0}$ > 40%. This finding indicates that the patient's condition may be underestimated if only traditional PFT data is used.

This prospective study has some limitations and biases. First, this was a small dataset from a single-center study. Therefore, there may be several confounding variables, and a large prospective study is needed to verify the findings. Second, there was no single surgical procedure, because the type of procedure used was based on lung cancer stage and the patient's physical condition. Third, COPD should not be defined by functional limitation and radiologic evaluation only. Other clinical criteria should have been taken into consideration [19]. It is possible that the use of other criteria for COPD could have produced different results.

6. Conclusion

For lung cancer patients with impaired pulmonary function, exercise testing is more feasible for predicting postoperative cardiopulmonary complications than stationary pulmonary function testing. 6MWT < 400 m, SCT height < 15 m, and SCT climbing pace < 8.5 m/min are useful values for predicting postoperative cardiopulmonary complications.

Disclosure Statements

All authors have no conflict of interest.

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