

Received: 2016.07.16  
Accepted: 2016.08.19  
Published: 2017.03.24

# Stair-Climbing Test Predicts Postoperative Cardiopulmonary Complications and Hospital Stay in Patients with Non-Small Cell Lung Cancer

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

ABDE **Jingsi Dong**  
BF **Yousheng Mao**  
BCF **Jiagen Li**  
FG **Jie He**

Department of Thoracic Surgery, Cancer Institute and Hospital, Chinese Academy of Medical Sciences, Beijing, P.R. China

**Corresponding Author:** Jie He, e-mail: jie\_he@aol.com  
**Source of support:** Departmental sources

**Background:** There is currently no reliable method to predict major postoperative cardiopulmonary complications for patients with non-small cell lung cancer (NSCLC). In this study, we hypothesized that exercise oxygen desaturation (EOD) and heart rate change results in a stair-climbing test (SCT) would predict postoperative cardiopulmonary complications for patients with NSCLC.





**Material/Methods:** We examined 171 patients (41 females and 130 males) with NSCLC by preoperative SCT from January 2010 to July 2015. Among them, 27 underwent wedge resection, 122 underwent lobectomy, and 22 underwent pneumonectomy. The correlation between postoperative cardiopulmonary complications and parameters of SCT and pulmonary function test (PFT) parameters were analyzed retrospectively.

**Results:** The overall 30-day postoperative morbidity of the patients was 46/171 (26.9%), with death occurring in 3/171(1.8%). The age, FEV1%, MVV, height of climbing, EOD, and heart rate change were found to be significantly different between the group with postoperative cardiopulmonary complications and those without. Binary logistic regression analysis showed that EOD and heart rate change were independently correlated with postoperative cardiopulmonary complications. In addition, a model predicting the probability of postoperative cardiopulmonary complication based on logistic regression for multivariable analysis was used to confirm our findings.

**Conclusions:** A symptom-limited SCT with oxygen saturation monitoring is a safe, simple, and low-cost method to evaluate cardiopulmonary function preoperatively.

**MeSH Keywords:** **Carcinoma, Non-Small-Cell Lung • Causality • Postoperative Complications**

**Full-text PDF:** <http://www.medscimonit.com/abstract/index/idArt/900631>

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## Background

For patients with non-small cell lung cancer (NSCLC), physicians have long been puzzled by the task of identifying candidates who may suffer major postoperative cardiopulmonary complications if they were to undergo lung resection surgery. Among the few available tests, the cardiopulmonary exercise test (CPET) is a standard tool to assess the surgical risk of patients with NSCLC [1–3]. Specifically, maximal oxygen uptake (VO<sub>2</sub>max) during symptom-limited exercise was found to be a more reliable than other parameters of spirometry, such as forced expiratory volume in 1 second (FEV<sub>1</sub>) or the ratio of FEV<sub>1</sub> against forced vital capacity (FVC), to predict postoperative morbidity and mortality among NSCLC patients [3].

As an alternative to CPET, excise-based diagnostic tests, such as stair-climbing test (SCT), have been reported to be a safe, economical way to assess risk-associated factors of patients [4–7]. Interestingly, for patients with NSCLC, since SCT requires patients to ride cycles, it is more stressful than cardiopulmonary exercise and can be considered as valid tool to detect any abnormalities in the oxygen transport system [8]. Thus, it is plausible that SCT may be helpful in predicting cardiopulmonary complications after lung resection [9]. However, definitive evidence is lacking to determine whether SCT is superior to CPET to predict postoperative cardiopulmonary complications for patients with NSCLC.

In this study, we used statistical methods to assess whether the key parameters of SCT, including exercise oxygen desaturation (EOD), may be independent and proficient prognostic factors predicting postoperative cardiopulmonary complications among patients with NSCLC who received various extents of lung resection.

## Material and Methods

### Ethics statement

In this study, all protocols were reviewed and approved by the Ethics Committee at the Cancer Hospital (Institute), Chinese Academy of Medical Sciences in Beijing, China. All patients signed consent forms before cardiopulmonary function tests and the surgical procedure.

### Patients

A total of 413 patients with non-small cell lung cancer (NSCLC) performed the stair-climbing test between January 2010 and July 2015. We excluded 74 patients due to lack of complete clinical data, 53 patients were excluded because they failed to correctly perform the pulmonary function test, 12 patients

were excluded as they received lung resection and esophagectomy at the same time, and 103 patients were excluded because they did not receive surgery afterwards. Thus, 171 eligible NSCLC patients were enrolled in this study, including 41 females and 130 males. None of the patients had received any antineoplastic therapy such as radiotherapy and/or chemotherapy in the 6 months prior to surgery.

### Stair-climbing test

All patients in the study participated in the symptom-limited stair-climbing test preoperatively by climbing 5 floors from the 1<sup>st</sup> floor to the 6<sup>th</sup> floor in our surgical building. There are 20 steps and 1 intermediate landing between each floor, and each step is 0.153 m in height. The patients were instructed before the stair-climbing test and encouraged to climb the stairs as fast as they could without stopping to rest until they reached the highest floor possible. The maximum height (to the 6<sup>th</sup> floor) was 18.4 m. The test was complete when patients reached either the 6<sup>th</sup> floor or the patients presented an apparent symptom such as severe dyspnea with oxygen desaturation, severe leg fatigue, or chest pain, which indicated exhaustion and they could not climb any more. All patients were accompanied by 2 physicians all the time during the test, who would monitor their symptoms and recorded test results simultaneously. Heart rate and capillary oxygen saturation were recorded before the test, at each floor during the test, and after resting for 15 min after completing the test, using a portable pulse-oxy meter with finger probe, called the Autobox (Newtech, Shenzhen, China). We also recorded the time taken to reach the highest floor possible. The resting oxygen saturation (O<sub>2</sub>sat) and lowest O<sub>2</sub>sat during the test were recorded and used to calculate the desaturation level. For air leak management, single thoracic drainage in the chest was induced into the 2<sup>nd</sup> intercostal space, midclavicular line (pneumonectomy), and the 7<sup>th</sup> intercostal axillary line (wedge resection and lobectomy). With the exception of pneumonectomy, all the drainage tubes were put into the chest with the front-most end reaching the top of the chest. At the end of the operation, water was introduced into the chests when the anesthesiologist started to induce 2-lung ventilation. Residual lung tissues were carefully examined, and then air-leak tissue was stitched by Prolene thread until there was no air leak from the residual lung tissue.

### Pulmonary function tests

Spirometry, flow-volume curves, and absolute lung volumes were measured using a pulmonary function test apparatus [10]. The diffusion capacity for carbon monoxide (DLCO) was determined using a standard single-breath technique. Best results were selected in 2 acceptable measuring results at intervals of at least 5–10 min between 2 measurements.

**Table 1.** Postoperative complications of NSCLC patients.

Postoperative complications	Patients n (%)
Acute carbon dioxide retention (Pa CO <sub>2</sub> >6 kPa)	4 (2.4)
Prolonged mechanical ventilation (>48 h)	8 (4.7)
Treated symptomatic cardiac arrhythmia	32 (18.8)
Myocardial infarction	0 (0)
Pneumonia (temperature >38°C, purulent sputum and infiltrate on radiography)	3 (1.8)
Pulmonary embolism (high probability on ventilation perfusion scan or angiogram)	0 (0)
Lobular atelectasis (necessitating bronchoscopy)	6 (3.5)
Death	3 (1.8)
Total	46 (27.0)

Pa CO<sub>2</sub> – arterial carbon dioxide tension.

### Surgical procedures and postoperative care

All patients underwent surgical resection for lung cancer by either thoracotomy (n=129) or video-assisted thoracoscopic surgery (VATS, n=42). Procedures included pneumonectomy in 22 cases, lobectomy in 122 cases, and pulmonary wedge resection in 27 cases. Postoperative treatment was focused on early mobilization, chest physiotherapy and physical rehabilitation, pain control, and antibiotic and anti-thrombotic prophylaxis. Postoperative complications and deaths were defined as those occurring 0–30 days postoperatively, according to the guideline reported by Bolliger et al. [11], Smith et al. [12], and Brutsche et al. [13].

### Statistical analysis

Statistical analyses were performed using SAS software (SAS Institute, Cary, NC). Categorical variables of clinical characteristics are shown as percentages and were compared using the chi-square test. Continuous variables are presented as means ± standard deviations and compared by use of the *t* test. The utility of the complication as a predictive marker for drainage tube length of postoperative stay and hospital stay was investigated using Kaplan-Meier analysis. Logistic regression analysis was used to determine the association of preoperative factors with postoperative complications. Univariate analysis was first performed to determine the significance of predictive variables. Factors with a significant difference in univariate analysis (*P* value <0.05) were measured again by multivariate analysis to determine their independence. A *P* value <0.05 was considered as statistically significant.

## Results

A total of 171 non-small cell lung cancer patients were included in the study. Postoperative complications are listed in Table 1. The overall postoperative morbidity was 26.9%. The rate of perioperative deaths was 1.8% (n=3). One of these deaths was a 75-year-old male and another was a 59-year-old female, whose exercise oxygen desaturation (EOD) were both greater than 5, and both died from respiratory failure 1 and 80.5, respectively, days postoperatively despite being supported by mechanical ventilation. The third patient was a 64-year-old male who died from postoperative bleeding in the chest after a lobectomy. He was then excluded from the analysis of this study. There was therefore only 1 death according to the definition of postoperative mortality. There was no air leak from the chest of patients for more than 2 days before closing the chest, and no patient had empyema.

Baseline information and the comparison between the complication group and the complication-free group are shown in Table 2. There were no significant differences in sex ratio, BMI, smoking, lung resection, spirometry measurements (FEV<sub>1</sub>, MVV%, DLCO and DLCO%), or stair-climbing test results (pre-climb SaO<sub>2</sub>, climbing-end SaO<sub>2</sub>, and climbing-end heart rate) between the groups. While comparing those parameters between the complication group and the complication-free group, there were significant differences in age, FEV<sub>1</sub>%, MVV, height of climbing, EOD, and heart rate change between the 2 groups.

Finally, logistic regression analysis showed that EOD and heart rate change were independent predictors of complications (Table 3). A model for predicting the probability of postoperative complications based on logistic regression was hypothesized as:  $\text{Probability} = e^{\chi} / (1 + e^{\chi})$ ,  $\chi = 1.136 + (0.114 \times \text{EOD}) + (-0.040 \times \text{heart rate change})$ , in which *e* represented the base of natural logarithms and the  $\chi$  was the regression coefficient in the logistic regression.

The accuracy of the model was evaluated by use of the ROC curve, which showed that the area under the ROC curve (AUC) was 0.750 (95% CI: 0.668–0.831) (Figure 1). If the cutoff probability value was larger than 0.193, the patient was considered to have high risk of suffering from postoperative cardiopulmonary complications, and vice versa. The sensitivity and specificity of this model was 80.4% and 50.3%, respectively. Patients without a postoperative cardiopulmonary complication had a median length of drainage time of 4.3 days (95% CI, 3.4–4.5) and a median length of hospital stay of 9.4 days (95% CI, 8.9–9.8), as compared to 5.9 days (95% CI, 5.3–6.4) (Figure 2, *P*<0.001), and 13.1 days (95% CI, 10.9–15.3) (Figure 3, *P*<0.001) for patients with postoperative complications.

**Table 2.** Patients' baseline characteristics of patients and univariate analysis between patients with and without complications.

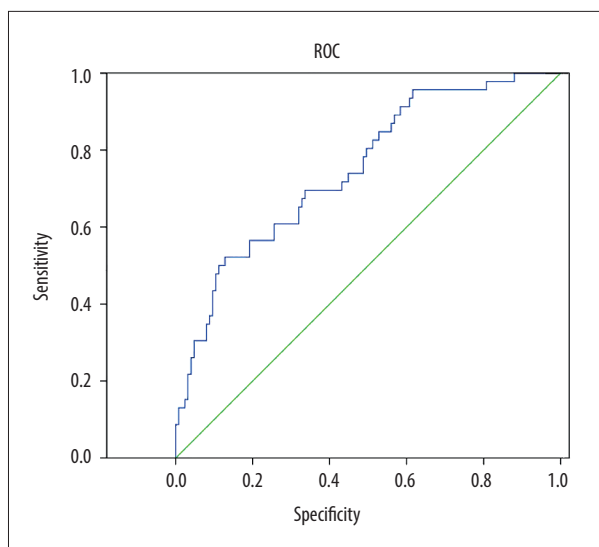
	All patients	No complications	Complications	P-value
Patients (n, %)	170	124	46	
Age	65±9	64±9	68±9	0.006
Male (n, %)	130 (76.0)	93 (71.5)	32 (78.0)	0.412*
BMI (kg·m <sup>-2</sup> )	24.5±4.0	24.7±3.5	25.2±5.3	0.204
Cardiopulmonary comorbidities (n, %)	24 (14.1%)	17 (13.7%)	7 (15.2%)	0.302
VATS (n, %)	42 (24.7%)	30 (24.2%)	12 (26.1%)	0.211
Smoking (pieces years)	724±685	690±707	815±623	0.290
FEV1 L	1.72±0.49	1.75±0.49	1.63±0.44	0.125
FEV1%	70.5±13.7	71.8±12.7	67.1±15.7	0.047
MVV L	53.7±18.1	55.3±18.8	49.4±15.3	0.036
MVV%	51.4±16.3	52.6±17.3	48.1±12.8	0.071
DLCO L	5.24±1.62	5.37±1.62	4.87±1.56	0.091
DLCO%	63.7±18.2	65.1±18.6	59.8±16.4	0.094
Height of climbing m	18.2±0.90	18.3±0.49	17.9±1.52	0.022
% Saturation (pre-climb)	96.6±0.94	96.6±0.94	96.5±0.91	0.302
% Saturation (at the end of climb)	92.3±4.5	92.6±4.23	91.4±5.14	0.109
EOD (%)	4.62±4.62	4.06±3.94	6.15±5.86	0.008
Heart rate(pre-climb) per/min	79.4±11.8	78.5±11.9	81.8±11.0	0.096
Heart rate (at the end of climb) per/min	132.1±15.3	132.6±14.6	130.6±17.1	0.455
Heart rate change per/min	52.7±14.4	54.1±14.5	48.8±13.5	0.030
Resection (%)	21.9±12.4	21.4±11.9	23.4±13.4	0.357

\* Chi-squared test; BMI – body mass index; EOD – exercise oxygen desaturation FEV1 – forced expiratory volume in one second; FEV1% – ratio of FEV1to forced vital capacity (FVC); DLCO – carbon monoxide lung diffusion capacity; MVV – maximum ventilatory volume; Resection – lung tissue resection, pneumonectomy=50%, bilobectomy=31%, lobectomy=20%, segmentectomy/wedge resection=5%. Cardiopulmonary comorbidities include hypertension, coronary heart disease, chronic arrhythmia and chronic obstructive pulmonary disease.

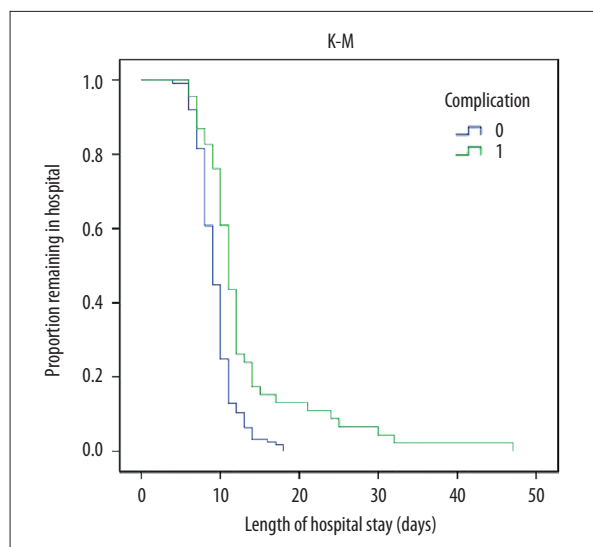
**Table 3.** Logistic regression analysis with cardiopulmonary morbidity as dependent variable.

	Coefficient	SE	OR	Wald	P-value	95% CI
Age	0.039	0.026	1.040	2.219	0.136	0.988–1.094
FEV1%	-0.017	0.015	0.983	1.286	0.257	0.955–1.012
MVV L	0.001	0.014	1.001	0.003	0.955	0.973–1.029
Height of climbing (m)	-0.115	0.243	0.891	0.226	0.634	0.554–1.434
EOD%	0.114	0.045	1.121	6.308	0.023	1.025–1.225
Heart rate change (per/min)	-0.040	0.016	0.961	6.127	0.013	0.931–0.992

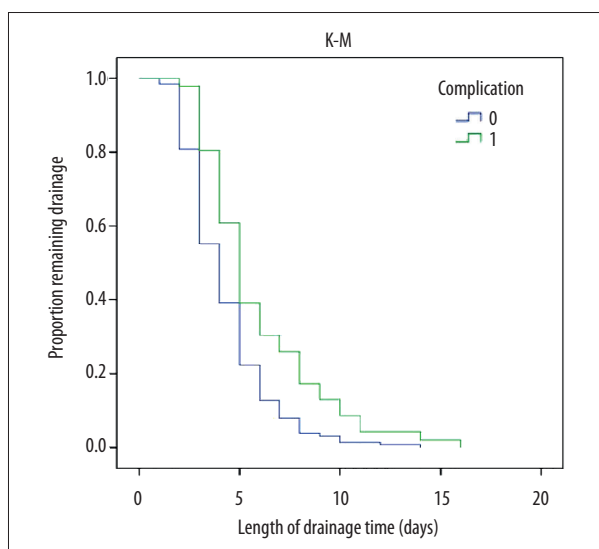
FEV1 – forced expiratory volume in one second; FEV1% – ratio of FEV1to forced vital capacity (FVC); MVV – maximum ventilatory volume; EOD – exercise oxygen desaturation.



**Figure 1.** The accuracy of the model for predicting the probability of postoperative complications was evaluated by use of the ROC curve. The area under the ROC curve (AUC) was 0.750 (95% CI: 0.668–0.831).



**Figure 3.** Patients without postoperative cardiopulmonary complications had a median length of hospital stay of 9.4 days (95% CI, 8.9–9.8) vs. 13.1 days (95% CI, 10.9–15.3) in patients with postoperative complications.



**Figure 2.** Patients without postoperative cardiopulmonary complication had a median length of drainage time of 4.3 days (95% CI, 3.4–4.5) vs. 5.9 days (95% CI, 5.3–6.4) in patients with postoperative complications.

## Discussion

In developing countries such as China, many NSCLC patients are heavy smokers. Complications such as chronic obstructive pulmonary disease (COPD) and coronary artery disease are very common among those patients, with high risk of surgical morbidity and mortality. Thus, it is critical to perform preoperative assessment on cardiopulmonary function to predict the risk of postoperative complications and death.

Use of vital capacity for the prediction of surgical risk was first reported as early as 1955 [14]. Since then, lung functional testing has been used to predict the risk of postoperative complications and even mortality. The 2 most commonly used parameters of conventional pulmonary function test are FEV1 and DLCO, which were confirmed by univariate analysis in our study. However, multivariate analysis showed that FEV1% was not an independent predictor of postoperative complications for patients with NSCLC.

Before this study, poor exercise capacity has long been used as the major predictor of postoperative cardiopulmonary complications after lung resection in patients with NSCLC. However, NSCLC patients with poor exercise capacity not only have high risk of postoperative cardiopulmonary complications, but also have longer hospital stay [15]. In the present study, our results showed that EOD and heart rate change were independent predictors of postoperative cardiopulmonary complications for patients with NSCLC, confirming the predictions from other studies [16,17]. Brunelli reported that complication rates in patients with and without EOD >4% and <4% were 36% and 22%, respectively [18]. In addition, a previous study by our team found the rate of postoperative cardiopulmonary complications was significantly higher in patients with EOD  $\geq$ 5% and heart rate change <55 beats/min than that in the group with EOD <5% and heart rate change  $\geq$ 55 beats/min [19]. Therefore, in the present study, we successfully established a model to predict the risk of postoperative cardiopulmonary complication using SCTs parameters of EOD and heart rate change.

It is worth noting that, in the present study, the patients without postoperative cardiopulmonary complication had a shorter hospital stay than those with postoperative cardiopulmonary complications. Also, the patients without postoperative cardiopulmonary complication had a shorter drainage time than those with postoperative cardiopulmonary complications. The possible explanation is that a patient who has postoperative cardiopulmonary complications creates more pleural effusion than one does not, further confirming that SCT may be an effective method to predict postoperative cardiopulmonary complications in NSCLC patients. However, well-established formal cardiopulmonary exercise testing (CPET) is still be recommended for precise assessment of these patients with high EOD or low heart beat change during the stair-climbing test [20].

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## Conclusions

We provided definitive evidence that EOD and heart rate change in SCT are independent predictors for postoperative cardiopulmonary complications in NSCLC patients. A follow-up study with a much larger patient pool would undoubtedly further verify our hypothesis. However, based on the information of our study, it is highly recommended for all lung resection candidates with poor conventional function test results to perform a stair-climbing test.

## Conflict of Interest

None.