


ORIGINAL ARTICLE

Evaluation of the 3-minute chair rise test as part of preoperative evaluation for patients with non-small cell lung cancer

Mathilde Azzi MD^{1,2}, David Debeaumont MD^{1,3}, Tristan Bonnevie PT, MSc^{4,5}, Bernard Aguilaniu MD, PhD⁶, Damiano Cerasuolo MD⁷, Fairuz Boujibar PT, MSc^{8,9}, Antoine Cuvelier MD, PhD^{2,5} & Francis-Edouard Gravier PT, MSc^{4,5} 

- 1 Department of Respiratory and Exercise Physiology, Rouen University Hospital, Rouen, France
- 2 Pulmonary, Thoracic Oncology and Respiratory Intensive Care Department, Rouen University Hospital, Rouen, France
- 3 CIC-CRB 1404, Rouen University Hospital, Rouen, France
- 4 ADIR Association, Rouen University Hospital, Rouen, France
- 5 Normandy University UNIROUEN, UPRES EA 3830, Haute Normandie Research and Biomedical Innovation, Rouen, France
- 6 Faculty of Medicine, Grenoble-Alpes University, Grenoble, France
- 7 Department of Biostatistics, Rouen University Hospital, Rouen, France
- 8 Normandy University UNIROUEN, INSERM U1096, Haute Normandie Research and Biomedical Innovation, Rouen, France
- 9 Department of Thoracic Surgery, Rouen University Hospital, Rouen, France

Keywords

Cardiopulmonary exercise testing; field test; lung surgery; non-small cell lung cancer; preoperative assessment.

Correspondence

Francis-Edouard Gravier, ADIR Association, Rouen University Hospital, 147 Avenue du Maréchal Juin, 76230 Bois-Guillaume, France.
Tel: +33 2 35 59 29 70
Fax: +33 2 35 59 29 71
Email: f.gravier@adir-hautenormandie.com

Received: 13 May 2020;

Accepted: 5 June 2020.

doi: 10.1111/1759-7714.13548

Thoracic Cancer **11** (2020) 2431–2439

Abstract

Background: Peak oxygen uptake ($\dot{V}O_{2\text{peak}}$) measured by a cardiopulmonary exercise test (CPX) is the gold-standard for predicting surgical risk in patients with non-small cell lung cancer (NSCLC). The 3-minute chair rise test (3CRT) is a simple test requiring minimal resources. This study aimed to determine the ability of 3CRT to predict $\dot{V}O_{2\text{peak}}$ in patients with NSCLC.

Methods: Retrospective data from CPX and 3CRT carried out in 36 patients with NSCLC between March 2018 and February 2019 were included. A multivariate analysis was undertaken to derive a predictive $\dot{V}O_{2\text{peak}}$ equation based on performance on the 3CRT. In addition, sensitivity-specificity analysis was carried out to estimate a threshold 3CRT value for the prediction of $\dot{V}O_{2\text{peak}} \geq 15$ mL/kg/minute.

Results: The following equation was obtained: $\dot{V}O_{2\text{peak}} \text{ predicted} = (0.04765 \times \text{FEV1}) - (0.20759 \times \text{BMI}) - (0.11589 \times \text{age}) + (0.38609 \times \text{vertical distance}) + 16.62869$; $r^2 = 0.75$, $P < 0.01$. The bias between the $\dot{V}O_{2\text{peak}}$ values predicted and measured during CPX was 0.0 ± 1.7 mL/kg/minute (95% limits of agreement [−3.5 to 3.5]). A performance ≥ 49 chair rises predicted $\dot{V}O_{2\text{peak}} \geq 15$ mL/kg/minute with a sensitivity of 0.75 and a specificity of 0.81.

Conclusions: The level of error in the prediction of $\dot{V}O_{2\text{peak}}$ from 3CRT performance was too great to recommend that 3CRT should replace CPX as the sole measurement of $\dot{V}O_{2\text{peak}}$. Nevertheless, the 3CRT could help to identify those patients that require CPX prior to lung resection surgery for NSCLC, larger prospective study is needed to confirm this hypothesis.

Key points

Significant findings of the study: Cardiopulmonary exercise tests can stratify the surgical risk. Prediction of the peak oxygen uptake ($\dot{V}O_{2\text{peak}}$) value from the

3CRT yields an unacceptable level of error. However, a performance of 49 chair rises or more during the 3CRT could indicate a $\dot{V}O_{2\text{peak}} \geq 15$ mL / kg / minute.

What this study adds: The 3CRT is a useful screening tool to determine the necessity for a comprehensive cardiopulmonary exercise test, whose access is limited in clinical practice. It could also allow early screening of patients requiring specific prehabilitation programs.

Introduction

Pulmonary resection is the most effective treatment for non-small cell lung cancer (NSCLC).¹ Unfortunately, many patients with lung cancer also have numerous comorbidities that increase the risk of postoperative complications.² The incidence of postoperative complications after lung cancer surgery is very heterogeneous according to the studies, it is estimated to be around 5% to more than 40%.³ These complications are associated with significantly poorer long-term outcomes.⁴ For this reason, all patients with NSCLC undergo comprehensive preoperative assessment to determine the benefits and risks of surgery in order to make appropriate therapeutic decisions.

Cardiopulmonary exercise test (CPX) is an important part of the preoperative assessment. It is used to measure and calculate variables that have been shown to be powerful indicators of the postoperative risk of morbidity and mortality. These variables include maximal oxygen uptake ($\dot{V}O_{2\text{max}}$) or, if maximal effort is not achieved, peak oxygen uptake ($\dot{V}O_{2\text{peak}}$).^{5, 6} Although the oxygen uptake capacity is now considered as the gold standard measurement to determine postoperative risk, access to CPX may be limited in some centres due to limitations in equipment and resources. As a result, other simpler tests have been developed.

The shuttle walking test (SWT) and the stair climbing test (SCT) are both currently recommended as screening tools to determine the necessity to perform CPX.⁷ Performance of 25 shuttles (ie, 5 minutes or 250 meters) in the SWT has been shown to be predictive of a $\dot{V}O_{2\text{peak}} \geq 15$ mL/kg/minute.⁸ For the SCT, an ascension of more than 22 meters has been associated with a $\dot{V}O_{2\text{peak}} \geq 15$ mL/kg/minute and fewer postoperative complications.^{9, 10} Therefore, these tests are useful to identify patients at low risk of postoperative complications. Patients who are at higher risk of postoperative complications and who do not achieve these test results often have a $\dot{V}O_{2\text{peak}} < 15$ mL/kg/minute.^{6, 11} Those patients require CPX in order to determine their risk more precisely; a $\dot{V}O_{2\text{peak}} < 10$ mL/kg/minute is considered a high surgical risk.^{7, 12}

Although the SWT and SCT are relatively simple tests, they still require space and stairs respectively. A new test,

the semi-paced 3-minute chair rise test (3CRT), has recently been standardized and validated in patients with chronic obstructive pulmonary disease.¹³ It has the advantage of requiring very little space and only a chair and a pulse oximeter. Therefore, the 3CRT can be performed in nearly any care setting, including very limited spaces such as consultation rooms. However, the results of 3CRT have not yet been compared with the definitive data obtained by CPX in patients with NSCLC, as has been undertaken for the SWT and SCT methods. This could allow the method to be used as a practical preoperative screening tool.

The aim of this study, therefore, was to investigate the relationship between the measurement of metabolic power by CPX ($\dot{V}O_{2\text{peak}}$) and the measurement of mechanical power developed during the 3CRT. More specifically, the aim was to determine the ability of 3CRT to predict the $\dot{V}O_{2\text{peak}}$ in patients with NSCLC and/or its ability to identify patients with a $\dot{V}O_{2\text{peak}} < \text{or} \geq 15$ mL/kg/minute in order to provide indications regarding either suitability for surgery, or the need for further testing.

Methods

Population and design

All patients in this paper were retrospectively included in the analysis. The institutional ethics committee of the Rouen University Hospital approved the data extraction for this study (n°E2019-67). Patients all had been diagnosed with NSCLC and had either a predicted postoperative forced expiratory volume in 1 second (ppoFEV1) or a predicted postoperative diffusing capacity for carbon monoxide (ppoDLCO) $< 60\%$,⁷ and been referred for complementary tests by thoracic surgeon or pneumologist. The predicted postoperative values of FEV1 and DLCO were estimated by preoperative value/total number of functioning segments before the operation, and \times the residual number of functioning segments after the operation.¹² The patients had undergone CPX as part of their preoperative assessment for pulmonary resection between March 2018 and February 2019. In addition, they had all also been assessed using 3CRT in

the physiology department of Rouen university hospital, France, since the department was trialing the test to determine if it was clinically feasible. All tests were carried out by the physiology medical team trained in carrying out stress assessment tests.

Assessments

Pulmonary function

Pulmonary function tests were carried out according to the American Thoracic Society and the European Respiratory Society guidelines¹⁴ using plethysmography (Masterscreen, Jaeger, Witsburg, Germany). Values were expressed as percentages of established theoretical values for European populations.¹⁵

Cardiopulmonary exercise test

The CPX room was air-conditioned and kept at a constant temperature of 19°C for all tests, and the hygrometry was not controlled in current practice. The measuring instruments were recalibrated every half day with a reading of the atmospheric pressure. Patients were advised to avoid strenuous exercise and the consumption of alcohol, tobacco or caffeine for 24 hours prior to examination. CPX was performed on an electromagnetic ergometer (Ergoselect 200, Ergoline, Bitz, Germany) using a standardized, incremental protocol.¹⁶ Following a three-minute warm-up, incremental ramp exercise (5 to 15 W/minute) was maintained until exhaustion. Markers used to consider the CPX as maximal were determined according to current guidelines.¹⁶ A face mask (Hans Rudolph, Inc., Kansas City, MO), pneumotach and gas analyzer (Ergocard,

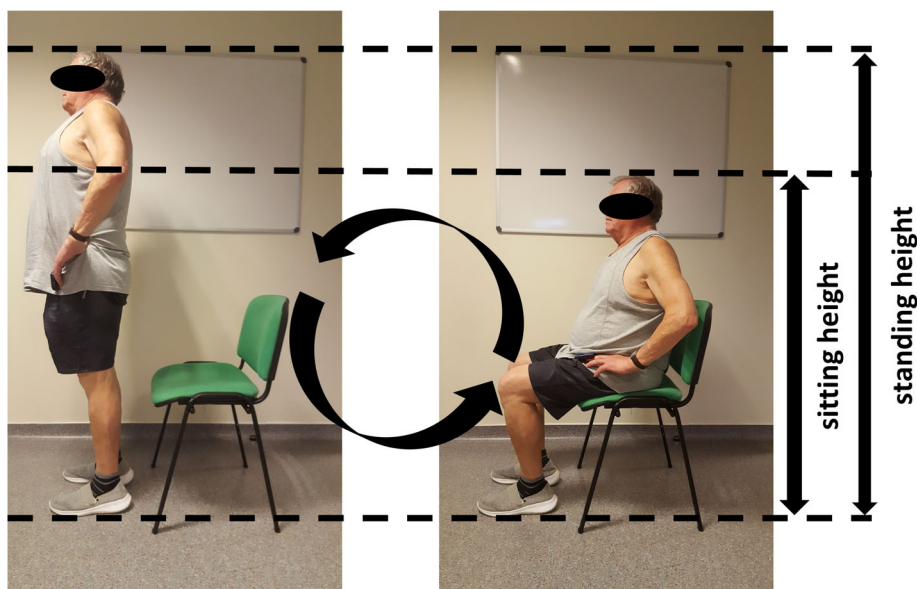
Medisoft, Louvain, Belgium) were used to measure breath-by-breath oxygen uptake ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$). Heart rate (HR) was continuously monitored with a 12-lead electrocardiogram (Ergocard, Medisoft, Louvain, Belgium).

3-minute chair rise test (3CRT)

The 3CRT was performed in the same condition (CPX room) according to the methodology validated by Aguilaniu *et al*¹³ Test instructions and instructions for rating the 0 to 10 points Borg scale (dyspnea and fatigue) were given while the patient was sitting at rest on a standard chair (floor to seat height 48 cm); this chair was then used for the test: “The aim of the exercise is to stand up and sit down repeatedly for three minutes. You must keep your hands on your hips all the time. I’ll give you the pace for the first minute by saying: “sit”, “stand” or by doing the sit-to-stand with you. During the last two minutes try to stand up and sit down as many times as possible. I’ll let you know how much time is left, for example: “1 minute and 30 seconds to go”, “1 minute to go”, “30 seconds to go”. You can slow down or speed up at any time. If the exercise is too difficult, you can have a little rest then continue. You can also stop the test before the end of three minutes if you feel too tired or breathless to finish it.” A chair rise was defined as one complete movement from sitting to standing and then sitting again (Fig 1).

Depending on the patient’s FEV1 value, the pace during the first minute was set to ensure that either 12 (FEV1 < 1200 mL) or 20 (FEV1 ≥ 1200 mL) rises were performed, in order to reduce interindividual variability at the start of the test.¹³ At the end of the test, physiological data

Figure 1 Installation and execution of the 3-minute chair rise test (3CRT). The patient was asked to stand up and sit down repeatedly for three minutes keeping their hands on their hips all the time. In the study the number of rises and the vertical distance reached (= [patient’s standing height - sitting height] x number of chair rises) were recorded.



(SpO₂, HR) and symptoms (dyspnea and leg fatigue with the Borg scale) were recorded. The number of chair rises was also recorded and two variables were calculated: (i) the vertical distance reached (in meters) = (patient's standing height - sitting height) x number of chair rises and (ii) the weight displaced (patient's weight x the number of chair rises).

Statistical analysis

Categorical data are expressed as numbers (percentages). Continuous data are expressed as means ± standard deviation or medians (interquartile range) according to their distribution; normality was assessed using the Shapiro-Wilk test. Paired *t*-tests or Wilcoxon matched-pairs signed rank tests were used for the comparison of continuous data depending on the normality of the distributions.

In order to predict the $\dot{V}O_{2peak}$, a multiple regression was undertaken using $\dot{V}O_{2peak}$ as the dependent variable. First, the univariate relationships between the $\dot{V}O_{2peak}$ measured during CPX and each demographic variable (age, BMI and FEV1) and each performance outcomes of the 3CRT (number of rises, vertical distance reached and weight displaced) were assessed using a Pearson's correlation test. The variables identified as related to $\dot{V}O_{2peak}$ with a *P*-value <0.10 were assessed for interrelationships and entered in a multivariate analysis. In the case of a strong interrelationship (*r* > 0.80), only the variable most related

with $\dot{V}O_{2peak}$ was used. Finally, a multivariate forward/backward stepwise regression was used to derive the best model to predict $\dot{V}O_{2peak}$. Agreement between the measured $\dot{V}O_{2peak}$ (during CPX) and predicted $\dot{V}O_{2peak}$ was evaluated using a Bland-Altman analysis and the mean absolute difference (MAD) between both results was calculated. Clinical equivalence between measured and predicted $\dot{V}O_{2peak}$ was defined a priori as: limits of agreements (upper and lower bounds) < 1.5 mL/kg/minute, corresponding to less than 10% of risk of bias.

The ability of the 3CRT to predict a cutoff $\dot{V}O_{2peak} \geq 15$ mL/kg/minute was evaluated by sensitivity, specificity and receiver operating characteristic (ROC) curve analyses. A *P*-value < 0.05 was considered statistically significant in all cases. GraphPad Prism 5.03 and R 3.6.1 software were used for all analyses.

Results

Patients

Between March 2018 and February 2019, 51 patients were referred for CPX as part of a preoperative evaluation for NSCLC. Of these, 13 did not undergo the 3CRT because of orthopedic limitations associated with disabling pain. A further two CPXs were uninterpretable due to submaximality of effort. The flow chart of these results is presented in Fig 2. Patient characteristics for the 36

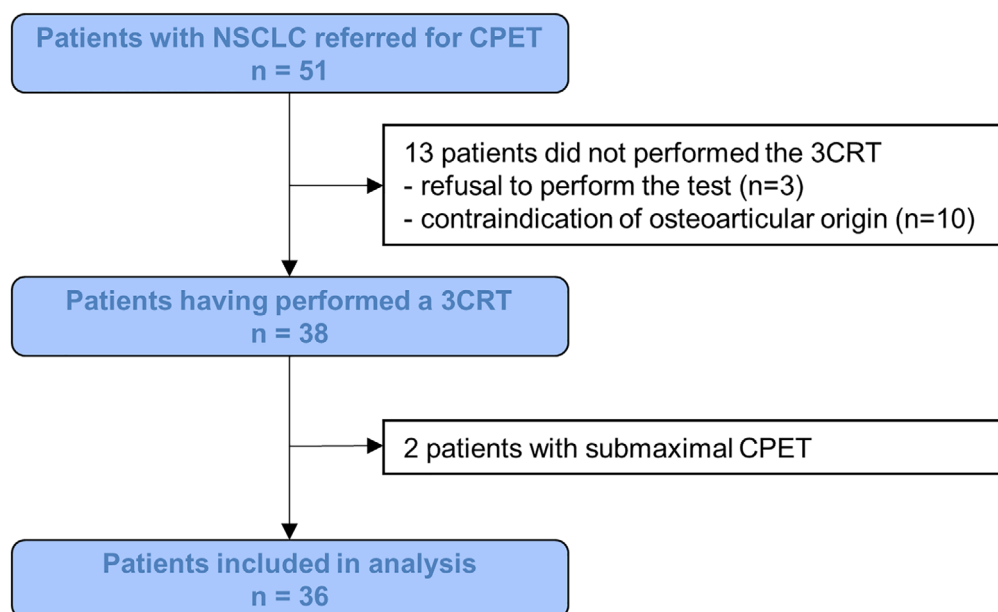


Figure 2 Flow-chart of patients included in the study; NSCLC, non-small cell lung cancer; CPX, cardiopulmonary exercise test; 3CRT, 3-minute chair rise test.

Table 1 Patient characteristics (n = 36)

| Variable (units) | |
|-------------------------------------|---------------------|
| Age (years), mean ± SD | 65.6 ± 7.7 |
| Male, n (%) | 27 (75%) |
| BMI (kg/m ²), mean ± SD | 25.4 ± 5.4 |
| Lung function | |
| FEV1/FVC (%), mean ± SD | 54.1 ± 13.4 |
| FEV1 (L), median (Q1 to Q3) | 1.7 (1.2 to 2.0) |
| FEV1 (% predicted), mean ± SD | 58.4 ± 18.6 |
| RV/TLC (%), median (Q1 to Q3) | 49.5 (43.3 to 60.0) |
| DLCO (%), mean ± SD | 60.7 ± 20.3 |
| mMRC, mean ± SD | 1.5 ± 1.0 |
| Tobacco | |
| Pack-years, median (Q1 to Q3) | 50.0 (36.3 to 60.0) |
| Former, n (%) | 24 (66%) |

BMI, body-mass index; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; RV, residual volume; TLC, total lung capacity; DLCO, diffusing capacity of the lung for carbon monoxide; mMRC, modified Medical Research Council dyspnea scale.

participants are shown in Table 1. Comorbidities and treatments are shown in Table S1. The CPX and 3CRT results are summarized in Table 2.

Correlation between $\dot{V}O_{2PEAK}$ and 3CRT

There was a significant correlation between the $\dot{V}O_{2peak}$ and the number of chair rises in three minutes ($r^2 = 0.37$, $P < 0.01$) as well as the vertical distance reached during the 3CRT ($r^2 = 0.62$, $P < 0.01$) (Fig 3). The other variables that were significantly correlated with $\dot{V}O_{2peak}$ were: age

($r^2 = 0.29$, $P < 0.01$), BMI ($r^2 = 0.18$, $P = 0.01$) and FEV1 ($r^2 = 0.12$, $P = 0.04$).

Capacity of the 3CRT to predict $\dot{V}O_{2PEAK}$

The best model determined by the multivariate analysis to predict $\dot{V}O_{2peak}$ was: $\dot{V}O_{2peak}$ predicted = $(0.04765 \times \text{FEV1 in \% predicted}) - (0.20759 \times \text{BMI in kg/m}^2) - (0.11589 \times \text{age in years}) + (0.38609 \times \text{vertical distance in m}) + 16.62869$; $r^2 = 0.75$, $P < 0.01$. The mean $\dot{V}O_{2peak}$ measured during CPX and predicted by the previous equation was not significantly different 14.6 ± 3.6 vs. 14.6 ± 3.1 , $P = 0.99$ (Table 2).

The bias between the $\dot{V}O_{2peak}$ predicted using this equation and the measured $\dot{V}O_{2peak}$ was 0.0 ± 1.7 mL/kg/minute, but the 95% limits of agreement were -3.5 to 3.5 . The corresponding Bland-Altman (B&A) plots are presented in Fig 4. The mean absolute difference (MAD) was 1.5 ± 1.0 mL/kg/minute. These results indicate that even if the r-square of the predictive model was high, it did not provide an adequate fit for our data.

Capacity of the 3CRT to predict a $\dot{V}O_{2PEAK} > 15$ mL/kg/minute

During CPX, there were 16 patients with a $\dot{V}O_{2peak} \geq 15$ mL/kg/minute and 20 who did not reach this capacity. The ROC curve analysis is presented in Fig 5 and detailed in Table S2.

Table 2 Cardiopulmonary exercise testing (CPET) and 3-minute chair rise test (3CRT) (n = 36)

| | CPET | 3CRT | P-value |
|--------------------------------------------------|--------------------|-------------------------|----------|
| Number of chair rises (n), mean ± SD | - | 51.0 ± 11.7 | |
| Vertical distance reached (m), mean ± SD | - | 20.9 ± 4.7 | |
| $\dot{V}O_{2peak}$ (mL), mean ± SD | 1048.0 ± 280.0 | - | |
| $\dot{V}O_{2peak}$ (mL/kg/minute), mean ± SD | 14.6 ± 3.6 | 14.6 ± 3.1 (predicted) | 0.99 |
| $\dot{V}O_{2peak}$ (% predicted), mean ± SD | 61.6 ± 14.1 | 61.6 ± 11.6 (predicted) | 1.00 |
| W_{peak} (watts), mean ± SD | 81.6 ± 23.9 | - | |
| W_{peak} (% predicted), mean ± SD | 65.9 ± 18.7 | - | |
| $\dot{V}E/\dot{V}CO_2$ slope, mean ± SD | 37.3 ± 7.7 | - | |
| HRmax (bpm), mean ± SD | 127.0 ± 21.4 | 115.9 ± 18.9 | < 0.01 * |
| HRmax (%predicted), mean ± SD | 75.7 ± 11.7 | 69.0 ± 11.0 | < 0.01 * |
| Δ HR (bpm), mean ± SD | 45.2 ± 17.7 | 33.0 ± 15.4 | < 0.01 * |
| Δ SpO ₂ (%), median (Q1 to Q3) | -2.0 (0.0 to -3.0) | -2.0 (-1.0 to -5.0) | 0.28 |
| Rest dyspnea (Borg), median (Q1 to Q3) | 0.0 (0.0 to 0.0) | 0.0 (0.0 to 0.5) | 0.65 |
| Δ dyspnea (Borg), mean ± SD | 5.0 ± 1.8 | 3.7 ± 2.2 | < 0.01 * |
| Rest fatigue (Borg), median (Q1 to Q3) | 0.0 (0.0 to 0.1) | 0.0 (0.0 to 1.0) | 0.19 |
| Δ fatigue (Borg), mean ± SD | 4.8 ± 2.3 | 4.0 ± 2.1 | 0.12 |

$\dot{V}O_{2peak}$, peak of oxygen consumption during CPET; W_{peak} , peak power reached during CPET; $\dot{V}E/\dot{V}CO_2$ slope, linear regression of the ratio between the increase in minute ventilation ($\dot{V}E$) and the expired carbon dioxide flow ($\dot{V}CO_2$); HR, heart rate; Δ , delta between rest and the end of the test; SpO₂, pulsed oxygen saturation.

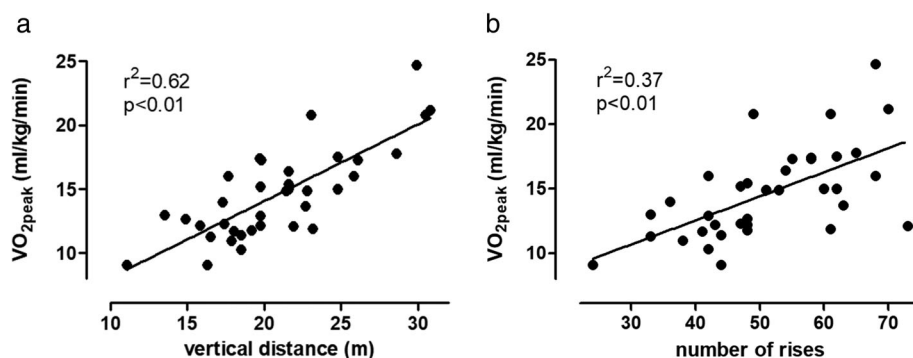


Figure 3 Correlation between the peak oxygen uptake ($\dot{V}O_{2peak}$) measured during cardiopulmonary exercise test with (a) the vertical distance reached, and (b) the number of chair rises, during the 3CRT.

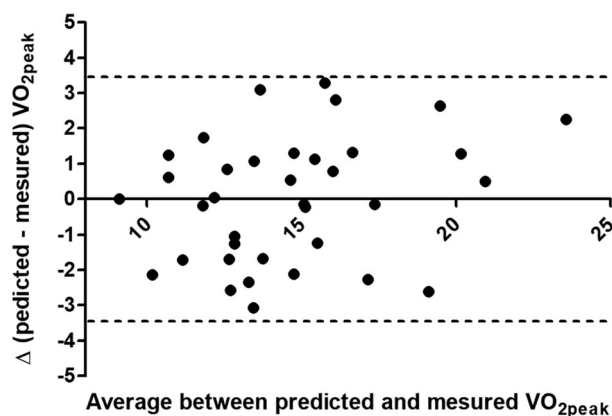


Figure 4 Bland-Altman plots for the estimation of the peak oxygen uptake ($\dot{V}O_{2peak}$) using the predictive equations derived from the 3-minute chair rise test (3CRT) performance. The point-to-point difference (Δ) between the two values (actually predicted minus measured) is plotted against the mean of the two values; bias = 0.0, 95% CI limits of agreement (lower and upper bounds) were -3.5 to 3.5 mL/kg/minute.

The area under the curve (AUC: 95% CI) was 0.82 (0.67 to 0.96). A number of chair rises ≥ 49 predicted a $\dot{V}O_{2peak} \geq 15$ mL/kg/minute with a sensitivity of 81% and a false-positive rate of 25% (specificity: 75%). The false-positive rate reduced to 15%, 10% and 5% for patients who achieved 54, 62 and 65 rises, respectively.

In this cohort, the threshold of 49 chair rises was associated with a positive predictive value (PPV) and a negative predictive value (NPV) to detect a $\dot{V}O_{2peak} \geq 15$ mL/kg/minute of 72% and 83%, respectively.

Discussion

The incidence of lung cancer is increasing worldwide.¹⁷ Access to curative surgical treatment for patients with NSCLC requires an assessment of functional capacity in order to identify patients at risk.^{7, 12} Since $\dot{V}O_{2peak}$ is a powerful predictive marker in many chronic pathologies, the demand for CPX is exploding in many institutions.

The need to develop field tests to estimate oxygen uptake is particularly topical. This study demonstrated a significantly positive relationship between performance on the 3CRT and $\dot{V}O_{2peak}$ measured during CPX in patients with NSCLC. The vertical distance reached during 3CRT was particularly strongly correlated with $\dot{V}O_{2peak}$ results. According to the multivariate analysis, the four independent variables related to $\dot{V}O_{2peak}$ during the 3CRT were the vertical distance reached, age, BMI and FEV1. Although the equation derived from the multivariate regression did not accurately predict specific $\dot{V}O_{2peak}$, the number of 49 or more rises performed during the 3CRT predicted a $\dot{V}O_{2peak} \geq 15$ mL/kg/minute with a sensitivity of 81% and a specificity of 75%.

To our knowledge, this is the first study to assess the ability of the 3CRT method as a tool to determine the need for presurgical CPX in patients with NSCLC. The 3CRT is one of a set of many sit-to-stand-tests (STST). Although they all evaluate the ability to get up from a chair without using the upper limbs as a measure of physical capacity, the specific aims and methods of each differ. The 1-minute STST (1-STST) particularly is used in patients with COPD. It is well correlated to quadriceps strength,¹⁸ as well as distance walked during the 6-minute walk test (6MWT), thus providing an estimate of functional capacity with less hemodynamic stress.^{19, 20} However, such quick tests do not reflect cardiorespiratory capacity, especially as $\dot{V}O_2$ kinetics are known to be slowed and related to the severity of the respiratory disease.^{21, 22} For patients with NSCLC, a longer evaluation over 3 minutes seems more appropriate since respiratory function is often altered and it may take 3 minutes for cardiorespiratory function to adapt to a constant load test.

We believe this test is valuable since it can easily be performed during a consultation to provide data to guide further therapeutic decisions. Similarly, to tests such as the SWT, the SCT and CPX, the main contraindication to its use is disabling lower limb pain. Patients with peripheral arteriopathy and hip prostheses were able to perform the 3CRT in the present study.

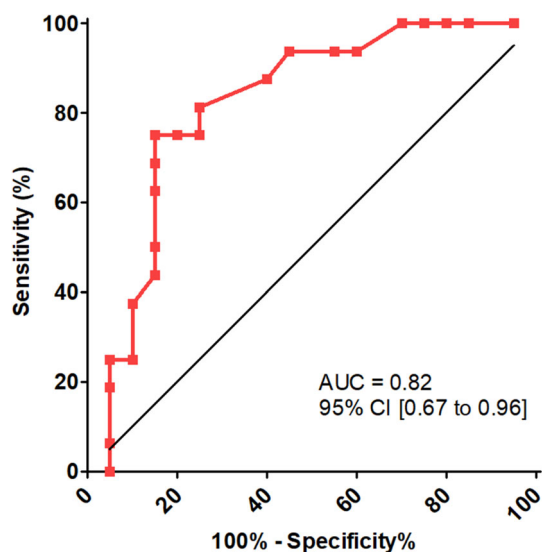


Figure 5 Receiver operating characteristic curve (ROC curve) performed to determine a threshold of the number of chair rises to predict a $\dot{V}O_{2\text{peak}} > 15$ mL/kg/minute: sensitivity (% of patients positively considered with a $\dot{V}O_{2\text{peak}} \geq 15$ mL/kg/minute) is plotted against 100%-specificity% (% of patients with a $\dot{V}O_{2\text{peak}} < 15$ mL/kg/minute falsely considered positive) at each possible threshold. Accuracy is measured by the area under the curve (AUC). An area of 1 = perfect; an area of 0.5 = inadequate.

The lack of accuracy of the prediction of specific $\dot{V}O_{2\text{peak}}$ value by the multivariate regression equation prohibit its use in clinical practice to predict $\dot{V}O_{2\text{peak}}$. The fact HR_{max} and Borg rating of dyspnea were significantly higher during the CPX suggests that the 3CRT was physiologically less stressful, or the evaluators did not motivate the patient as much as during the CPX during this new test. It is also possible that the sample size was too small and thus the dispersion of the data was relatively high. Larger studies should therefore be conducted to refine the equation and assess the influence of the evaluation conditions.

The ROC analysis showed that performance of 49 rises or more during the 3CRT was predictive of a $\dot{V}O_{2\text{peak}} \geq 15$ mL/kg/minute, with a high level of sensitivity (81%) and a moderate false-positive rate (25%) (specificity: 75%). To compare with other field tests used in screening NSCLC patients in the preoperative assessment, the PPV and NPV for the threshold of 49 rises during the 3CRT were calculated (72% and 83%, respectively). A study of the SWT found higher PPV and NPV (90% each) for a distance ≥ 250 meters to predict a $\dot{V}O_{2\text{peak}} > 15$ mL/kg/minute.⁸ For the SCT, a high PPV (86%) was found for a climb ≥ 22 meters to predict a $\dot{V}O_{2\text{peak}} > 15$ mL/kg/minute; however, the NPV was only 62%.¹⁰ The SWT is therefore the most

accurate of these tests in determining which patients need to be referred for CPX. However, it is also the most difficult to carry out in everyday practice, as none of the thoracic surgeons interviewed in a recent American survey prescribe a SWT.²³ Comparatively to the SWT and SCT, the 3CRT can be performed in nearly any care setting, including very limited spaces such as consultation rooms by surgeons themselves, or allied health professionals, and could be sufficient to determine the need for presurgical CPX in patients with NSCLC.

During the 3CRT validation study in COPD patients, Aguilaniu *et al.* reported that patients who were able to perform more than 50 rises during the 3 minutes had a lower score on the disability related to COPD tool (DIRECT) questionnaire, suggesting less impaired function.¹³ Similarly, Lévesque *et al.* reported a mean number of 51.9 ± 13.1 rises during the 3CRT in patients with COPD whose BODE index score was in the first favorable quartile (0–2 /10).²⁴ These results are consistent with the threshold of 49 rises found in the present study to predict a $\dot{V}O_{2\text{peak}} \geq 15$ mL/kg/minute in the present cohort.

This study had several limitations. First, there may have been selection bias due to the retrospective design. Second, even if the multivariate regression analysis model ($r = 0.75$, $P < 0.01$) and ROC curve analyses (AUC 0.82 [0.67 to 0.96]) were statistically significant, the study was not powered a priori and was probably underpowered. The measurement of post hoc statistical power is questionable and has not been recommended by several authors.²⁵ We took the option not to include this measure in the present paper, as we felt that it would not strengthen the level of evidence of this preliminary retrospective study. Third, a separate validation with an independent cohort of patients is necessary to confirm the PPV and NPV for the threshold of 49 rises during the 3CRT to predict a $\dot{V}O_{2\text{peak}} \geq 15$ mL/kg/minute. Finally, this study only focused on the evaluation of performance on the 3CRT in relation to the $\dot{V}O_{2\text{peak}}$ as a postoperative risk factor, and did not directly evaluate postoperative complications.

Nevertheless, the results of this preliminary, retrospective study suggest that this simple tool is promising as a screening test prior to CPX in patients with NSCLC and thus larger, prospective studies are justified. Moreover, the data relating to the relationship between 3CRT performance and $\dot{V}O_{2\text{peak}}$ can be used to determine the appropriate design of a prospective study with a larger number of patients.

In conclusion, performance of at least 49 chair rises during the 3CRT indicated a $\dot{V}O_{2\text{peak}} \geq 15$ mL/kg/minute, similar to results from the SCT and the SWT. However, prediction of the specific $\dot{V}O_{2\text{peak}}$ value based on the 3CRT performance was insufficiently accurate or sensitive to be used as a standalone method for determining the specific

$\dot{V}O_{2\text{peak}}$ value. The 3CRT is a simple field test that could be very useful as a screening test to indicate patients with NSCLC who require further testing with CPX and those who can be safely referred for surgery. Prospective studies with larger sample sizes are needed to validate these results.

Acknowledgments

We thank the Aide à Domicile aux Insuffisants Respiratoires (ADIR) Association for supporting this work, the Rouen University Hospital Physiology Department team for their help with data entry, and Johanna Robertson and Jennifer Dandrea-Palethorpe for language assistance and constructive criticism.

Disclosure

The authors report having no conflict of interest to disclose in relation to the present study.

References

- Howington JA, Blum MG, Chang AC, Balekian AA, Murthy SC. Treatment of stage I and II non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2013; **143**(5 Suppl):e278S–e313S.
- Grose D, Morrison DS, Devereux G *et al.* Comorbidities in lung cancer: Prevalence, severity and links with socioeconomic status and treatment. *Postgrad Med J* 2014; **90** (1064): 305–10.
- Gagne S, McIsaac DI. Modifiable risk factors for patients undergoing lung cancer surgery and their optimization: A review. *J Thorac Dis* 2018; **10** (Suppl 32): S3761–s3772.
- Lugg ST, Agostini PJ, Tikka T *et al.* Long-term impact of developing a postoperative pulmonary complication after lung surgery. *Thorax* 2016; **71** (2): 171–6.
- Benzo R, Kelley GA, Recchi L, Hofman A, Sciarba F. Complications of lung resection and exercise capacity: A meta-analysis. *Respir Med* 2007; **101** (8): 1790–7.
- Brunelli A, Belardinelli R, Refai M *et al.* Peak oxygen consumption during cardiopulmonary exercise test improves risk stratification in candidates to major lung resection. *Chest* 2009; **135** (5): 1260–7.
- Brunelli A, Kim AW, Berger KI, Addrizzo-Harris DJ. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2013; **143**(5 Suppl):e166S–e190S. <https://doi.org/10.1378/chest.12-2395>.
- Benzo RP, Sciarba FC. Oxygen consumption, shuttle walking test and the evaluation of lung resection. *Respiration* 2010; **80** (1): 19–23.
- Brunelli A, Refai M, Xiume F *et al.* Performance at symptom-limited stair-climbing test is associated with increased cardiopulmonary complications, mortality, and costs after major lung resection. *Ann Thorac Surg* 2008; **86** (1): 240–7; discussion 247–248.
- Brunelli A, Xiume F, Refai M *et al.* Peak oxygen consumption measured during the stair-climbing test in lung resection candidates. *Respiration* 2010; **80** (3): 207–11.
- British Thoracic Society, Society of Cardiothoracic Surgeons of Great Britain and Ireland Working Party. BTS guidelines: Guidelines on the selection of patients with lung cancer for surgery. *Thorax* 2001; **56** (2): 89–108.
- Brunelli A, Charloux A, Bolliger CT *et al.* ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients (surgery and chemo-radiotherapy). *Eur Respir J* 2009; **34** (1): 17–41.
- Aguilaniu B, Roth H, Gonzalez-Bermejo J *et al.* A simple semipaced 3-minute chair rise test for routine exercise tolerance testing in COPD. *Int J Chron Obstruct Pulmon Dis* 2014; **9**: 1009–19.
- Miller MR, Crapo R, Hankinson J *et al.* General considerations for lung function testing. *Eur Respir J* 2005; **26** (1): 153–61.
- Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report working party standardization of lung function tests, European Community for Steel and Coal Official Statement of the European Respiratory Society. *Eur Respir J Suppl* 1993; **16**: 5–40.
- American Thoracic Society, American College of Chest Physicians. ATS/ACCP statement on cardiopulmonary exercise testing. *Am J Respir Crit Care Med* 2003; **167** (2): 211–77.
- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin* 2019; **69** (1): 7–34.
- Zanini A, Aiello M, Cherubino F *et al.* The one repetition maximum test and the sit-to-stand test in the assessment of a specific pulmonary rehabilitation program on peripheral muscle strength in COPD patients. *Int J Chron Obstruct Pulmon Dis* 2015; **10**: 2423–30.
- Ozalevli S, Ozden A, Itil O, Akkoclu A. Comparison of the sit-to-stand test with 6 min walk test in patients with chronic obstructive pulmonary disease. *Respir Med* 2007; **101** (2): 286–93.
- Reychler G, Boucard E, Peran L *et al.* One minute sit-to-stand test is an alternative to 6MWT to measure functional exercise performance in COPD patients. *Clin Respir J* 2018; **12** (3): 1247–56.
- Puente-Maestu L, Sanz ML, Sanz P, Nunez A, Gonzalez F, Whipp BJ. Reproducibility of the parameters of the on-transient cardiopulmonary responses during moderate exercise in patients with chronic obstructive pulmonary disease. *Eur J Appl Physiol* 2001; **85** (5): 434–41.

- 22 Pessoa BV, Beltrame T, Di Lorenzo VA, Catai AM, Borghi-Silva A, Jamami M. COPD patients' oxygen uptake and heart rate on-kinetics at cycle-ergometer: Correlation with their predictors of severity. *Braz J Phys Ther* 2013; **17** (2): 152–62.
- 23 Clark JM, Marrufo AS, Kozower BD *et al.* Cardiopulmonary testing before lung resection: What are thoracic surgeons doing? *Ann Thorac Surg* 2019; **108** (4): 1006–12.
- 24 Levesque J, Antoniadis A, Li PZ *et al.* Minimal clinically important difference of 3-minute chair rise test and the DIRECT questionnaire after pulmonary rehabilitation in COPD patients. *Int J Chron Obstruct Pulmon Dis* 2019; **14**: 261–9.
- 25 Zhang Y, Hedro R, Rivera A, Rull R, Richardson S, Tu X. Post hoc power analysis: Is it an informative and meaningful analysis? *General Psychiatry* 2019; **32**: e100069.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Table S1: Comorbidities and treatments ($n = 36$). **Table S2:** Receiver operating characteristic analysis of the number of chair rises versus peak oxygen consumption ($\dot{V}O_{2\text{peak}} \geq 15$ mL/kg/minute; binary outcome).