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Pulmonary function tests in the preoperative evaluation of lung cancer surgery candidates. A review of guidelines

Marzena Trzaska-Sobczak, Szymon Skoczyński, Władysław Pierzchała

Department of Pneumology, Medical University of Silesia in Katowice, Poland

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Abstract

Before planned surgical treatment of lung cancer, the patient's respiratory system function should be evaluated. According to the current guidelines, the assessment should start with measurements of FEV_1 (forced expiratory volume in 1 second) and DLco (carbon monoxide lung diffusion capacity). Pneumonectomy is possible when FEV_1 and DLco are > 80% of the predicted value (p.v.). If either of these parameters is < 80%, an exercise test with VO_2 max (oxygen consumption during maximal exercise) measurement should be performed. When VO_2 max is < 35 % p.v. or < 10 ml/kg/min, resection is associated with high risk. If VO_2 max is in the range of 35-75% p.v. or 10-20 ml/kg/min, the postoperative values of FEV_1 and DLco (ppoFEV_1, ppoDLco) should be determined. The exercise test with VO_2 max measurement may be replaced with other tests such as the shuttle walk test and the stair climbing test. The distance covered during the shuttle walk test should be > 400 m. Patients considered for lobectomy should be able to climb 3 flights of stairs (12 m) and for pneumonectomy 5 flights of stairs (22 m).

Key words: lung cancer, preoperative evaluation, exercise testing.

Streszczenie

Przed planowanym operacyjnym leczeniem raka płuca należy dokonać oceny czynności układu oddechowego. Według aktualnych wytycznych w pierwszej kolejności powinno się dokonać pomiaru natężonej objętości wydechowej pierwszosekundowej (FEV_1) i zdolności dyfuzyjnej płuc dla tlenku węgla (DLco). Zabieg pneumonektomii można przeprowadzić, gdy wartość zarówno FEV_1, jak i DLco przekracza 80% wartości należnej. Jeśli jeden z powyższych parametrów jest niższy niż 80% wartości należnej, należy na kolejnym etapie wykonać badanie wysiłkowe z pomiarem VO_2 max. Gdy VO_2 max jest < 35% wartości należnej lub < 10 ml/kg m.c./min, leczenie operacyjne jest obarczone dużym ryzykiem. Jeśli wartość VO_2 max mieści się w przedziale 35–75% wartości należnej lub wynosi 10–20 ml/kg m.c./min, należy wyliczyć należne pooperacyjne wartości FEV_1, DLco (ppoFEV_1, ppoDLco). Badanie wysiłkowe z oceną VO_2 max może być zastąpione testem marszowym wahadłowym lub testem wchodzenia po schodach. Pacjent w teście marszowym wahadłowym powinien pokonać dystans > 400 m. Zdolność pokonania 3 kondygnacji schodów w teście wchodzenia po schodach (12 m) kwalifikuje do lobektomii. Chory planowany do pneumonektomii powinien pokonać różnicę wysokości równą 5 kondygnacjom (22 m).

Słowa kluczowe: rak płuca, ocena przedoperacyjna, testy wysiłkowe.

Introduction

Lung cancer is currently responsible for the largest number of "neoplastic" deaths both among women and men [1, 2]. Surgical treatment is one of the methods for treating this disease. The option of surgical treatment is largely determined by the stage of the neoplasm according to the TNM (tumor, node, metastasis) classification [3]. However, in some patients, the surgical options are also limited by concomitant respiratory system diseases, which impair lung function. One such disease, which most often limits the possibility of resection, is chronic obstructive pulmonary disease (COPD). It is, moreover, a risk factor for lung cancer independent of smoking [4]. Establishing the respiratory reserve is an important element of qualifying patients for resection of lung parenchyma. The currently binding recommendations of the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS) from 2009 underscore the significance of cooperation within multispecialist teams consisting of pneumonologists, thoracic surgeons, oncologists, and radiation therapists in determining the optimal treatment strategy for individual patients [5]. In the proposed algorithm for conducting the qualifica-

Address for correspondence: Marzena Trzaska-Sobczak, Department of Pneumology, Medical University of Silesia in Katowice, Medyków 14, 40-752 Katowice, phone: +48 501 459 101, e-mail: trzaska@mp.pl

tion procedure, the subsequent function tests are aimed at increasing both perioperative safety and the percentage of patients qualified for surgical treatment.

The aim of the study was to present the current guidelines concerning the assessment of respiratory system function before qualifying patients for the surgical treatment of lung cancer and to highlight the changes in relation to previous recommendations.

Preliminary assessment – spirometry and exercise capacity testing

According to the current guidelines of ERS and ESTS, both spirometry, aimed at measuring FEV_1 (forced expiratory volume in 1 second), and the assessment of the diffusing capacity of the lungs (DLco), performed by measuring gas diffusion within the lungs, are recommended during the first stage of qualifying patients for lung parenchyma resection [5].

Previous guidelines, both those published by the American College of Chest Physicians (ACCP) in 2007 and those published by the British Thoracic Society (BTS) in 2001, recommended only spirometry with FEV_1 measurement as the preliminary examination [6, 7]. The DLco examination was recommended only for patients with lowered FEV_1, post-exercise dyspnea disproportionate to FEV_1, or suspicion of interstitial lung disease [6, 7]. The latest guidelines include the DLco measurement in the preliminary function examination, as numerous studies have demonstrated that reduced DLco levels constitute an independent risk factor for increased mortality and perioperative complications, even in patients with normal FEV_1 [8-13]. In a large study encompassing 872 patients qualified for lung parenchyma resection, Brunelli *et al*. found reduced DLco levels in 508 patients (63%) with normal FEV_1, which resulted in an increased frequency of perioperative complications. This is one of the reasons for the recommendation that DLco assessment be performed routinely in all candidates for pulmonary parenchyma resections [9].

Spirometry should be conducted in accordance with the ERS/ATS standards [14]. The previously published guidelines established independent boundary values of FEV_1 for planned lobectomy and pneumonectomy (1.5 l and 2 l, respectively) [6]. Later guidelines added that FEV_1 should not be lower than 80% of the predicted value (p.v.), both in the case of planned lobectomy and pneumonectomy [7]. The current values employ only a percentage threshold value, which is 80% of the predicted value for both FEV_1 and DLco (Fig. 1) [5]. The preliminary assessment of respiratory function may be concluded if the values of both indices (FEV_1 and DLco) exceed 80% p.v. This means that surgical treatment is not burdened with an increased risk of complications and perioperative mortality [5].

When at least one of the parameters (FEV_1 or DLco) is lowered (< 80% p.v.), the next stage of the qualification process for lung parenchyma resection should establish the patient's exercise capacity (Fig. 1).

Exercise tests

Exercise tests are widely used in pulmonary diagnostics (including the process of qualifying patients for the surgical treatment of lung cancer) due to their higher prognostic value with regard to FEV_1 and DLco measurement. Engaging large groups of muscles, exercise tests significantly burden the circulatory and respiratory systems, enabling the estimation of the physiological functional reserve before the planned surgical procedure [15]. Exercise tests should be performed in patients with FEV_1 or DLco lower than 80% p.v. (Fig. 1) [5]. The best test among them is the cardiopulmonary exercise test (CPET), also known as ergospirometry. Cardiopulmonary exercise test may be performed on a treadmill or, as recommended for respiratory system diseases, on a cycloergometer [15]. The measurement of exercise capacity in ergospirometry is peak oxygen uptake expressed by the VO_2 max parameter [15].

Reduced VO_2 max results in an increased risk of post-resection complications [16].

This pertains especially to patients with VO_2 max < 65% p.v. (or < 16 ml/kg/min) [17]. Brunelli *et al*. reported that all deaths after lung resections that were at least as extensive as lobectomy occurred among patients whose VO_2 max was < 20 ml/kg/min [18].

Low-cost exercise tests

In Poland, CPET is relatively inaccessible and costly, and requires trained personnel. Other, lower-cost methods of assessing exercise capacity include the 6-minute walk test (6MWT), shuttle walk test (SWT), and stair climbing test.

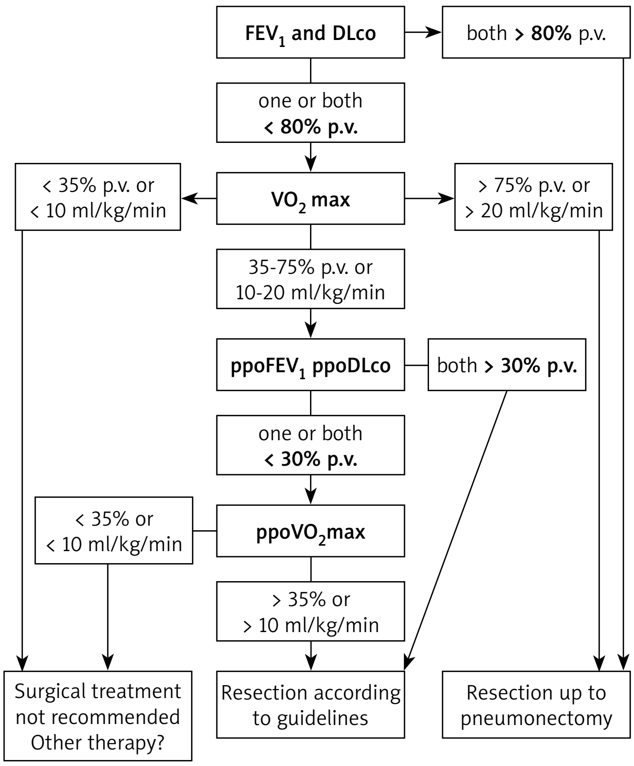

Fig. 1. Algorithm for assessing respiratory system function in lung cancer surgery candidates

The 6-minute walk test

The distance covered during 6MWT correlates well with VO_2 max in lung transplantation candidates [19]. However, it is not a good prognostic indicator in terms of the probability of complication occurrence after lung resection [20-30].

The shuttle walk test

During the test, the patient walks between 2 points, which are 10 m apart, at an increasing speed set by a test-specific sound signal. The distance covered during this test correlates well with VO_2 max [24-26]. Previous guidelines recommended 250 m to be the boundary value for increased complication frequency after lung resection [6].

Later reports demonstrated no significant difference in the distance covered during this test by patients with and without postoperative complications [27, 28]. On the other hand, it was revealed that some patients covered distances shorter than 250 m in spite of the fact that their VO_2 max values exceeded 15 ml/kg/min [28]. In the study group, all patients who walked more than 400 m in distance achieved VO_2 max values exceeding 15 ml/kg/min [28].

As a result, the shuttle walk test is currently recommended as a screening exercise test for patients qualified for resection due to lung cancer [29]. All patients with results over 400 m should undergo additional CPET in order to establish their VO_2 max [29].

Stair climbing

Stair climbing is another examination recommended for qualifying patients for lung cancer surgery [30, 31]. During this simple test, the patient climbs flights of stairs, thus ascending a certain distance and number of floors. As demonstrated by Brunelli *et al.*, patients who climb less than 12 m (3 floors) are twice as likely to suffer from complications, while mortality among them increases 13-fold, and the costs of their treatment rise 2.5-fold in comparison with patients who can climb 22 m (5 floors) [32].

Thus, the stair climbing test may be employed as a screening examination for the identification of patients who are able to ascend 22 m (5 floors) of stairs and can, therefore, undergo lung resection up to pneumonectomy without increased risk [32].

Lately, reports have been published, pointing to the significance of the speed of stair climbing with regard to the frequency of complications after lung resection procedures (the majority of the studied patients were operated on for non-neoplastic reasons) [33, 34]. It was demonstrated that climbing 20 m within 80 s (speed ≥ 15 m/min) correlates well with VO_2 max [33]. All patients who achieved a result of less than 80 s had VO_2 max above 20 ml/kg/min [33].

Also, Ambrozini *et al.* demonstrated that climbing 12.16 m in a time exceeding 37.5 s indicates a higher risk of complications after thoracic surgery procedures [34].

Perhaps a larger number of reports assessing the stair climbing speed of patients qualified for resections due to lung cancer will result in the preparation of appropriate expert guidelines.

Predicted postoperative values of FEV_1 and DLco ($ppoFEV_1$, ppoDLco)

After exercise tests, the next stage of preoperative function evaluation consists in calculating the predicted postoperative values of FEV_1 and DLco [5].

Previous guidelines recommended calculating $ppoFEV_1$ and ppoDLco if FEV_1 is lowered (< 1.5 l for lobectomy and < 2 l for pneumonectomy) [6, 7]. The current guidelines place $ppoFEV_1$ and ppoDLco calculations after exercise capacity tests and VO_2 max measurements (Fig. 1) [5].

Moreover, the latest guidelines include the calculation of predicted oxygen consumption after resection (VO_2 max) [5]. This pertains to patients in whom $ppoFEV_1$ or ppoDLco is lower than 30% p.v. (in previous guidelines, the boundary value of $ppoFEV_1$ and ppoDLco in qualifying patients for resection was 40% p.v.) [6, 7]. Considering the improving standards of perioperative care and the modern, less invasive surgical techniques, the boundary value of $ppoFEV_1$ and ppoDLco was lowered to 30% p.v. [5].

The formulae enabling the calculation of predicted postoperative values are similar for FEV_1, DLco, and VO_2 max [35].

When lobectomy is planned, the values of $ppoFEV_1$, ppoDLco, and $ppoVO_2$ max are calculated with consideration to the number of all resected segments (Formula 1) or obstructed segments whose number can be assessed using CT or bronchoscopy (Formula 2) [35]. In the case of pneumonectomy, scintigraphy and an assessment of perfusion within the resected lung are required [5-7].

Calculating predicted postoperative values (ppo)

A. Lobectomy

Formula 1.

$$\text{ppo } FEV_1 \text{ (DLco, } VO_2 \text{ max)} = \text{pre } FEV_1 \text{ (DLco, } VO_2 \text{ max)} \times \frac{\times (19 - \text{number of excised segments})}{19}$$

Right lung:	Left lung:
upper lobe – 3	upper lobe – 3
middle lobe – 3	lingula – 2
lower lobe – 5	lower lobe – 4

Formula 2.

ppo = preoperative value × (1 – a/b)

a – number of excised patent segments
b – total number of patent segments

B. Pneumonectomy

ppo = preoperative value × (1 – perfusion percentage within the resected lung)

New indicators in the preoperative assessment of lung cancer patients

The assessment of physical activity by means of simple tests evaluating daily energy expenditure correlates with perioperative mortality among adults [36].

Measuring motor activity with a pedometer facilitates the determination of the degree of exercise capacity impairment resulting from COPD or other diseases [37, 38]. Its usefulness in predicting negative effects of surgery, including thoracic surgery, requires further study.

The slope of the VE/VCO_2 curve obtained during CPET is an independent indicator of mortality in patients with moderate and severe COPD undergoing resection due to non-small-cell lung carcinoma [39]. The slope of VE/VCO_2 is a better predictive factor than VO_2 max, with regard to both mortality and perioperative complications in patients undergoing lung resection [40].

The increasing number of reports concerning the usefulness of these indicators in evaluating the risk of complications after lung cancer surgery procedures may well result in their routine use in preoperative evaluation in the future.

Special circumstances in the preoperative assessment of lung cancer patients

It should be remembered that surgical treatment of lung cancer is also possible in patients with significantly reduced lung function parameters (as long as FEV_1 and DLco are not lower than 20% p.v.) if the tumor is located in the upper lobes affected by emphysematous changes [7, 41]. In such cases, concurrent resection of emphysematous bullae serves the role of lung volume reduction surgery in COPD and improves lung ventilation. Another exception occurs if the exercise tests cannot be performed by a patient with orthopedic ailments, e.g. advanced degenerative changes of the hip or knee joints, in which case only the calculation of predicted postoperative lung function indicator values is required.

Conclusions

The qualification of lung cancer patients for resection is a multistage process. Qualifying for the procedure requires not only meeting histopathological and radiological criteria, but also having normal, good lung ventilation and diffusion capacity. In doubtful cases, it must be verified by assessing the patient's exercise capacity. Proper qualification is aimed at both increasing perioperative safety and raising the percentage of patients qualified for lung resection due to cancer.

Disclosure

The authors report no conflict of interest.

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