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Review Article

# Prehabilitation and rehabilitation for surgically treated lung cancer patients

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ABSTRACT

According to the published data, lung cancer was the most common and deadly malignancy between 2002 and 2008 in Taiwan, with a significant difference between the 5-year survival rate of patients who underwent surgery and those who did not receive surgical intervention. The anatomic resection with radical lymph node dissection is a curative treatment for lung cancer. Although there is insufficient evidence to support the routine functional assessment before surgery, the assessment of exercise capacity before surgery is considered pivotal in the management of patients with lung cancer, both for prognostic and therapeutic reasons. Prehabilitation could improve exercise capacity, and might increase the number of inoperable-to-operable patients and reduce postoperative morbidity and mortality. Furthermore, rehabilitation after surgery approach seems to improve patient physical performance and quality of life. Despite advances in research over the past decade on the role of rehabilitation in patients with lung resection, only a few physicians incorporate this type of treatment into the daily care of lung cancer patients. Therefore, the integration of rehabilitation with medical optimization in the perisurgical period deserves to receive more attention by clinicians to elucidate the most comprehensive interventions.



## 1. Introduction

Lung cancer is the most common and deadly malignancy in Taiwan, the cause of an estimated 33,919 new cases between 2002 and 2008. Although the 5-year survival rate is only 15.9%, the overall survival rate is as high as 60.7% in patients whose tumors are confined to the primary site at time of diagnosis. Unfortunately, this number only accounts for just 12.5% of the patients, and only 16.4% patients received surgical resection with a median survival of 13.2 months.[1]

Anatomic resection with radical lymph node dissection is a curative treatment for lung cancer. There is a significant difference between the 5-year survival rate of patients who underwent surgery (57.2%) and those who did not receive surgical intervention (7.5%), according to the published data in Taiwan. Patients who underwent lobectomy have a higher 5-year survival rate compared with patients who underwent other surgical procedures.[1]

Given the relatively poor prognosis for patients with lung cancer who cannot be treated surgically, every effort should be made to increase the number of patients eligible for surgery. Approximately 73% of men and 53% of women are diagnosed with chronic obstructive pulmonary disease (COPD) along with lung cancer.[2] These patients often have hyperinflation and increased labored breathing which leads to decreased activity levels, subsequent muscle deconditioning and poor exercise tolerance. Surgery in these patients can be associated with increased risk of morbidity and mortality after lung resection.[3] For lung cancer patients with no underlying chronic respiratory disease, physical symptom burden, fatigue and performance status may have a negative effect on general function and poor postoperative outcomes.[4,5]

The benefits of pulmonary rehabilitation in COPD are well-documented. Advances in research over the past decade, particularly supporting the use of exercise training, have rapidly

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progressed the role of rehabilitation in lung resected patients. This review article discusses the preoperative assessment of patients awaiting lung cancer surgery and the potential role of rehabilitation associating with the number of patients eligible for tumor resection. Finally, the impact of pulmonary rehabilitation on surgical outcomes during and after surgery are reviewed.

## 2. Preoperative evaluation

Surgical options in cases of lung cancer include pneumonectomy, lobectomy or sub-lobar resection, and are available for patients who are eligible for surgery. The advantages of limited pulmonary resection are in part the ability to preserve a greater amount of lung volume and reducing the risk of physiological impairment after surgery. Although surgery is the best option for treating patients with early-stage non-small-cell lung cancer (NSCLC), abnormal pulmonary function still occurs in patients with potentially resectable tumors. These patients may be at an increased risk of both immediate perioperative complications and long-term disability following surgical resection.[6] The level of acceptable risk for postoperative complications is somewhat subjective, and efforts persist to ensure the best predictive tests and define the threshold values necessary for minimizing surgical risk. Consequently, in considering whether the patient should undergo curative-intent surgical resection of lung cancer, the possible short-term perioperative risk from comorbid cardiopulmonary disease and the long-term risk of pulmonary disability must be balanced against the possible risk of reduced survival if an oncological suboptimal treatment strategy is chosen. The task of the preoperative assessment is to identify patients at an increased risk of both perioperative complications and long-term disability from lung cancer. This assessment is essential to allow communication between clinicians and their patients about treatment options and risks, so that informed decisions can be made. Preoperative functional evaluation is deemed necessary for all types of operations. Diffusing capacity of the lung (DLCO), one of the most clinically valuable tests of lung function, was established for predicting postoperative complications in patients with normal Forced Expiratory Volume in One Second (FEV1). The clinicians should not ignore the assessment of exercise capacity and Maximum Oxygen Uptake (VO2 max), which has been proven to be inversely correlated with post-operative morbidity and mortality, as shown by the guidelines laid down by the European Respiratory Society and the European Society of Thoracic Surgeons joint task force. The suggested tests include measurement of preoperative pulmonary function, calculation of predicted postoperative pulmonary function, measures of gas exchange, and exercise testing.[7]

In 2013, the American College of Chest Physicians provided a guideline to the preoperative physiological assessment of patients being considered for surgical resection of lung cancer.[6] It has been recommended that patients must be assessed by a multidisciplinary team before operation, regardless of age. During the preoperative period, optimal medical care for patients who have chronic respiratory disease should include smoking cessation, optimal pharmacologic and oxygen therapy when indicated, and prompt treatment of exacerbations. Patients with lung cancer are predisposed to atherosclerotic cardiovascular disease because of cigarette smoking, and the prevalence of underlying coronary artery disease is about 11–17%.[8,9] The risk of major postoperative cardiac complications, including myocardial ischemia, pulmonary edema, ventricular fibrillation or primary cardiac arrest and cardiac-related death, is about 2–3% following lung resection.[8,9] As a consequence, a preoperative cardiovascular risk assessment should be first performed. The Thoracic Revised Cardiac Risk Index (ThRCRI) is the preferred risk scoring tool to assess cardiac risk in patients undergoing noncardiac surgical procedures.[10] The risk score was based on weight values of high-risk surgery as follows (including lobectomy or pneumonectomy): 1.5 points; previous ischemic heart disease: 1.5 points; previous stroke or transient ischemic attack: 1.5 points; and serum creatinine $\geq$ 2 mg/dL: 1 point. Patients with ThRCRI $\geq$2 or any cardiac condition requiring medication or a newly suspected cardiac condition or limited exercise tolerance (inability to climb two flights of stairs) should be referred for a cardiac consultation and noninvasive testing, and the treatment results should be noted in these patients (Fig. 1).[10]

The next step is to assess FEV1 and DLCO. The Predicted Post-Operative (ppo) lung functions should be calculated by the operation methods. For pneumonectomy candidates, ventilation/perfusion scan (V/Q scan) method was suggested to calculate the ppo values of FEV1 or DLCO (ppo values = preoperative values $\times$ (1 − fraction of total perfusion for the resected lung), where the preoperative values are taken as the best measured postbronchodilator values. For lobectomy patients, ppo values of FEV1 or DLCO was calculated by segmental counting (ppo values = preoperative values $\times$ (1 − y/z), where the preoperative values are taken as the best measured postbronchodilator value, y is the number of functional or unobstructed lung segments to be removed and z is the total number of functional segments. If both the percent of ppoFEV1 and ppoDLCO values are greater than 60%, the patient is considered to be at low risk. This indicates that the expected risk of mortality is below 1% for perioperative death and cardiopulmonary complications following resection, and major anatomic resections including pneumonectomy can be safely performed. No further tests are required in this group. If either the percent ppoFEV1 or the percent of ppoDLCO are within 30–60% of predicted values, a low technology exercise test (e.g. stair climb test or shuttle walk test) should be performed. If either stair climbing test is greater than 22 m or shuttle walk distance greater than 400 m, patients are regarded as at low risk of anatomic resection. A formal cardiopulmonary exercise test is indicated when the percent of ppoFEV1 or ppoDLCO <30%, or when the performance of the stair-climbing test or the shuttle walk test is not satisfactory. On the other hand, VO2 max >20 mL/kg/min or at 75% indicates a low risk. If VO2 max is between 10 and 20 mL/kg/min or 35–75%, the patients will be considered moderate risk which implies that the morbidity and mortality rates may vary according to the values of split lung functions, exercise tolerance and extent of resection. The risks and benefits of the operation should be thoroughly discussed with the patient. The actual risks are affected by patient factors (comorbidities, age), structural aspects (center volume, specialization), process factors (management of complications) and surgical access (thoracotomy vs. minimally invasive). Conversely, VO2 max <10 mL/kg/min or 35% predicted indicates a high risk of mortality which may be higher than 10%. This will cause considerable risk of severe cardiopulmonary morbidity and residual functional loss. At this point, patients should be advised about alternative surgical (minor resections or minimally invasive surgery) or nonsurgical options. For patients who are considered for surgery but have a high risk outcome, a preoperative or postoperative pulmonary rehabilitation is recommended.[6] In patients with lung cancer being considered for surgery who undergo neoadjuvant therapy, it is suggested that repeated pulmonary functional testing with diffusion capacity be performed after completion of neoadjuvant therapy.[6]

## 3. Preoperative rehabilitation

Severe pulmonary function impairment was considered inoperable in approximately 37% of patients with anatomically resectable lung cancer.[11] The surgical morbidity and mortality rates for

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