

Clinical consensus on preoperative pulmonary function assessment in patients undergoing pulmonary resection (first edition)

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Introduction

While surgery is an important treatment option for lung diseases, its value can be compromised in patients with impaired lung function. The decreased lung ventilation or diffusion function in these patients increases the risk of perioperative complications and affects long-term survival. Therefore, the extent of resection should be defined according to disease stage; based on the pulmonary function, the risk of perioperative complications and long-term quality of life should be evaluated and predicted before surgery. Thus, the feasibility of surgical treatment and the extent of resection should be decided after weighing the pros and cons.

Since Borelli first measured expiratory volume in 1679, the development of lung function tests has evolved tremendously. Pulmonary function testing has been applied in thoracic surgery for more than 50 years. In 1971, Boushy and colleagues (1) found one second forced expiratory volume (FEV₁) can be used as an essential indicator of surgical tolerance before a thoracic surgery. Later, in a study enrolling 2,340 patients by Miller (2), when the results of a comprehensive analysis of pulmonary functions including FEV₁, maximum voluntary ventilation (MVV), and forced expiratory flow rate from 25% to 75% (FEF₂₅₋₇₅) were applied, a more precise method of selecting patients for various types of pulmonary resection has resulted in a lower mortality. In 1987, Bechard and

Wbtstein (3) concluded that exercise was an essential criterion in the preoperative evaluation of patients for pulmonary surgery as cardiopulmonary exercise testing (CPET) could effectively simulate the status of patients after pneumonectomy by testing cardiac and pulmonary load and function simultaneously; meanwhile, a maximal exercise O₂ consumption (VO₂max) less than 10 mL/kg/min was significantly associated with morbidity and mortality. In 1988, Ferguson *et al.* (4) demonstrated the role of diffusing capacity of the lung for carbon monoxide (DLCO) in predicting the prognosis of postoperative patients with lung cancer. Since then, FEV₁ and DLCO have been used as standard preoperative pulmonary evaluation of the lung resection candidates. In 1999, Wyser *et al.* (5) developed an algorithm that incorporated FEV₁, DLCO, and VO₂max as well as their respective ppo values for the preoperative functional evaluation, which further decreased the complication rate by 50%. Since then, the British Thoracic Society (6), the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS) (7), and the American College of Chest Physicians (ACCP) (8) have issued relevant guidelines to guide preoperative pulmonary function testing.

The purpose of preoperative pulmonary function assessment is to accurately assess lung function by using non-invasive or minimally invasive methods, to predict the risk of perioperative complications and the long-term

Table 1 Categories of recommendations

Category	Risks and benefits	Supporting evidence	Applications
IA	Definite	Results from a randomized controlled clinical trial without any flaw	A strong recommendation that can be unreservedly applied to most patients in various environments
IC+	Definite	Definite results from an observational study, with its level of evidence equal to that from a RCT	A strong recommendation that can be applied to most patients in various environments
IB	Definite	Results from a randomized controlled clinical trial with flaws	A strong recommendation that can be applied to most patients
IC	Definite	Results from an observational study	A moderate recommendation that may be changed as new reliable evidence becomes available
IIA	Indefinite	Results from a randomized controlled clinical trial without any flaw	A moderate recommendation that can be applied per the real conditions of the patients
IIC+	Indefinite	Definite results from an observational study, with its level of evidence equal to that from a RCT	A weak recommendation that can be applied according to different conditions including the patient's conditions and economic considerations
IIB	Indefinite	Results from a randomized controlled clinical trial with flaws	A weak recommendation that may be replaced by more optimal options based on the patient's real conditions
IIC	Indefinite	Results from an observational study	An extremely weak recommendation whose effect may be achieved by other method or recommendation

survival of patients after radical surgery and to make an informed decision on the extent of surgical resection. Based on the assessment results, effective prevention and control measures can be taken to reduce complications and improve the long-term quality of life.

This consensus document aligns existing literature and international clinical guidelines and attempts to offer clinicians with guidance on the standardized preoperative assessment of lung function.

The categories of recommendations are shown in *Table 1*.

Ventilation and diffusing capacity of the lungs

Spirometry

The FEV₁ and the predicted postoperative (PPO)-FEV₁ are the main parameters for measuring the ventilation function. The decline in FEV₁ and PPO-FEV₁ suggests an increased risk of postoperative complications and perioperative mortality. According to the standard guidelines (6,9), the screening of surgical candidates is mainly based on the absolute value of FEV₁: patients are suitable for pneumonectomy if FEV₁ is greater than 2 L and for lobectomy is FEV₁ is greater than 1.5 L. No further

physiologic evaluation is required for these patients.

FEV₁ is highly diverse among individual patients, and it is not feasible to screen surgical patients based on the absolute value of FEV₁ alone. A model was established based on large data sets, including patients' gender, height, weight, age, and other factors to estimate the expected lung function. The introduction of FEV₁% provided an excellent solution to account for individual differences. Most studies have shown that a PPO-FEV₁ of less than 40% predicted suggests an increase in perioperative complication rates, which are 16–50% in the literature (10–14). Nakahara *et al.* (15) found a mortality rate as high as 60% when ppo-FEV₁ was <30% predicted. Therefore, a PPO-FEV₁ of less than 40% of predicted is typically used as a cut-off value to categorize operations as “high risk”.

The cut-off screening value for ventilation function changes with the advances in relevant research. Research has suggested that FEV₁ is an independent risk factor for surgery: The incidence of perioperative respiratory complications was 43% in patients with preoperative FEV₁ <35% predicted and was only 12% in patients with FEV₁ >60% predicted. In a study of 1,046 patients by Ferguson *et al.* (16), FEV₁ was an independent risk factor for predicting perioperative mortality due to pulmonary

complications (OR, 1.1; FEV₁ decreased by 10%) and also a risk factor for perioperative deaths from cardiovascular complications (OR, 1.13; FEV₁ decreased by 10%). In a cohort of 1,239 patients, Licker *et al.* (17) found FEV₁ could be used to predict surgical complications, with FEV₁ <60% predicted being the optimal predictor of perioperative mortality and respiratory morbidity.

Diffusing capacity test

The diffusion capacity is mainly assessed by measuring the DLCO. In 1988, Ferguson *et al.* (4) found that DLCO was an independent predictor of complications and death after lung resection: patients with a DLCO of less than 60% predicted had a postoperative respiratory complication rate of 40% and a perioperative mortality rate of 25%. Berry *et al.* (18) studied 340 patients and found the perioperative mortality rate was 5% and the complication rate was 48% in patients having either FEV₁ or DLCO below 60% predicted after lobectomy, and both FEV₁ and DLCO were independent risk factors. Cerfolio *et al.* (19) enrolled 906 patients and also confirmed that both DLCO and FEV₁ were important predictors; meanwhile, they proposed that DLCO/VA% was another important predictor of postoperative complications after pneumonectomy. Further studies have demonstrated the association between DLCO and long-term survival of patients after lung resection. In a study conducted by Liptay *et al.* (20), patients were divided into different DLCO groups after adjusted for FEV₁, and the results showed that the long-term survival rates dropped with the decrease of DLCO. Ferguson *et al.* (21) found on univariate analysis that the hazard ratio between DLCO of <60% group and DLCO of ≥80% group was 1.35, and multivariate analysis revealed DLCO was an independent predictor of long-term survival.

For patients undergoing pulmonary surgery, the current international guidelines recommend the use of both FEV₁ and DLCO for evaluation, along with the calculation of PPO-FEV₁ and PPO-DLCO. According to the current ERS/ESTS guidelines, FEV₁ and DLCO are still recommended during the first stage of qualifying patients for lung resection. If both of them are greater than 80% predicted, no further evaluation is needed, and elective surgery can be planned. According to the ACCP guidelines, however, the calculation and evaluation of PPO-FEV₁ and PPO-DLCO are required based on the resection extent; if both of them are greater than 60% predicted, no further evaluation is required, and

surgery (e.g., total pneumonectomy) can be performed. The calculation of PPO-FEV₁ and PPO-DLCO uses the number of functioning lung segments and the number of lung segments to be removed. Before a lobectomy, segmentectomy, combined segmentectomy/subsegmentectomy, and/or combined lobectomy, the lung function can be assessed by calculating PPO-FEV₁ and PPO-DLCO according to the calculation methods provided in the guidelines. The actual situations can be a lot more complicated. For instance, the lung tissues to be removed by surgical or non-surgical means may have inconsistent functions (the presence of non-functioning area or heterogeneous lesions, especially in patients presented with heterogeneously distributed diffuse lung disease). Under such conditions, CT or radionuclide perfusion imaging should be performed to assess the number of functioning lung units, to predict PPO-FEV₁ and PPO-DLCO more accurately. It has been found that preoperative CT three-dimensional reconstruction can be used for the evaluation of PPO-FEV₁ and PPO-DLCO (22). Le Roux *et al.* (23) used gallium-68 and strontium-99-macroaggregated polymeric albumin lung perfusion PET/CT to detect 22 patients undergoing lung surgery and performed preoperative and postoperative pulmonary function tests and follow-up; they found the lung function in different lobes significantly differed among different patients.

Recommendations

For all patients who may undergo radical surgery, it is recommended to measure both FEV₁ and DLCO and calculate and evaluate PPO-FEV₁ and PPO-DLCO according to the resection sizes (Category IB).

For all patients who may undergo radical surgery, no further evaluation is required if the PPO-FEV₁ and PPO-DLCO are greater than 60% predicted according to the resection size, and surgical resection can be scheduled (Category IC).

For all patients who may undergo radical surgery, low-technology exercise tests [including stair climbing test (SCT) and shuttle walk test (SWT)] are recommended if either PPO-FEV₁ or PPO-DLCO is less than 60% predicted and both are greater than 30% predicted according to the resection size (Category IC).

For all patients who may undergo radical surgery, CPET is recommended to measure VO₂max if either PPO-FEV₁ or PPO-DLCO is less than 30% predicted according to the resection size (Category IB).

Low-technology exercise tests

SCT

SCT is a simple pulmonary exercise testing that requires no special equipment or staffing. Patients have to mobilize a large number of muscles during SCT. Compared with other sports, SCT exerts a certain pressure on the patient and can, to some extent, reflect the cardiopulmonary function. In 1987, Bolton *et al.* (24) confirmed the association between SCT and lung function: FVE₁ was >1.7 L in patients who could climb three flights of stairs and >2.0 L in those who could climb five flights of stairs. However, SCT has certain limitations: factors including climbing speed, the height of stairs, and body weight of patients can dramatically affect the results. Thus, efforts have been made to standardize SCT.

- (I) Changing the floor count to the total height of the stairs climbed. In a series of 160 patients, Brunelli *et al.* (25) found that the postoperative cardiopulmonary complication rate was 6.5% in patients reached an altitude of 14m and 50% in those who could only climb less than 12 m. A larger study in 2008 showed the cardiopulmonary complication rate of patients whose climbing altitude was lower than 12 m was two times of that in patients who could climb more than 22 m, along with 13 times higher mortality rate (26). The climbing altitude was significantly correlated with the results of CPET: 56% of patients with a climbing altitude of less than 14 m had a VO₂max of less than 15 mL/kg/min, while 98% of patients with an altitude of more than 22 m had a VO₂max of greater than 15 mL/kg/min (27).
- (II) Adjusting for body weight and climbing speed. In a recent study, Novoa *et al.* (28) established a modified formula after the patients' body weight, and climbing speed was adjusted, which represented a meaningful exploration in low-technology exercise tests.

In summary, stair climbing can offer general information on the cardiopulmonary function; for patients with subnormal lung function, the cardiopulmonary function test is more feasible.

SWT

SWT is another simple cardiopulmonary function test, during which a patient is asked to walk back and forth between two markers 10 meters apart. Walking speed is increased each minute in a graded fashion and paced by an

audio signal. The test is stopped when the patient is too breathless to maintain speed. Singh *et al.* (29) found an inability to complete 25 shuttles (250 m) on two occasions suggested a VO₂max of <10 mL/kg/min. Win *et al.* (30) suggested that the walking distance had a certain correlation with VO₂max, although SWT might underestimate VO₂max. Benzo *et al.* (31) demonstrated a definite linear correlation between SWT results and the VO₂max: the average VO₂max was 55 mL/kg/min in 55 subjects who had completed 25 shuttles. Although SWT is not a common test in clinical practice and its value in assessing clinical lung function is slightly lower than that of SCT, it can still be used as a supplementary test to improve the accuracy of low-technology exercise tests.

6-minute walking test (6MWT)

There are currently no detailed definitions of the methods and standards of 6MWT. Few studies have investigated 6MWT, and the results were significantly inconsistent. Currently, 6MWT is not recommended for preoperative lung function assessment in most international guidelines. A recent study (32) described a modified 6MWT and proposed that measuring the heart rate and oxygen saturation during 6MWT could improve the accuracy of preoperative lung function assessment. Such studies shed new light on the improvements in low-technology exercise tests.

Recommendations

For all patients who may undergo radical surgery, CPET is recommended to measure VO₂max if the walking distance is less than 25 shuttles (<400 m) during SWT or if the climbing altitude is below 22 m during SCT (Category IC).

For all patients who may undergo radical surgery, the surgical risk is assessed to be low if the walking distance is more than 25 shuttles (>400 m) during SWT or if the climbing altitude is higher than 22 m during SCT (Category IC).

CPET

CPET is a relatively complex physiologic evaluation technique that enables the real-time recording of ECG, exercise heart rate, minute ventilation, and oxygen intake per minute during exercise. CPET can yield the maximal oxygen consumption (VO₂max), which is recommended by the

previous guidelines as an important indicator for assessing cardiopulmonary function and surgical tolerance (9,33), allowing for even more accurate assessment of surgical risks. CPET is highly recommended by the guidelines issued by ERS/ESTS in 2009. For all patients scheduled for preoperative lung function tests, CPET is recommended for assessing surgical risk for patients with either FEV₁ or DLCO less than 80% predicted. If CPET reveals that the VO_{2max} is greater than 20 mL/kg/min or greater than 75% predicted, all the scheduled operations (including total pneumonectomy) can be performed. For patients with VO_{2max} less than 20 mL/kg/min, PPO-FEV₁ and PPO-DLCO need to be calculated according to resection size. If both of them are larger than 30% predicted, the planned resection can be performed; if either of them is less than 30% predicted, PPO-VO_{2max} can be calculated according to resection size; and if PPO-VO_{2max} is larger than 10 mL/kg/min or larger than 35% predicted, the scheduled resection can be performed. Studies have confirmed that the risk of postoperative death is closely related to VO_{2max}, and patients with VO_{2max} less than 10 mL/kg/min have extremely high postoperative mortality rate (3,11,34). A meta-analysis (including 14 studies, n=955) conducted by Benzo *et al.* (35) showed that VO_{2max} decreased by 3 mL/kg/min in patients with postoperative complications compared with those without postoperative complications. Loewen *et al.* (36) found in 346 patients that VO_{2max} <65% predicted was associated with more postoperative complications and a VO_{2max} of <15 mL/kg/min prompted poorer long-term survival. These findings provided multicenter validation for the use of VO_{2max} for preoperative assessment of lung cancer patients, and the authors encouraged an aggressive approach when evaluating these patients for surgery. Bayram *et al.* (37) did not find postoperative cardiopulmonary complications in patients with a VO_{2max} of >15 mL/kg/min; in contrast, patients with VO_{2max} <15 mL/kg/min had significantly increased postoperative lung complication rate and were at significantly increased risk for cardiovascular complications. Torchio *et al.* (38) investigated 145 COPD patients undergoing resection and found CPET is an important tool for assessing postoperative cardiopulmonary complications in these patients. They believed VO_{2max} and V_E/V_{CO2} are valuable indicators. Similarly, Bobbio *et al.* (39) concluded that VO_{2max} measured during CPET was significantly correlated with the prognosis. Recently, Brunelli *et al.* (40) found in a study enrolled 200 patients that the postoperative mortality rate was 0% and the pulmonary

complication rate was only 7% in patients with a VO_{2max} of >20 mL/kg/min; in contrast, those with a VO_{2max} of <12 mL/kg/min had 5-fold and 13-fold higher rates, respectively, of total cardiopulmonary complications and perioperative mortality rate.

Due to the presence of lung disease and long-term smoking, patients may have concurrent coronary atherosclerosis and cardiac insufficiency. CPET can also be used to evaluate and detect myocardial perfusion. Many guidelines recommend the use of CPET as a preoperative assessment tool for patients with a history of myocardial ischemia to assess and learn the patient's myocardial perfusion reserves and cardiac function. Meanwhile, since CPET is a stress test, the patient should be assessed for cardiac function before CPET to avoid cardiovascular events induced during the test. The guidelines released by both American Heart Association/American College of Cardiology (41) and European Society of Cardiology/European Society of Anesthesiology (42) recommend the use of revised cardiac risk index (RCRI) (43) for assessing the operational risk in patients with cardiovascular diseases. Brunelli *et al.* (44) conducted a study in 1,696 patients undergoing lung resection and found four outcome variables were in the RCRI were reliably associated with major cardiac complications: cerebrovascular disease (1.5 points), cardiac ischemia (1.5 points), renal disease (creatinine >2 mg/dL or >176.8 μmol/L; 1 point), and pneumonectomy (1.5 points). Currently, these four variables have been used as thoracic RCRI (ThRCRI). Patients are scored according to their medical history and related tests before surgery. If ThRCRI is <2 points, no further cardiac assessment is required; pulmonary function assessment can be performed directly, and CPET can be carried out based on lung function. If ThRCRI is ≥2 points, the myocardial perfusion and cardiac function shall be assessed; if surgical intervention is required, no other assessment including CPET will be performed. The patients can be treated by the percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). A second assessment will be performed six weeks after the treatment before subsequent treatment is applied. In patients with a ThRCRI score of ≥2 points but without an indication for surgical intervention, CPET and lung function testing can be performed under drug treatment and other interventions.

In summary, CPET plays an important role in the assessment of operative risk in patients undergoing lung resection. CPET in nature is an exercise stress test that can simultaneously assess the cardiopulmonary functions;

thus, it can evaluate both pulmonary complications and cardiovascular complications. Since CPET can effectively simulate the functioning of cardiopulmonary systems after surgery, it enables more accurate and intuitive assessments. However, CPET requires sophisticated equipment and professional testing personnel. At present, CPET is performed in only a few large clinical centers, and its values have not been fully recognized.

Recommendations

For all patients who may undergo radical surgery, patients can be categorized as a low-risk group if the VO_2max is higher than 20 mL/kg/min or higher than 75% predicted during CPET; a surgery (e.g., total pneumonectomy) can be performed (Category IC).

For all patients who may undergo radical surgery, patients can be categorized as a high-risk group if the VO_2max is lower than 10 mL/kg/min or lower than 35% predicted during CPET; treatment options should be carefully selected, including the re-calculation and assessment of the resection size and the use of non-surgical treatments (Category IC).

For all patients who may undergo radical surgery, the PPO- VO_2max should be calculated based on resection size in patients with a VO_2max of 10–20 mL/kg/min or 35–75% predicted during CPET. If the calculated PPO- VO_2max is higher than 10 mL/kg/min or larger than 35% predicted, a surgery performed within the calculated extent of resection is recommended; however, the operational risk is still high in these patients (Category IC).

Arterial blood gas (ABG) analysis

ABG analysis has previously been regarded as an important preoperative evaluation method. In particular, when pulmonary diffusion capacity testing is not available, ABG analysis combined with spirometry can, to some extent, evaluate the diffusion capacity of lungs. Hypercapnia ($\text{PaCO}_2 > 45$ mmHg) has long been considered a relative surgical contraindication as it might have been associated with increased incidences of postoperative adverse events (45,46). However, new studies have shown that hypercapnia is not an independent perioperative risk factor for perioperative complications or death associated with lung resection. Stein *et al.* (47) found no correlation between $\text{PaCO}_2 > 45$ mmHg and postoperative mortality. Two other studies have also demonstrated that patients

with hypercapnia, as indicated by ABG analysis, showed no significant increase in perioperative complication rates compared with otherwise normal patients (48,49). In another study, the incidence of perioperative complications significantly increased in patients with preoperative hypoxemia (50). Furthermore, ABG analysis may reflect the diffusion capacity of lung tissues. For clinical centers that have difficulty in measuring DLCO, ABG analysis combined with imaging scans can be used to evaluate some low-risk patients. If blood gas analysis yields normal results, chest CT reveals that there is no visible lesion in lung tissue except the resected part and the lung texture is even and normal, and the clinical measurement of DLCO is difficult, the combined method can be applied for assessing diffusion capacity. However, for patients with abnormal blood gas profile or imaging findings, measurement of DLCO is recommended for assessing the diffuse capacity.

Preoperative pulmonary function tests in patients with specific conditions

Preoperative pulmonary assessment in patients undergoing surgery for simultaneous bilateral lung cancer

The diagnosis rate of primary simultaneous bilateral lung cancer has increased with the wider application of CT examination and thus, the earlier diagnosis of lung cancer. However, the preoperative pulmonary function tests and the decision-making on resection sizes in such patients can be challenging (51,52). Many studies have demonstrated the feasibility of surgical therapy for bilateral multiple primary lung cancer (53–57). Some recent articles have reported the radical surgery for simultaneous bilateral lung cancer (58–60), prompting the possibility of treating this malignancy with simultaneous bilateral surgery. However, compared with the unilateral surgeries, the bilateral surgeries are associated with a larger loss of lung function within a short period and higher perioperative complication rate due to the simultaneously damaged integrity of bilateral thoracic cavity and the lack of compensation by a healthy side. For bilateral sub lobectomy or unilateral lobectomy combined with contralateral sub lobectomy, the preoperative assessment can follow the pulmonary assessment methods used for unilateral surgery. However, the preoperative pulmonary assessment for simultaneous bilateral major lung resection remains controversial. Our study on patients undergoing unilateral lobectomy combined with resection

of two or more contralateral segments has shown that the incidences of perioperative complications in these patients were significantly higher than those in patients receiving a unilateral surgery. The results suggest the preoperative pulmonary assessment for bilateral pneumonectomy should be performed with caution due to the simultaneous bilateral destruction of the integrity of the thoracic cavity and the lack of contralateral compensation. However, limited by its small sample size, our study only confirmed that the cut-off values needed to be further increased during pulmonary assessment for a simultaneous bilateral surgery, whereas the specific cut-off values need to be further investigated in studies with large sample sizes.

Preoperative pulmonary assessment in patients with chronic obstructive pulmonary disease (COPD) and/or other diffuse lung diseases

The difference in lung function between patients with COPD and otherwise, healthy patients needs to be further clarified as lung volume reduction may occur after lung resection. Brunelli *et al.* (61) found that COPD patients with a PPO-FEV₁ of <40% predicted had a perioperative mortality rate of only 4.8% after lobectomy. Linden *et al.* (62) investigated the outcomes of patients with preoperative FEV₁ <35% predicted (mean: <26% predicted) and concluded FEV₁ alone could not adequately predict perioperative complications and deaths. Thus, the accuracy of FEV₁ alone in preoperative pulmonary evaluation has been questioned. In lung cancer patients with moderate to severe COPD, the postoperative lung function loss can be smaller than predicted (and even increase in some cases) due to the effect of lung volume reduction if the resected lung parenchyma is also the main diseased area of COPD (63-65). These studies also showed that the lung volume reduction effect in these patients occurred immediately after surgery, suggesting the effect of radical surgery for lung cancer on lung function is smaller in these patients than in a patient without COPD. Thus, less strict assessment criteria may be applied in these patients, along with the use of multiple testing methods for a more detailed and accurate assessment. Notably, preoperative preparation of the respiratory system (e.g., clearing the respiratory tract with phlegm-resolving drugs and encouraging patients to perform physical exercises such as stair climbing) in COPD patients can remarkably improve lung function. In these patients, a second assessment can be performed after the

preparation to ensure the patient has achieved the required lung function criteria before surgery.

For preoperative pulmonary tests in patients with diffuse lung disease (e.g., diffuse bullae or interstitial lung disease), the assessment methods are theoretically similar to those for ordinary patients since these patients have no clear lesions or non-functional areas. However, certain adjustments need to be made in preoperative pulmonary tests, depending on the different characteristics of the disease. In COPD patients, since the lesions in two upper lobes are often larger than those in two lower lobes, the indication for resection of the upper lobes can be set wider; in contrast, the resection of the lower lobes should be more cautious. Interstitial lung disease is a group of clinicopathological entities with diffused pulmonary parenchyma, alveolar inflammation, and interstitial fibrosis as basic lesions and with active dyspnea, diffuse imaging changes, restrictive ventilatory dysfunction, decreased diffusing capacity, and hypoxemia as clinical manifestations. Preoperative pulmonary tests in patients with idiopathic pulmonary fibrosis (IPF) should be particularly cautious. The abnormal lung function in IPF patients is featured by the marked decrease in forced vital capacity (FVC) and DLCO, whereas the decrease in FEV₁ is not obvious. Research has confirmed that FVC is an independent risk factor during the surgical evaluation of such patients (66). FEV₁ is often used as a clinical assessment indicator for IPF patients, which often results in overestimated lung function; however, there is no widely-recognized cut-off value of FVC for the pre-operative pulmonary assessment in IPF patients. IPF Patients may suffer from rapid disease progression after surgery; for these patients, the pulmonary assessment should be based on FVC and DLCO as well as the functional and structural changes of the resected and preserved lung tissues. Preoperative pulmonary assessment should be stricter for patients undergoing upper lobe resection because patients with interstitial lung disease tend to have more severe lesions in lower lobes. Notably, for patients with idiopathic fibrosis, even if their preoperative pulmonary ventilation function and diffusion capacity meet the surgical requirements, patients and their families should be informed of the risk of death due to acute exacerbation of pulmonary interstitial lesions.

Pulmonary ventilation/perfusion imaging can be performed with the support of related equipment. However, the results provided by this technique are not three-dimensional. The functional areas of different lung lobes

have obvious overlap and cannot be separated. Since the lung function loss of patients undergoing upper lobe resection is often overestimated, the results of this test are just suggestive.

Preoperative pulmonary assessment in patients with a localized lesion or non-functioning lung tissue

Some benign lung diseases are risk factors for lung cancer, and lung cancer often occurs in the region of these underlying lesions such as COPD, interstitial lung disease, and tuberculosis (67). Also, tumors originating in the proximal bronchus can cause luminal obstruction, leading to post-obstructive pneumonia or atelectasis in the distal lung tissue. Benign diseases may be confined to a region where lung function is generally poor. The presence of an area with localized lesions or a non-functioning area results in the uneven distribution of functioning lung units. Thus, the preoperative pulmonary assessment should consider whether the surgical resection site includes such an area. A non-functioning area should be defined as tissues that cannot complete normal blood-gas exchange. These areas can be determined by pulmonary ventilation/perfusion scan, which can assess the level of ventilation/perfusion in each lung tissue area; specially, anterior-posterior overlap exists in lung tissue imaging, which may lead to over- or under-estimation of postoperative lung function (68). For lung cancer patients with impaired lung function, removal of tumor-containing lung tissues in the non-functioning area did not increase the risk of postoperative complications such as respiratory failure. Resection of non-functioning areas can increase the proportion of blood flow in the ventilated lung area. The cut-off values used in preoperative pulmonary assessment should be set wider for these patients. For patients undergoing only the resection of functioning lung units but not the removal of non-functioning areas, the preoperative pulmonary assessment should be more cautious. In patients having areas with impaired lung function, the lung function of the resected part is remarkably worse than that of normal lung units; thus, the preoperative pulmonary assessment often results in underestimated lung function. Single-photon emission computed tomography (SPECT) enables more accurate lung function assessment as SPECT can calculate the functional status in a specific lung area without being

affected by spatial overlap.

Pulmonary assessment before a second lung surgery

The preoperative pulmonary assessment before a second surgery is more complicated because the redistribution of blood flow and ventilation after the first operation results in the altered distribution of the function of each lobe. The ipsilateral and contralateral reoperation should be tailored following preoperative findings. If necessary, the pulmonary ventilation/perfusion scan can be performed to identify the functional proportions of the lateral and various parts, to determine the proportions of functional lung tissues removed. Subsequently, the corresponding formulas are used to calculate PPO-FEV₁ and PPO-DLCO, and the results are substituted into the path to evaluate the patient's surgical risk. Meanwhile, the following conditions should also be considered during preoperative evaluation.

Factors affecting lung function in a second lung surgery include:

- (I) Whether the two operations are performed ipsilaterally or contralaterally: if the second surgery is performed ipsilaterally, the reduction in postoperative pulmonary function is relatively small; if the second surgery is performed contralaterally, it can have a more severe impact on lung function and is more likely to induce respiratory failure.
- (II) The interval between two operations: if the interval between two operations exceeds six months, the decreased lung function after the first operation has almost completely recovered; if the interval is within six months, the decreased lung function following the first operation can be further restored.
- (III) Calculation of PPO-FEV₁ and PPO-DLCO: after the first operation, the residual pulmonary function at the operated side may be greatly affected due to factors including the shrunk thoracic cage on the operated side and the muscle damage on the chest wall. It is not advisable to calculate the PPO-FEV₁ and PPO-DLCO based directly on the number of lung segments. The postoperative residual lung function can be assessed by calculating the ventilation/perfusion ratio and lung ventilation function (*Figure 1*).

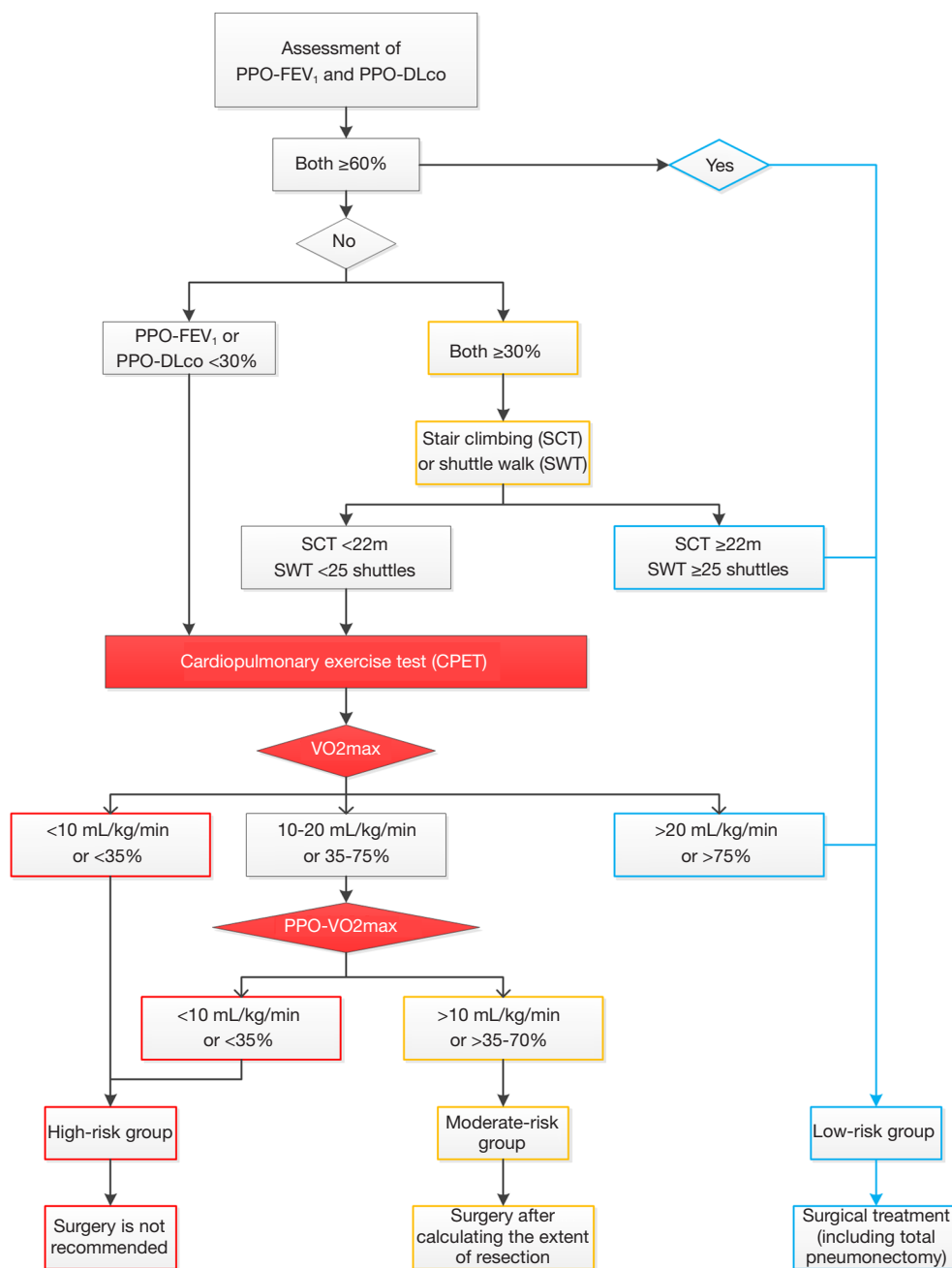


Figure 1 The recommended assessment protocol.

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Footnote

Conflicts of Interest: GJ serves as an unpaid Editor-in-Chief

of *Current Challenges in Thoracic Surgery*. CC serves as an unpaid Associate Editor-in-Chief of *Current Challenges in Thoracic Surgery*. HW and YY serve as unpaid Managing Editors of *Current Challenges in Thoracic Surgery*. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Calculation of PPO-FEV₁, PPO-DLCO, and PPO-VO₂max

Calculation of PPO-FEV₁

For patients undergoing total pneumonectomy: PPO FEV₁ = preoperative FEV₁ × (1 – a fraction of the total perfusion for the resected lung);

For patients undergoing lobectomy: PPO FEV₁ = preoperative FEV₁ × (1 – y/z).

Calculation of PPO-DLCO

For patients undergoing total pneumonectomy: PPO-DLCO = preoperative DLCO × (1 – a fraction of the total perfusion for the resected lung);

For patients undergoing lobectomy: PPO-DLCO = preoperative DLCO × (1 – y/z).

Calculation of PPO-VO₂max

For patients undergoing total pneumonectomy: PPO-VO₂max = preoperative VO₂max × (1 – a fraction of the total perfusion for the resected lung);

For patients undergoing lobectomy: PPO-VO₂max = preoperative VO₂max × (1 – y/z).

Note: y is the number of functional or unobstructed lung segments to be removed, and z is the total number of functional segments.

Summary of recommendations for patients scheduled for a radical surgery

(I) Measure both FEV₁ and DLCO and calculate and evaluate PPO-FEV₁ and PPO-DLCO according to the resection sizes (Category IB).

- (II) No further evaluation is required if the PPO-FEV₁ and PPO-DLCO are greater than 60% predicted according to the resection size, and surgical resection can be scheduled (Category IC).
- (III) Low-technology exercise tests (including SCT and SWT) are recommended if either PPO-FEV₁ or PPO-DLCO is less than 60% predicted and both are greater than 30% predicted according to the resection size (Category IC).
- (IV) Cardiopulmonary exercise test (CPET) is recommended to measure VO₂max if either PPO-FEV₁ or PPO-DLCO is less than 30% predicted according to the resection size (Category IB).
- (V) Cardiopulmonary exercise test (CPET) is recommended to measure VO₂max if the walking distance is less than 25 shuttles (<400 m) in SWT or if the climbing altitude is below 22 m during SCT (Category IC).
- (VI) Patients can be categorized as a low-risk group if the VO₂max is higher than 20 mL/kg/min or larger than 75% predicted during CPET; a surgery (e.g., total pneumonectomy) can be performed (Category IC).
- (VII) Patients can be categorized as a high-risk group if the VO₂max is lower than 10 mL/kg/min or lower than 35% predicted during CPET; treatment options should be carefully selected, including the recalculation and assessment of the resection size and the use of non-surgical treatments (Category IC).

The PPO-VO₂max should be calculated based on resection size in patients with a VO₂max of 10–20 mL/kg/min or 35–75% predicted during CPET; if the calculated PPO-VO₂max is higher than 10 mL/kg/min or larger than 35% predicted, a surgery performed within the calculated scope is recommended; however, the surgical risk is still high in these patients (Category IC).