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Review

Evaluation of preoperative cardiopulmonary reserve and surgical risk of patients undergoing lung cancer resection

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***Abstract*:** Lung cancer represents the second most frequent neoplasm and the leading cause of neoplastic death among both women and men, causing almost 25% of all cancer deaths. Patients undergoing lung resection—both for primary and secondary tumors—require careful preoperative cardiopulmonary functional evaluation to confirm the safety of the planned resection, to assess the maximum tolerable volume of resection or to exclude surgery, thus shifting the therapeutic approach toward less invasive options. Cardiopulmonary reserve, pulmonary lung function and mechanical respiratory function represent the cornerstones of preoperative assessment of patients undergoing major lung resection. Spirometry with carbon monoxide diffusing capacity, split function tests, exercise tests and cardiologic evaluation are the gold standard instruments to safely assess the entire cardiorespiratory function before pulmonary resection. Although pulmonary mechanical and parenchymal function, together with cardiorespiratory compliance represent the mainstay of preoperative evaluation in thoracic surgery, the variables that are responsible for fitness in patients who have undergone lung resection have expanded and are being continually investigated. Nevertheless, because of the shift to older patients who undergo lung resection, a global approach is required, taking into consideration variables like frailty status and likelihood of postoperative functional deterioration. Finally, the decision to go ahead with surgery in fragile patients being consideredfor lung resection should be evaluated in a multispecialty preoperative discussion to provide a personalized risk stratification. The aim of this review is to focus on preoperative evaluation of cardiopulmonary reserve and surgical risk stratification of patients candidate for lung cancer resection. It does so by a literature search of clinical guidelines, expert consensus statements, meta-analyses, clinical recommendations, book chapters and randomized trials (1980–2022).

Keywords: cardiopulmonary exercise testing, lung cancer, lung function tests, lung resection

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Introduction

Lung cancer represents the second most frequent neoplasm and the leading cause of neoplastic death among both women and men, causing almost 25% of all cancer deaths. On the other hand, since the lung is the second most frequent target of metastases originating from solid tumors, lung metastasectomy is the most frequently performed surgical resection in thoracic surgery departments.[1] Patients undergoing lung resection—both for primary and secondary tumors—require careful preoperative cardiopulmonary functional evaluation to confirm the safety of the planned resection and to assess the maximum tolerable volume of resection or to exclude surgery, thus shifting the therapeutic approach toward less invasive options. These patients are usually considered high-risk individuals because of their older age, coexisting diseases and global level of frailty. All these factors contribute to amplifying the risk of postoperative cardiopulmonary complications, resulting in more frequent intensive care unit admission, increased total length of stay and global postoperative morbidity and mortality.[2] Nowadays, preoperative risk assessment is constantly more difficult, given the flexibility of the limits to define borderline cardiorespiratory function; in fact, there is no standard cut-off to define unacceptable operative risk, thus limiting standard evaluation to low, medium or high risk.[3] Cardiopulmonary reserve, pulmonary lung function and mechanical respiratory function represent the cornerstones of preoperative evaluation of patients candidate for major lung resection.[4] Spirometry and carbon monoxide diffusing capacity, split function tests, exercise tests and cardiologic evaluation are the gold standard instruments to safely assess the entire cardiorespiratory function before pulmonary resection.[5] Patients who are candidates for pulmonary resection due to cancer often suffer from concurrent obstructive airway disease and/or restrictive lung diseases., These conditions encompass a broad range of thoracic diseases that cause lung tissue inflammation, scarring, or filling of air spaces with exudate and debris, such as diffuse parenchymal lung diseases. Additionally, many patients have atherosclerotic cardiovascular disease mainly due to exposure to noxious particles or gases, including smoking history, ambient air pollution and/or professional exposure. This clinical scenario places this cohort of patients at a higher risk both of post-resection complications and long-term pulmonary function impairment, thus resulting in potential pulmonary disability and reduced quality of life after surgery.[6] A thorough preoperative functional evaluation of patients who are candidates for lung resection for cancer, not only reduces the risk of postoperative major complications and post-resectional mortality rate but allows a proper selection of patients who might profit most from surgery without long-term quality of life impairment. Although ERS/ETS clinical guidelines published in 2009 still represent a cornerstone for preoperative evaluation of cardiopulmonary reserve and surgical risk stratification of patients who are candidates for lung cancer resection,[5] many further data have recently arisen and will be analyzed in this paper (Table 1).

Thoracic surgery operability criteria

Every surgical procedure can impact the lung, including supine decubitus and general anesthesia that determine a displacement of the diaphragm and impair vital capacity, tidal volume and respiratory frequency. The cough reflex is suppressed, and atelectasis may develop in various pulmonary areas when mechanical ventilation is not optimized. Patients who undergo anatomical resection can show the whole spectrum of adverse events from general anesthesia and surgery.

The British Thoracic Society (BTS) guidelines for lung cancer surgery suggest performing pulmonary function tests with carbon monoxide diffusion capacity of the lung (DLCO) and arterial blood gas analysis in all patients candidate for thoracic surgery.[7] Patients are considered safely operable with an acceptable operative risk when FEV1 is >1.5 L and >2 L in the case of pneumonectomy or with a ppoFEV1 $\geqslant 40\%$, DLCO is $\geqslant 40\%$ predicted and oxygen saturation $>90\%$. On the basis of the above-mentioned BTS guidelines, when one or more of these criteria are not fulfilled, more exams have to be done, including the six-minute walking test, a cardiopulmonary exercise test or a quantitative perfusion scanning, the latter providing a proper forecast of the ppoFEV1, although it can be evaluated by some mathematic formulae.[7] The exercise testing is helpful when lung function criteria are not satisfied. The BTS guidelines define the peak rate of oxygen consumption (VO2) as the most significant variable for the operability assessment. The threshold for VO2 indicated by guidelines for acceptable operative risk is VO2 >15 mL/kg/min; on the other hand, in case of VO2 $\leqslant 15$ mL/kg/min, patients are classified as “high risk” candidates.[8]

Lung function tests

Predicted postoperative FEV 1 (ppo-FEV1)

One of the best spirometric parameters for preoperative functional evaluation of patients undergoing lung resection is predicted postoperative forced expiratory volume in 1 s (ppo-FEV1); this shows if further tests are needed before offering surgical resection if patients could undergo the operation directly or if patients should be excluded from surgery without receiving further tests.[9] Ppo-FEV1 is usually calculated by counting the unobstructed lung segments to be resected and detracting that number from the number of all non-obstructed lung segments of the two lungs. In the case of standard lobectomy, ppo-FEV 1 is obtained by

Table 1. Clinical guidelines and statement on physiologic evaluation of the patient with lung cancer being considered for resectional surgery.

Guidelines/Statement	Year	Society
British Thoracic Society; Society of Cardiothoracic Surgeons of Great Britain and Ireland Working Party. BTS guidelines on the selection of patients with lung cancer for surgery[7]	2001	British Thoracic Society (BTS) and Society of Cardiothoracic Surgeons (SCTS) of Great Britain and Ireland
ATS statement: guidelines for the six-minute walk test[19]	2002	American Thoracic Society (ATS)
Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: ACCP evidenced-based clinical practice guidelines (2nd edition)[9]	2007	American College of Chest Physicians (ACCP)
ERS Task Force Recommendations on the use of exercise testing in clinical practice[26]	2007	European Respiratory Society (ERS)
ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients (surgery and chemo-radiotherapy)[5]	2009	European Respiratory Society (ERS) and European Society of Thoracic Surgeons (ESTS)
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[6]	2013	American College of Chest Physicians

ACCP, American College of Chest Physicians; ATS, American Thoracic Society; BTS, British Thoracic Society; ERS, European Respiratory Society; ESTS, European Society of Thoracic Surgeons; SCTS, Society of Cardiothoracic Surgeons.

this formula: ppo-FEV1 = preoperative FEV1 × (1 – number of unobstructed lung segments to be resected/total number of functional or unobstructed segments).[10] When ppo-FEV 1 is <40% of the predicted rate, higher postoperative mortality rates have been reported[11]; the cut-off value of ppo-FEV1 of 40% is therefore nowadays applied to discriminate between higher risk and normal risk patients.[12] According to the most recent "ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients" this threshold should be lowered to 30%, considering the recent substantial advancement in postoperative care and minimally invasive resections.[5] Moreover, these standard operability criteria—like others based on static pulmonary function analysis—have recently been questioned when applied to some cohort of patients: in fact, it has been shown that ppo-FEV 1 might not correctly predict postoperative complications in patients with preoperative FEV1 >70 as well as with a ppo-FEV1 <40%.[13] These results have been interpreted as a consequence of the lung volume reduction (LVR) effect, decreasing respiratory deficit in operated patients with emphysema. Several studies disclosed limited functional damage or even some level of increase in chronic obstructive pulmonary disease (COPD) patients although this effect has been clearly shown during the immediate postoperative period rather than in long-term follow-up.[14] We can therefore conclude that ppoFEV1 underestimates the immediate postoperative risk in predominantly obstructed patients with COPD and pulmonary emphysema.

It has also been observed that ppo-FEV1 is reasonably precise in forecasting actual postoperative FEV 1 at 3 or 6 months after lung resection, while it significantly overstates real postoperative FEV 1 in the early postoperative period.[15] In light of these results, the ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients state that ppo-FEV 1 should not be utilized as the only parameter to stratify operative risk for patients who are candidates for lung resection, in particular in the case of COPD patients. It might underestimate functional deficit in the early postoperative period and should not be considered a very predictable variable in terms of respiratory complications in COPD patients receiving lung surgery.[5]

As mentioned above, PpoFEV1 is the most widely adopted parameter to stratify the perioperative risk, but only one value of FEV1 without a clear connection with other variables may result in effective and insidious. Guidelines suggest realizing the whole PFTs[7]; anyway, in daily clinical practice, FEV1 is the parameter most commonly adopted, and often the only measurement used for the indication to undergo surgery in an individual patient. Ppo-FEV1 has been shown to be an independent risk factor for perioperative morbidity and mortality, but—as suggested by guidelines—all functional parameters should be taken into account to define the phenotype of every individual patient and to direct physicians toward the ideal management of each case, "tailoring" the surgery on patient's peculiarities.[7]

The FEV1/FVC ratio plays a pivotal role in the phenotype of the functional pattern of the patients to be operated on, whether it is an obstructive and/or restrictive ventilatory failure or normal. A careful perioperative functional assessment of the patient is a basic step to selecting the best surgical strategy to be adopted.

Diffusing capacity of the lung for carbon monoxide (DLCO)

The diffusing capacity of the lung for carbon monoxide (DLCO) is a useful surrogate estimation of alveolar oxygen exchange for patients receiving lung resection for cancers.[15] It has been widely demonstrated—both by early and more recent studies—that DLCO normally lowers after lung resection and a reduced preoperative DLCO correlates with additional postoperative mortality rate after major pulmonary resection.[5] A threshold of predicted postoperative DLCO (ppo-DLCO) of 40% is nowadays applied to discriminate between higher risk and normal-risk lung resection candidates. Anyway, similarly to ppo-FEV 1, "ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients" suggest that this threshold should be lowered to 30%, considering the recent substantial advancement in perioperative care and minimally invasive surgical procedures.[5]

Although some controversial opinions have been reported about the need for DLCO measurement only in surgical candidates with impaired respiratory function, nowadays routine measurement of diffusing capacity is recommended in every patient, despite the spirometric standard evaluation results. It has been widely demonstrated and it is nowadays well known that diffusing capacity is an effective predictor of postoperative complications in surgical patients irrespective of COPD status.[5]

DLCO is therefore an important tool to assess the operability of the patients. According to BTS guidelines, patients are defined as "average risk" when DLCO is greater than 40% of the predicted value.[7] Anyway, many factors may cause a reduction in the preoperative DLCO, including ventilation heterogeneity, vascular/epithelial or alveolar injuries,[8] which may differently condition exercise capacity and gas exchange in the perioperative period.[16] Thoracic surgeons should thus also take into account preoperative DLCO value. In fact, the preoperative DLCO has been shown to foresee postoperative complication risk, early and long-term outcomes and total length of stay in patients who have undergone lung resection.[17]

Split function studies

Perfusion scanning is the most commonly adopted technique to forecast post-resectional pulmonary function in patients who are candidates for pneumonectomy.[7] It is not routinely used in the case of planned lobectomy because of the complexity of identifying the involvement of each single lobe in global ventilation or perfusion. Both perfusion and ventilation scintigraphy provide effective forecasts of postoperative lung function but there is no evidence of any further advantage in performing both.[5] However, it should be taken into account that both perfusion and ventilation scintigraphy might underestimate the real postoperative function. In conclusion, "ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients" recommend using ventilation or perfusion scanning to determine postoperative respiratory function in patients candidate for pneumonectomy and quantitative computed tomography (CT) scan before lobectomy in patients with marginal respiratory reserve.[5] Single-side pulmonary artery occlusion is a test that can be applied to predict postoperative cardiorespiratory activity, in particular of the right ventricle, but it is nowadays performed only exceptionally because it is a highly invasive procedure with several major risks. It consists of whole lung or single-lobe pulmonary artery selective occlusion using a balloon catheter, thus reproducing the typical postoperative scenario of reduced pulmonary vascular bed and consequent right heart modification. In any event, major complications like arrhythmia, pulmonary thrombosis and cardiac arrest have been observed due to potential catheter migration or misplacement.[15]

Exercise tests

The goal of exercise testing is to evaluate the total cardiorespiratory system's capacity to deliver oxygen under stressful conditions and predict postoperative physiological reserve. Physical exercise simulates the postoperative clinical phase by increasing lung ventilation, CO_2 output and O_2 uptake, and total blood flow, thus proving significantly correlated to postoperative outcome. It has been observed, in fact, that postoperative cardiopulmonary complications rate after pulmonary resections is significantly higher in patients disclosing lower exercise capacity before surgery, expressed as VO2 max (maximum volume of oxygen consumed per minute).[18] However, exercise testing is suggested only in cases with reduced FEV 1 or DLCO.

The six-minute walking test (6MWT) is widely adopted to evaluate functional capacity, define prognosis and measure the response to medical intervention across a wide range of chronic respiratory diseases.[19]

The distance walked or the distance saturation product (DSP), the latter defined as the product of distance walked and lowest oxygen saturation during the 6MWT,[20] helps to stratify the risk of complications. Almost all patients with ppo values $<60\%$ achieved the 6MWD >400 m or DSP value >350 m%, representing the cohort with reduced risk of complications despite reduced lung function.[21]

Nevertheless, a significant correlation between poor preoperative VO2 max and unfavorable postoperative course has been reported, having been demonstrated that preoperative VO2 max values lower than 60% of predicted are related to raised postoperative mortality risk. In the case of patients with preoperative spirometric values of FEV 1 and DLCO lower than 80% of the predicted rate, measurement of VO2 max is strongly advised and VO2 max values lower than 10 mL/kg/min or 40% of the expected value contraindicate surgical resection. On the other hand, preoperative VO2 max higher than 20 mL/kg/min or 75% of the expected rate allows safe lung resection up to pneumonectomy. As a consequence of these observations, exercise testing is suggested in all patients who are candidates for pulmonary resection with FEV1 or DLCO $<80\%$ of predicted values. The most used ergometric tests to assess the feasibility and safety of major lung resection are the stair climbing test (SCT) and the shuttle walk test (SWT). The SCT is a basic functional screening exam to be suggested in the group at intermediate risk. Patients able to climb >22 m—without presenting any cardiorespiratory distress—are defined as eligible for lung resection; on the contrary, patients who cannot climb at least 12 m are at higher risk of suffering cardiopulmonary postoperative complications.[22] In the SWT, patients walk between two markers usually set 10 m apart and gradually increase their speed; patients able to accomplish 400 m on the SWT are deemed adequate for surgery. Patients failing to complete the SCT or the SWT are not automatically excluded from surgery but require further study by cardiopulmonary exercise testing (CPET).[23] According to ERS/ESTS clinical guidelines, the SWT tends to underestimate exercise capacity and should not be applied alone for preoperative patient selection but only as a low-cost first-line screening test. Similarly, the SCT can predict postoperative morbidity and mortality rate better than static functional tests but requires additional and more complex second-level functional tests to exclude patients from curative lung surgery. In fact, exercise oxygen desaturation greater than 4% during the SCT predicts an increased postoperative morbidity and mortality rate, but CPET is required for a more correct assessment of the cardiopulmonary system.[5]

The role of cardiopulmonary exercise testing

It is well known that cardiorespiratory and muscle energetic systems may fail under stressful conditions, when an increase in cardiac output, O_2 uptake, CO_2 output and ventilation is required in proportion to the intensity of stress.[24] CPET stresses both cardiorespiratory and muscle-energetic systems and records every cardiorespiratory variable in this setting, thus offering a reliable evaluation of cardiopulmonary reserve.

Two main types of exercise tests have been applied in the preoperative evaluation of high-risk patients undergoing lung resection for cancer, these being incremental exercise testing and the fixed exercise challenge.

In incremental exercise testing, the work rate is gradually increased to a required cut-off value, while in the fixed exercise challenge, there is a constant work rate. Both types of exercise can be defined as maximal or submaximal exercise testing: in the first case, the patient is required to complete an incremental exercise until reaching a plateau at which additional work does not generate any further VO2 increase. In the second case, the patient is required to perform an assigned sub-maximal workload exercise for a defined period of time and is usually used in patients unable to tolerate exercise stress because of fatigue or dyspnea, such as elderly or COPD patients, and who might therefore not be able to complete the exercise to exhaustion. These standard cut-off values for VO2 peak should be adopted: >75% of predicted or >20 mL/kg/min qualifies for any lung resection up to pneumonectomy; <35% of predicted or <10 mL/kg/min suggests high risk for any resection. Evidence is not strong enough to identify proper cut-off values for lobectomy.[5]

Cardiological evaluation before lung resection

Cardiac complications have been reported in about 30% of operated thoracic patients and postoperative atrial fibrillation is the most frequent. On the other hand, postoperative or intraoperative acute myocardial infarction is relatively rare, having been reported in about 5% of operated patients; however, when it occurs after lung resection, mortality can rise to 40%.[25] Right ventricle dysfunction has been reported after lung resection, and its severity is strictly related to the volume of pulmonary tissue resected, being significantly more critical following right pneumonectomy rather than left.[26] Right ventricle dysfunction after pulmonary resection is mainly due to the increment of the right ventricle afterload and uncoupling of the right ventricle-pulmonary artery association. It may last up to 8 weeks after surgery and culminate in a mortality rate higher than 70%.[27]

The ThRCRI (Thoracic Revised Cardiac Risk Index) has been proposed for stratifying postoperative cardiac events in patients receiving thoracic non-cardiac surgery, with a cut-off value of 2.[6] Patients presenting a ThRCRI ⩾2 have a raised perioperative cardiac risk, thus requiring additional cardiologic assessment before considering the feasibility of lung surgery; on the other hand, patients showing a ThRCRI < 2 do not require additional cardiac assessment before lung surgery. Metabolic equivalents (METs) are commonly used to determine functional capacity: a cut-off value lower than 4 METs—corresponding to the incapacity to climb two flights of stairs—indicates the reduced functional capacity and therefore the need for further exams before proceeding with lung surgery. On the other hand, its reliability is somewhat questionable because it standardly relates to the basal metabolic rate of a 40-year-old 70-kg man which is not the typical lung cancer patients.[6] Another interesting index to assess preoperative cardiac risk in patients receiving lung resection is the Duke Activity Status Index (DASI): it has been observed that a DASI score lower than 34 predicts an increased risk of postoperative cardiac complications; it corresponds to about 5 METS and a VO2 peak of 17 to 18 mL/kg/min.[3] When the DASI score is lower than 25, it predicts a +50% risk of postoperative cardiac complications; this result, therefore, not only requires further cardiac assessment but also strongly suggests a different therapeutic approach rather than lung surgery. Brain natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) are cardiac biomarkers predicting cardiac dysfunction, thus further contributing to preoperative risk evaluation in non-cardiac surgery. Increased preoperative BNP levels >30 pg/mL and >100 pg/mL are significantly related to a higher incidence of postoperative cardiac complications after pulmonary resection including postoperative atrial fibrillation.[3]

Patients undergoing lung resection and presenting satisfactory exercise tolerance do not usually require extensive cardiac assessment for coronary heart disease.[28] Patients with reduced exercise tolerance should be further examined—by non-invasive testing—to exclude ischemic diseases, arrhythmias or heart failure. When more aggressive cardiac examinations or revascularization procedures are required, aggressive long-term anti-platelet therapy needs to be started and its influence on perioperative setting of lung resection should be taken into consideration. With regard to protective cardiac medical therapy, beta-blockers have been advocated to decrease postoperative myocardial infarction; on the other hand, they could increase the risk of stroke—probably related to hypotension and bradycardia.

Their prophylactic use thus remains somewhat controversial.[29]

Preoperative risk factors

Malnutrition

Nutritional risk must be evaluated before every elective thoracic surgical procedure. Body mass index (BMI) is a manageable tool to assess preoperative malnutrition in oncologic patients: in fact, patients with a BMI of <18.5 are considered underweight and it has been shown that they more frequently develop postoperative complications and prolonged air leaks when compared to normal weight patients.[30] Similarly, lower preoperative serum albumin levels are related to a higher postoperative morbidity rate although not always related to malnutrition, as liver or kidney diseases may affect serum albumin levels. Patients with an impaired preoperative nutritional status should receive an implementation nutritional program before surgery whenever possible to reduce postoperative complications and surgical mortality rate.[31]

Obesity

Obesity—defined as BMI $\geqslant 30$—causes physiologic modifications reducing pulmonary volumes and worsening ventilation/perfusion mismatch, thus resulting in hypoxemia which is even more significant under general anesthesia and one-lung ventilation.[32] We have previously demonstrated that the risk of pulmonary complications in obese and overweight patients receiving pneumonectomy is 5.3 times higher when compared to patients whose BMI is less than 25. Thoracic surgeons and anesthesiologists should take this finding into consideration before offering pneumonectomy in obese and overweight patients.[33]

Smoking

It has been demonstrated that smokers have an elevated postoperative morbidity rate which is significantly related to the increasing number of pack-years. On the other hand, there seems to be no correlation between preoperative smoking interruption and postoperative complications rate.[34] In fact, patients who have quit smoking present a lower risk of postoperative pulmonary complications when compared with active smokers; on the other hand, the ideal extent of smoking interruption is unclear.[35]

Obstructive sleep apnea

Obstructive sleep apnea (OSA) is defined as episodes of hypopnea or apnea because of the collapse of upper airway tissues during sleep. As a result, patients suffering from OSA present recurring episodes of hypercarbia and hypoxia. Obesity, male gender, increased neck circumference and older age are risk factors for developing OSA which can be observed also in patients with anatomical craniofacial abnormalities predisposing to pharyngeal airway collapse. Patients suffering from OSA present an increased postoperative morbidity and mortality rate when receiving lung surgery and should continue using their positive pressure airway device after surgery.[20]

Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is the most frequent comorbidity observed in patients candidate for lung resection for cancer. It is characterized by pathological dilatation of the airspaces in the lungs and crushing of the alveolar wall determining a reduction of gas exchange membrane and air trapping with consequent hyperinflation of the alveoli. As a consequence of this pathophysiology, patients with COPD suffer from dyspnea, hypercapnia, hypoxia and impaired lung dynamics and more frequently experience postoperative complications after thoracic surgery, in particular, prolonged mechanical ventilation, recurrent pneumonia and ventilatory failure as well as myocardial infarction or cardiac arrest[20,36] (Table 2). Bronchoscopic LVR with endobronchial valve is a minimally invasive endoscopic technique improving the pulmonary function of patients presenting advanced emphysema; in particular, patients disclosing critical hyperinflation with an appropriate emphysema treatment and without collateral ventilation maximally benefit from this therapy. Anyway, due to the severity of underlying COPD, when diagnosed with lung cancer, these patients are not routinely offered a surgical approach and other less invasive treatments are recommended.[37]

Asthma

Patients suffering from severe asthma have more chance to develop postoperative pulmonary complications after major surgical procedures on the chest. Patients presenting active wheezing should be deferred even in the case of optimal response to bronchodilatation, because of needing to better

Table 2. Classification of COPD as defined by global initiative for chronic obstructive lung disease.

	COPD Classification	**Definition**
Classification of airflow limitation (post-bronchodilatation FEV_1)	Mild—GOLD Stage I	$FEV_1 \geqslant 80\%$ predicted
	Moderate—GOLD Stage II	$FEV_1 \geqslant 50\%$ predicted but $<80\%$ predicted
	Severe—GOLD Stage III	$FEV_1 \geqslant 30\%$ predicted but $<50\%$ predicted
	Very severe—GOLD Stage IV	$FEV_1 <30\%$ predicted
Classification of symptoms/risk of exacerbation	GOLD category A	mMRC 0–1 or CAT <10 (low symptom burden) History of 0 or 1 moderate or severe exacerbations (not leading to hospital admission)
	GOLD category B	mMRC ⩾2 or CAT ⩾10 (higher symptom burden) History of 0 or 1 moderate or severe exacerbations (not leading to hospital admission)
	GOLD category C	mMRC 0–1 or CAT <10 (low symptom burden) History of ⩾2 moderate/severe exacerbations or ⩾1 exacerbation (leading to hospital admission)
	GOLD category D	mMRC ⩾2 or CAT ⩾10 (higher symptom burden) History of ⩾2 moderate/severe exacerbations or ⩾1 exacerbation (leading to hospital admission)

CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; mMRC, modified Medical Research Counsel questionnaire.

reduce the inflammatory modifications in the bronchial tree. Inhaled bronchodilators and steroids should be administered before surgery and should be carefully prolonged throughout the perioperative period.[20]

Conclusion

Although lung mechanical and parenchymal function, together with cardiopulmonary reserve, represent the mainstay of preoperative evaluation in thoracic surgery, the variables responsible for fitness in patients who have undergone lung resection have increased and are being continually checked. The spirometry and cardiopulmonary exercise testing risk thresholds suggested in the referenced international guidelines refer mainly to thoracotomy and major lung resection. They do not automatically refer to the patient receiving a minimally invasive approach or sub-anatomical resection. Patients with ppoFEV1 and DLCO thresholds as low as 20% to 30%, whom we can define as "high-risk" patients, may now receive minimally invasive surgery without a substantial increase in the perioperative risk. Cardiac risk is another important discriminator. Nevertheless, because of the shift to older patients who undergo lung resection, a global approach is required, considering variables like frailty status and likelihood of postoperative functional deterioration. Finally, the decision to consider surgery in complex patients candidate for lung resection should be evaluated in a multidisciplinary preoperative discussion to provide a personalized risk stratification.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Author contributions
Francesco Petrella: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

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