Preoperative assessment of patients for lung cancer surgery

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Purpose of review
The aim of this work was to present and analyze the latest published documents about the functional evaluation of patients undergoing lung resection and review articles from the past two years addressing the same topic.

Recent findings
In 2009 and 2010, two important task forces, appointed by international scientific societies, have published documents to guide the preoperative evaluation and risk stratification of lung resection candidates. In both documents, cardiac evaluation is prioritized. Detailed cardiologic guidelines have been proposed. After this first step, functional assessment should include a spirometric assessment, a systematic measurement of carbon monoxide diffusion capacity and a cardiopulmonary exercise test evaluation. Differences in the relative importance of these tests in the two guidelines were discussed. Most recent evidences focused on the role of cardiopulmonary exercise test and the use of several direct and indirect ergometric parameters that may refine risk assessment.

Summary
The use of evidence-based clinical guidelines on preoperative evaluation is recommendable. Nevertheless, scientific evidence is still suboptimal in this field. Aggregate analyses on larger series are needed to improve risk stratification.

Keywords
carbon monoxide lung diffusion capacity, exercise testing, lung resection, risk, spirometry

INTRODUCTION
The present work aims to analyze the possible tests and pathways that clinicians can follow to define the risk of mortality and complications after lung resection. The two most recently published algorithms have been revised in order to identify the main steps of the preoperative functional evaluation, highlighting their similarities and differences. Moreover, we reviewed those papers that during the last two years added an outstanding contribution to the same topic.

STATE OF THE ART
The most recent guidelines about preoperative functional evaluation of patients undergoing lung resection were produced by two different task forces.

The first was published in 2009 as a joint effort of the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS) [1], the second was published in 2010 on behalf of the British Thoracic Society (BTS) and the Society for Cardiothoracic Surgeons (SCTS) of Great Britain and Ireland [2].

In both cases, a similar methodological approach was used and consisted of a systematic review of the literature by a group of experts and subsequent development of recommendations graded according to the Scottish Intercollegiate Guidelines Network Grading Review Group [3].

Whereas ERS/ESTS guidelines were aimed at stratifying a generic perioperative risk of death and major cardiopulmonary complications, the BTS/SCTS guidelines proposed a tripartite risk assessment (risk of mortality, myocardial events...
and residual dyspnea/impaired lifestyle). Furthermore, whereas the ERS/ESTS algorithm defined criteria to admit or exclude patients from operation, the BTS guidelines defined the level of risk to be presented and discussed with the patient. At this stage, the patient judgement becomes pivotal in the surgical selection process. If the patient accepts the risk and its potential impacts on lifestyle, then surgery can be offered. In spite of this different structure, the two documents stated similar messages and are often consistent with each other at the key points of the evaluation flowchart.

In fact, both groups recommended a preliminary cardiologic evaluation. They affirmed that all patients should undergo a detailed cardiac history, physical and electrocardiographic examination in order to be risk stratified according to the Revised Cardiac Risk Index (RCRI) [4] proposed by the American College of Cardiology (ACC) Foundation and the American Heart Association (AHA) [5]. Those patients with an RCRI of 3 or greater should be carefully evaluated with specific cardiac tests in order to identify pathological conditions that can be treated (in this regard, the ERS/ESTS article provides a detailed list of cardiologic approaches for reducing risks). On the other hand, patients with an RCRI of 2 or greater should be carefully evaluated with specific cardiac tests in order to identify pathological conditions that can be treated (in this regard, the ERS/ESTS article provides a detailed list of cardiologic approaches for reducing risks). On the other hand, patients with an RCRI of 2 or less can proceed to respiratory function evaluation. There is no indication to treat patients who would not have otherwise needed any treatment with the only intent to reduce cardiac risk after lung resection.

The interpretation and purpose of the respiratory function assessment differ in the two guidelines. Based on the results derived from the French Epithor Database [6], the BTS/SCTS guidelines proposed not to use forced expiratory volume in 1 s (FEV1) and the related predicted postoperative FEV1 (ppoFEV1) to predict postoperative mortality. The entire functional assessment [including spirometry, carbon monoxide lung diffusion capacity (DLCO) measurement and cardiopulmonary exercise test (CPET)] should be better reserved to define the risk of postoperative dyspnea and impaired quality of life, rather than surgical mortality. Notwithstanding the aim of the functional assessment (dyspnoea for BTS and mortality for ERS/ESTS), in both algorithms the first step in the evaluation of lung function is represented by the systematic measurement of DLCO (regardless of the FEV1 values) and FEV1.

After this stage, the ERS/ESTS task force recommended a more liberal use of CPET, which was not reserved only for those patients with impaired predicted postoperative values of FEV1 and DLCO. VO2 peak is regarded as a pivotal measure in the algorithm. Split lung function values are in fact reserved for a select group of patients in whom exercise testing showed a VO2 peak value between 35 and 75% or between 10 and 20 ml/kg per min (Fig. 1).

In the BTS/SCTS algorithm, ppoFEV1 or predicted postoperative DLCO (ppoDLCO) are instead calculated at the beginning of the algorithm for all the surgical candidates and CPET is reserved only for those patients with ppoFEV1 or ppoDLCO less than 40%. In this group, those patients with an oxygen consumption (VO2) peak less than 15 ml/kg per min are regarded as high-risk patients for posttreatment dyspnea and impaired quality of life (Fig. 2).

Considering specifically the stratification of the perioperative risk of death, the BTS/SCTS guidelines recommended the use of the Thoracoscore, which is

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**KEY POINTS**

- The two most recent evidence-based clinical guidelines that should inspire functional evaluation lung resection candidates are those published by the European Respiratory Society/European Society of Thoracic Surgeons and British Thoracic Society/Society for Cardiothoracic Surgeons task forces.
- FEV1 and DLCO must be assessed in all lung resection candidates.
- Cardiopulmonary exercise test is essential to precisely define deficits in the oxygen transport system and consequent surgical risk.
- More data and analyses are needed to improve the ability of stratifying the risk before lung resection.
a scoring system developed by the French Society of Thoracic and Cardiovascular Surgery [6], that quantifies the mortality risk in relation to multiple factors (individual variables, comorbidities, type and priority of the operation). This model had a high discrimination ability in the validation set (c-index 0.86) and was also validated in an external population with similar performance [7].

**MOST RECENT EVIDENCE**

Since the publication of the guidelines discussed above, only a small number of articles have addressed the issue of functional assessment of patients undergoing pulmonary resection.

Some of them contributed to highlight the weaknesses of FEV1 and DLCO when used alone to stratify the risk of pulmonary surgery.

In the past, Brunelli et al. [8] showed that the ppoFEV1 is unable to predict postsurgical cardiopulmonary complications in lung cancer patients with moderate to severe chronic obstructive pulmonary disease (COPD), representing a large portion of patients undergoing pulmonary resection. Moreover the same authors demonstrated that, 3 months following lobectomy, the actual to predicted postoperative ratios of FEV1 and DLCO in COPD patients were 115 and 122%, respectively [9].

Varela et al. [10] demonstrated that ppoFEV1 was rather imprecise in predicting the FEV1 immediately after surgery. In fact, ppoFEV1 was much higher than the actual FEV1 measured on the first postoperative days, a period when most of the complications occur. More recently, Berry et al. [11] confirmed that FEV1 and DLCO were not reliable predictors of morbidity in operated lung cancer patients. In particular, they reviewed data of more than three hundred patients older than 70 years, submitted to pulmonary lobectomy by thoracotomy or video-assisted thoracoscopy. After a multivariable analysis, they found that the only predictors of morbidity were age and having the operation performed via thoracotomy. Neither FEV1 nor DLCO resulted correlated with adverse outcomes in this study. Finally, in 2011 Takamochi et al. [12] published an article presenting predictors of morbidity after pulmonary resection in younger and older patients. They reviewed over one thousand lung cancer patients submitted to pulmonary resections (wedge, segmentectomy, lobectomy and pneumonectomy), dividing the population into two groups (patients less than 70 years, younger and patients 70 years or more, older). Analyzing clinical and pathological data, the authors found that parameters associated with postoperative course were different in the two groups. In fact, the risk
Several recent articles focused on cardiopulmonary exercise testing. In 2010, Brunelli et al. [13] published a review of the literature about different types of low-technology exercise tests used in the fitness evaluation of patients undergoing lung resection. They confirmed the paucity of scientific evidence in our setting, supporting the use of the 6-min walking test, which for this reason does not appear a useful parameter of patient selection. In the same review, the authors stated the importance of shuttle walk and stair climbing tests as instruments for an effective first level evaluation of the cardiopulmonary reserve of lung cancer surgical candidates. In particular, they highlighted the ability of these two low-tech tests of selecting subgroups of patients (those walking less than 400 m and those climbing less than 22 m) requiring a more sophisticated ergometric evaluation. In the same year Brunelli et al. [14] published another work that strengthened the role of the stair-climbing test in the preoperative functional assessment. They found an association between the altitude reached at preoperative stair climbing test and VO2 peak measured during the same test by a portable gas analyzer. In particular, they demonstrated that 98% of patients climbing more than 22 m had a VO2 peak greater than 15 ml/kg per min.

Two additional studies were published in 2010 about the use of high-tech cardiopulmonary exercise testing for lung resection candidates. Campione et al. [15] analyzed 99 patients with poor lung function and submitted to pulmonary resection (segmentectomy, lobectomy and pneumonectomy) after a CPET evaluation. They found a correlation between the postoperative outcomes (mortality and cardiopulmonary complications) and some ergonomic parameters such as the peak heart rate and the oxygen pulse. The logistic regression analysis however did not confirm the ability of the peak oxygen consumption in stratifying the risk of adverse outcome after lung resection.

Torchio et al. [16] verified whether ventilatory efficiency (expressed as the ventilation to CO₂ (VCO₂) production ratio, i.e. ventilatory efficiency/VCO₂ slope) measured during CPET was able to predict morbidity and mortality in 145 consecutive COPD patients submitted to pulmonary resection for lung cancer. They found that ventilatory efficiency/VCO₂ slope was the only predictor of mortality. VO₂ peak was instead associated with the occurrence of severe cardiopulmonary complications in the same group of patients.

Finally, in 2011, Puente-Maestú et al. [17**] published an article contributing to better defining the role of VO₂ peak in surgical candidates with impaired pulmonary function. They compared the postoperative outcomes of two groups of patients: group A, patients with ppoFEV1 and ppoDLCO more than 40% predicted, and group B, patients with either ppoFEV1 or ppoDLCO less than 40% predicted or both between 30 and 40% predicted and ppoVO₂ peak greater than 10 ml/kg per min. The authors found a similar complication rate among the two groups, but a higher 30-day mortality (1.9 vs. 13.5%) in group B.

**FUTURE DEVELOPMENTS**

Over the past 20 years, numerous studies have focused on the prediction of risk of complications and death after pulmonary resection. The effort of identifying parameters related to the postoperative outcomes (morbidity and mortality) has gradually expanded into three main research fields: the spirometric studies (considering in particular the role of FEV1 and its derivates), the DLCO measurement and CPET evaluation for the assessment of the whole oxygen delivery system. Although this has made possible the development of algorithms and guidelines for the preoperative evaluation of candidates for lung resection, limitations still exist in the risk estimation using the tools mentioned above.

These limitations can be in part overcome by a progressive large accumulation of data necessary to more precisely refine the role of FEV1, DLCO, and exercise testing. Larger numbers would be needed to stratify the risk within different categories of patients or treatments.

Works aimed at revising the role of traditional risk predictors in specific patient sub-groups or for specific operations are those published by Berry in 2009 [11] and 2010 [18].

On the other hand, there are encouraging results derived from more original lines of research on risk prediction. Examples in this regard are those represented by the works published by Varela et al. [19,20] in 2006 and 2007. They demonstrated that the observed FEV1 in the immediate postoperative period was lower than the ppoFEV1. Moreover, they found that the measured FEV1 in the first postoperative day was the best predictor of complications in patients submitted to lung resection. Following these findings, Brunelli et al. [21] published a model to predict the immediate postoperative FEV1.
Wang et al. [22] published a series of 57 lung resection candidates, in whom they assessed the changes of DLCO during exercise. These changes were associated, more than any other ergometric parameters, with postoperative complications.

In addition to VO2 peak, many other direct and indirect parameters are measured during CPET and can assist in the preoperative risk stratification.

As discussed above, some authors have already started to publish about such derived parameters [15,16,23]. Furthermore, CPET has been shown to accurately detect asymptomatic coronary artery disease [24–27].

Finally, some studies have suggested a possible role of daily physical activity in evaluating the surgical risk. In particular in 2011 Novoa et al. [28] demonstrated how the standardized measurement of the daily walked distance could be a predictor of VO2 peak in lung resection patients.

CONCLUSION

Most recent publications on functional evaluation before lung resection have allowed more precise definition of the following aspects:

1. the limited role of traditional spirometry and predicted postoperative FEV1;
2. the importance of a systematic measurement of carbon monoxide lung diffusion capacity;
3. the global approach in fitness evaluation, by assessing the entire oxygen transport system with cardiopulmonary exercise testing.

Nevertheless, studies on larger sample sizes are needed to improve statistical reliability and better define the individual roles of each single test in the context of preoperative evaluation. Aggregate data from International databases may serve as the natural platform for these future analyses. In addition to traditional outcomes, other more patient oriented metrics such as residual functional status, quality of life and dyspnea would hopefully be the subject of future studies. Finally, preoperative functional assessment should be tailored to accurately define the risk of morbidity and mortality according to specific subgroups of patients, operations or surgical approaches.

Acknowledgements

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 384).

Neoplasms of the lung

29. A prospective analysis performed on 38 lung resection candidates submitted to objective measurement of their daily basal preoperative activity using a pedometer. The authors showed that the distance recorded with the pedometer was correlated with VO2 peak.