Commentary: The ERS/ESTS clinical guidelines for evaluating fitness for radical treatment for lung cancer

The European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS) have recently established a joint task force, composed of leading multidisciplinary experts on the functional evaluation of lung cancer patients, with the purpose of developing clinical evidence-based guidelines on the evaluation of fitness for radical therapy in patients with lung cancer. The results of this joint endeavor have been published in the *European Respiratory Journal* [1, 2].

Approximately 20–25% of lung cancer patients are operable; however, lung resection remains the only curative treatment for lung cancer, despite advances in alternative treatments. Recent advances in operative and perioperative management and the reassessment of lung function tests and exercise test modalities justify the re-evaluation of the ideal surgical candidates. Nonsurgical patients are usually treated with chemo- or radiotherapy, which have specific toxicities that need to be taken into account. The task force aims to review acute and long-term risks related to chemo- and radiotherapy and make recommendations on alternative nonsurgical treatments. The conclusions of the guidelines will be summarised in this commentary to supplement the interesting and informative review by D. SUBOTIC in this edition of *Breathe*.

Cardiologic evaluation

All available information on the pre-operative cardiac risk was integrated into a functional algorithm for evaluation of the lung resection candidate. This algorithm was generated based on the best available scientific evidence and consensus opinion of experts and recommends that cardiac evaluation should be the first step to assess a patients risk for surgery (figure 1) emphasising the importance of preliminary cardiologic assessment.

Lung function tests

The next step for patients with a low cardiological risk or with optimised cardiological treatment is to proceed with pulmonary evaluation (figure 2). The panel of experts agreed that predicted post-operative (ppo) forced expiratory volume in 1 s (FEV_1) is not a reliable predictor of lung resection complications and should not be used alone to select lung cancer patients for surgery. However, it is a useful tool in combination with other diagnostics.

Diffusing capacity of the lung for carbon monoxide ($D_{L,CO}$) has been found to be an independent pre-operative predictor for the mortality and morbidity of lung resection [3–4]. The guidelines suggest that $D_{L,CO}$ should be routinely measured in lung resection candidates regardless of the results of spirometry. A cut-off ppo$D_{L,CO}$ value of 30% predicted has been recommended as a high-risk threshold.

Perfusion scintigraphy is the most widely used method of predicting post-operative lung function in lung cancer patients prior to pneumonectomy [5]. However, it has been reported that lung segment counting can predict ppoFEV_1 as accurately as perfusion scintigraphy [6, 7]. Therefore, it has been recommended that lung segment counting should be used to calculate residual lung function and only in patients with borderline function perfusion scintigraphy should be used.

Exercise tests

Exercise tests are commonly used to evaluate the whole cardiopulmonary and systemic oxygen delivery systems under stress in order to estimate the physiological reserve of the patient after surgery. It is predicted that if a patient cannot perform well on an exercise

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Figure 1

Algorithm for cardiac assessment before lung resection in lung cancer patients. RCRI: Revised cardiac Risk Index; ECG: electrocardiogram; AHA: American Heart Association; ACC: American College of Cardiology; CABG: coronary artery bypass graft; PCI: primary coronary intervention; TIA: transient ischaemic attack. Taken from [1].
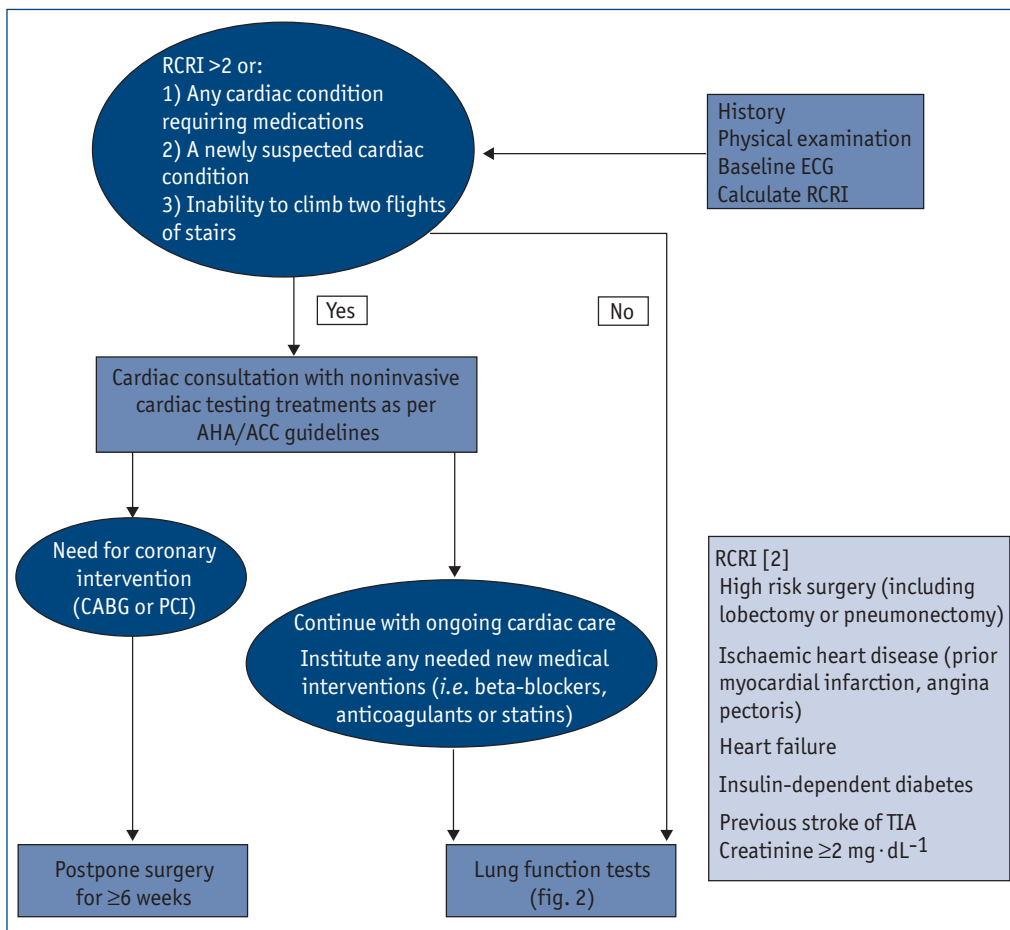
test that they will be unlikely to be able to withstand the stresses of surgery. However, a meta-analysis reported that exercise capacity was actually lower in patients who developed post-operative complications after lung resection [8]. Other studies have found a correlation between exercise capacity and mortality following lung resection and it is suggested that exercise tests should be carried out on patients with FEV1 and $D_{L,CO}$ <80% pred.

Low technology exercise tests

Stair, 6-min walk distance and shuttle tests are the most widely used low technology exercise tests. The shuttle walk test has not been found to discriminate between patients with or without complications after surgery or to be reliable in estimating exercise capacity at a lower range. It is only advised for screening and not as a stand alone test. In contrast, stair climbing has been found to be superior at predicting the likelihood of morbidity and mortality after lung resection compared with spirometry measurements. Stair climbing is a cost-effective method for first-line screening to immediately select patients who are

safe to undergo surgery and those who need further more sophisticated tests. The 6-min walk test has not been found to be reliable in distinguishing patients fit for surgery and therefore should not be used in pre-operative decisions.

Cardiopulmonary exercise testing

Cardiopulmonary exercise testing is usually performed on a bicycle or treadmill in a controlled environment allowing for good reproducibility and standardised results. Maximal oxygen consumption ($V_{O_2,peak}$) is used to measure exercise capacity. Currently there is a consensus that $V_{O_2,peak}$ >20 mL per kg or >75% pred qualifies patients for resection and $V_{O_2,peak}$ <10 mL per kg or <35% pred indicates a high risk for any resection and these should be used as cut-off values. $V_{O_2,peak}$ measurements should be considered as the most important factor for exercise capacity for predicting post-operative complications.

Future trends in pre-operative workup

The inclusion of daily physical exercise in the pre-operative work-up could be used as an additional

test to compliment more sophisticated measurements. Exercise $D_{L,CO}$ could also be an interesting parameter to measure since impairment of $D_{L,CO}$ reflects poor recruitment of pulmonary capillary and alveolar volume.

Patient care management
## Rehabilitation before and after surgery

Currently, evidence is insufficient to clearly recommend pulmonary rehabilitation in surgical lung cancer patients. However, pulmonary rehabilitation in COPD patients has been found to improve V_{O_2} rate before surgery which decreased the number of late complications after surgery [9]. In addition, pre-operative training programmes have led to a reduction in the length of hospital stays and complications in COPD patients with lung cancer [10]. Smoking cessation before surgery has a positive impact on the rate of complications after surgery [11] and it is therefore recommended to cease smoking 2–4 weeks prior to surgery.

Scoring systems

Scoring systems designed specifically for lung resection including the cardiopulmonary risk index, the predictive respiratory quotient and the EVAD system (age, FEV1 and $D_{L,CO}$) have all been unreliable at predicting the risk of morbidity and mortality for individuals [12–15]. Therefore, it is not recommended that scoring systems should be used as standard care; however, they may be a useful tool when assessing a group of patients for surgery.

Thoracotomies and the intensive care unit

The guidelines state that systematic admission to the intensive care unit (ICU) after thoracotomy should not be implemented and when a high-dependency unit (HDU) is available no patients should be admitted to the ICU. Only in an emergency situation such as organ failure, patients should be admitted to the ICU. Patients with a high risk of complication, those who have undergone complex pulmonary resection and those with a marginal cardiopulmonary reserve should be admitted to the HDU after surgery. Low risk patients should be sent to a specialised thoracic surgical unit after surgery.
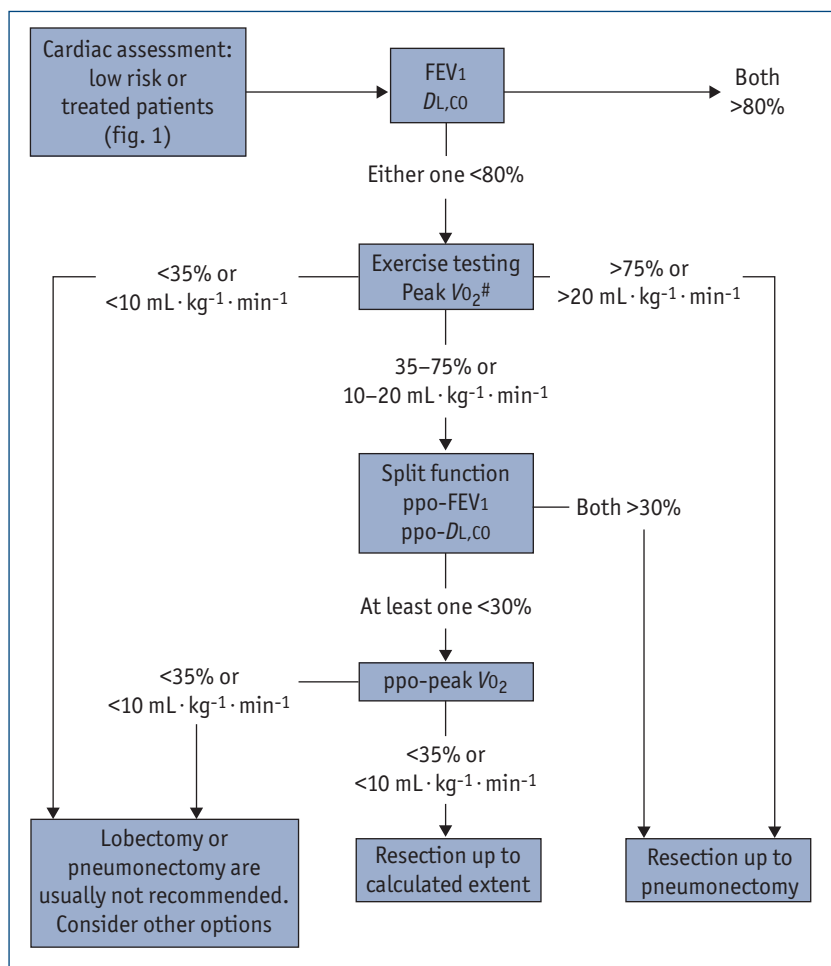
Figure 2
Algorithm for assessment of cardiopulmonary reserve before lung resection in lung cancer patients. #: If peak V_{O_2} is not available, cardiopulmonary exercise testing can be replaced by stair climbing; however, if altitude reaching during stair climbing is ,<22 m, cardiopulmonary exercise testing with peak V_{O_2} measurement is highly recommended. Taken from [1].

Surgical techniques
Combined cancer and lung volume reduction surgery

Lung volume resection surgery (LVRS) produced significant improvements in exercise capacity and survival in patients with upper lobe emphysema [16, 17]. Better health status and lung function has been noted after LVRS compared with normal medical treatment and rehabilitation [18, 19]. Long-term survival after LVRS has also been improved compared with other modalities of treatment. In selected high-risk patients with hyperinflated lung and a poorly perfused tumour-containing lobe anatomical lobectomy combined with LVRS has produced beneficial effects in terms of survival. Based on this evidence it was

recommended that anatomical lobectomy with or without LVRS should be performed in well selected COPD patients with lung cancer.

Compromised parenchymal sparing resections and minimally invasive techniques

Parenchymal sparing resection or sublobar resections include segmentectomy and wedge resection. Patients recommended for segmentectomy are as follows:

 a) Stage IA with margins of resection >1 cm.
 b) Stage I patients with poor lung function.
 c) Lung resection after prior lobectomy.

 Wedge resections are recommended in the following circumstances:

 a) Stage IA (tumours <2 cm)
 b) Small peripheral adenocarcinoma with air-containing image on high-resolution computed tomography scans.

Chemo- and radiotherapy
Neoadjuvant chemotherapy

The advantages of neoadjuvant treatments for resectable and operative lung cancer are currently being examined in future studies. To date, several studies have reported advantages for morbidity and mortality following induction therapy after pneumonectomy [20–22]. However, in recent trials induction chemotherapy in pneumonectomy has led to high levels of mortality and morbidity especially in right sided pneumonectomy [23, 24]. More studies are required to make a judgement on the use of induction chemo- and radiotherapy. It is recommended that after induction chemo- or radiotherapy, new functional evaluation should be carried out prior to surgery.

Definitive radio- and chemotherapy

The greatest limitation to definitive radiotherapy is radiotherapy-induced lung toxicity which is heterogenic across studies due to different scoring systems. The risk of developing radiation pneumonitis-induced lung toxicity can be estimated by calculating the dose–volume histogram of the lung, including V20 and mean lung dose [25, 26]. Therefore this calculation should be carried out prior to treatment to determine the risk of toxicity. There is too little evidence on the safety of definitive chemotherapy to make a formal recommendation on its use.

Alternatives to surgery

For medically inoperable nonsmall cell lung cancer (NSCLC) the best established method for treatment is radiation alone which appears to increase survival rates. Continuous, hyperfractionated, accelerated radiotherapy (CHART) is the preferred method compared with conventional radiotherapy because it has been shown to provide improved local control and survival. In stage I NSCLC patients at high surgical risk, stereotactic radiotherapy should be considered as a good alternative to surgery.

Who should treat thoracic patients and where should they be treated?

Ideally a multidisciplinary team made up of a thoracic surgeon specialising in lung cancer, a medical oncologist, a radiation oncologist and a pulmonologist should manage lung cancer patients. Lung cancer patients undergoing surgery should be admitted to specialised centres with qualified thoracic surgeons, since specialisation has been shown to improve resectability, post-operative mortality and long-term survival. Surgery should also be carried out in centres with an adequate volume of cases (minimum surgical volume of 20–25 major lung resections per year) as this has a positive impact on resectability, post-operative mortality and long-term survival. In addition, there is also a positive impact of volume on the results of chemotherapy and radiotherapy. Radiotherapy should be performed by radiologists that routinely treat patients with this modality.

Summary

Despite advances in alternative treatments, lung resection remains the only curative treatment for lung cancer. Preliminary cardiologic assessment should be the first step to assess patients for surgery followed by pulmonary evaluation for those with low cardiological risk. $D_{L,CO}$ should be routinely measured in lung resection candidates as it has been seen to be an independent pre-operative predictor of mortality and morbidity. Stair climbing can be used for first-line screening to select patients for more sophisticated tests. V_{O_2} peak is the most important factor for exercise capacity for predicting post-operative complications. There is

no clear evidence for scoring systems or rehabilitation in selecting lung resection candidates. ICUs should be reserved for patients with major complications such as organ failure. Anatomical lobectomy with or without LVRS should be performed in well selected COPD patients with lung cancer. Additional studies are required to make adequate judgements on induction chemo- and radiotherapy and definitive chemotherapy. Stereotactic radiotherapy should be considered as a good alternative to surgery in stage I NSCLC patients at high surgical risk. Surgery and radiotherapy should be carried out by trained specialists who routinely treat patients with this modality.

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