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## Perioperative Pulmonary Functional Assessment

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### 1. Introduction

Pulmonary resection is the first therapeutic option of various lung pathologies, among which localized non-microcytic bronchogenic carcinoma is the most prevalent. Due to the fact that many patients who develop non-microcytic bronchogenic carcinoma present significant comorbidity, lung resection is associated with an increased risk (between 2 and 5%) of perioperative death (Little et al., 2005). Therefore, it is important to assess the patient's operability, which is defined as the ability to survive the lung resection without leaving any disabling sequelae.

As most of these patients are or have been smokers, many of them have varying degree of obstructive lung disease. It is known that the pulmonary obstruction increases the risk of lung resection (Miller et al., 1981), which is why the decision to perform resection depends largely on the functional integrity of the lung not affected by tumor. As the excision supposes a loss of lung function, many years of research have led to a reasonably solid scientific evidence that the postoperative risk depends on post-surgery lung function, which can be estimated preoperatively by knowing the amount of tissue to be resected basing on anatomical size or quantifying it by perfusion scintigraphy (Wernly et al., 1980).

On the other hand, it is also known that the functional capacity measured by exercise tests is associated with postoperative mortality (Puente & Ruiz., 2003). This has led to the development of integrated strategies in which basal functional tests are followed by postoperative function estimate and, in borderline patients, by stress testing (Marshall & Olsen 1993).

### 2. Perioperative pulmonary physiology

The major cardiopulmonary complications that alter normal lung function occur as a result of surgery (thoracotomy and resection of lung parenchyma) and anaesthesia (table 1). The thoracic surgery causes restrictive changes in the lung function characterized by moderate to severe reductions (50%) in vital capacity and up to 70% decrease of functional residual capacity (FRC). As a result of the FRC decrease, the volume of airway closure is shifted, so

in the areas of pulmonary decline the end point of exhalation is below the closure volume, which causes an early closure of the airway and, therefore, of the areas of atelectasis. The factors that reduce FRC include supine position, pain, general anaesthesia and obesity. These functional changes occur without apparent obstruction of the airway, so that the ratio of forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) does not decrease.

The action of the anaesthetic and the muscle relaxant used in the surgical procedure, involves a decrease in lung volumes. In addition, the effects of these drugs on the diaphragm and the bulbar center responsible for regenerating respiratory impulses are the main reasons that justify changes in lung volumes.

The cause of the diaphragm muscle dysfunction is not clear yet. Direct damage to the muscles during the surgical intervention has been proposed as one of possible mechanisms, but transdiaphragmatic pressure measurements during maximal phrenic nerve stimulation suggest that the depression of the central nervous system efferent traffic on the diaphragm occurs as a result of inhibitory reflexes associated with pain and other stimuli to sympathetic or vagal receptors.

Hypoxemia and arterial hypercapnia that appear, especially in the postoperative period, are mainly due to the effects of anaesthesia used during the surgery and cause a decrease in the interrelation ventilation/perfusion (V/Q), and besides lead to deterioration of hypoxic pulmonary vasoconstriction, alveolar hypoventilation or low cardiac output. The gas exchange disorder is intensified with combination of hypoventilation, increase in dead space ventilation, rapid shallow breathing and a decrease in mixed venous oxygen saturation due to low cardiac output, anemia and arterial desaturation and increased peripheral oxygen consumption with pain, fever or stress (Beckles et al., 2003).

<b>Lung function changes with anesthesia and surgery</b>
Impairment of gas exchange
Reduction in lung volumes
Dysfunction of the diaphragm
Depression of ventilatory control
Inhibition of cough and mucociliary system

Table 1. Mechanism of lung function changes with anesthesia and surgery (Swenson, 1999).

Ventilatory depression is also typical of the postoperative period and is marked by the residual effects of anaesthesia that inhibit normal response to hypoxia and hypercapnia. Analgesics and other sedatives may enhance these effects, and impede the implementation of pulmonary rehabilitation. They can rarely lead to episodes of sleep apnea.

The lung defends itself from attacks of infectious and environmental agents with cough and mucociliary clearance. The former is suppressed both with excessive and poor pain treatment. The latter can be altered by an ineffective cough, limited by restrictive changes and weakened respiratory muscles and also by atelectasis and dysfunction and ciliary damage caused by anaesthetic gases (Swenson, 1999).

Finally, it should be noted that many of these functional alterations may come as a result of postoperative complications such as atelectasis, infections, respiratory failure or exacerbations of chronic obstructive lung disease (table 2).

<b>Postoperative pulmonary complications</b>
<b>General complications</b>
Atelectasis Infection (Pneumonia or bronchitis) Bronchospasm Respiratory failure Prolonged mechanical ventilation Exacerbation of chronic lung disease Pulmonary embolism Obstructive sleep apnea
<b>Specific thoracic surgical complications</b>
Pleural effusion Phrenic nerve injury Bronchopleural fistula and empyema Sternal wound infection Gastroesophageal anastomotic leak

Table 2. Postoperative pulmonary complications in patients with thoracic surgery (Swenson, 1999).

### 3. Lung function tests

In the preoperative thoracic surgery the functional assessment schemes have varied over the past 50 years. Most respiratory function tests which were utilized in order to minimize morbidity and postoperative mortality (table 3) are no longer used today, being replaced by simpler techniques that provide similar or better information. Today the process of lung function assessment is spread out over several phases comprising a series of breathing tests that the patients scheduled for thoracic surgery will be given according to their baseline pulmonary function and the amount of lung tissue for resection. These steps complement each other, so that the degree of severity of impairment of lung function is the fact that determines whether or not to go a step higher.

<b>Pulmonary function test</b>	<b>Parameter</b>
Spirometry	FVC, FEV1, ppo-FEV1
Lung volumes	TLC, RV, TLC/RV%
Diffusing capacity of the lung for CO	DLCO, ppo-DLCO
Arterial gasometry	PaO <sub>2</sub> , PaCO <sub>2</sub>
Pulmonary hemodynamic	PAP, PVR
Perfusion scintigraphy	% Perfusion en each lung
Ventilation scintigraphy	% Ventilation in each lung
Exercise test (6-min walking, shuttle walk and stair climbing)	Distance walked
Cardiopulmonary exercise test	VO <sub>2</sub> peak

Table 3. Pulmonary function test used in the preoperative assessment. FVC: Forced vital capacity. FEV1: Forced expiratory volume in 1 second. ppo: postoperative. TLC: Total lung capacity. RV: Residual volumen. DLCO: Diffusion capacity of the lung for carbon monoxide. PaO<sub>2</sub>: Oxygen partial pressure of artery. PaCO<sub>2</sub>: Carbon dioxide partial pressure of artery. PAP: Pulmonary artery pressure. PVR: Pulmonary vascular resistance. VO<sub>2</sub>: Oxygen uptake.

### 3.1 Spirometry

Spirometry is a simple, inexpensive test of high reproducibility, easy to perform. From the standpoint of the preoperative evaluation the most important variables are the FEV1 and FVC. In the early 1950s spirometry was already considered as the most valid technique to assess morbidity and postoperative mortality in the thoracic surgery.

The first authors who used the predictive power of FEV1 in such surgery observed that the complications derived from the resection of bronchial carcinoma were associated with absolute values of FEV1 lower than 2 liters (Boushy et al., 1971). Subsequently, the measurements of spirometry were combined with those of lung volumes and there was observed an increase in complications with a FEV1 less than 1.20 liters, reserve volume (RV) greater than 3.30 liters and total lung capacity (TLC) greater than 7.90 liters (Lockwood, 1973). On the other hand, there was an attempt to link the value of FEV1 with the type of lung resection and it was noticed that the requirement for pneumonectomy was a FEV1 more than 2 liters, for lobectomy more than 1 liter and for segmentectomy or wedge resection more than 0.6 liter (Miller et al., 1981).

Considering FEV1 in absolute values can lead to errors in the estimation of lung function, especially in patients of advanced age or low height. In this sense, there have been some studies whose data contemplate a reduction in complications when the FEV1 is greater than 60% (Richter et al., 1997) or  $89 \pm 19\%$  (Wang et al., 2000) of predicted values (table 4). Therefore, it is preferable to place greater emphasis on FEV1 percentage value in relation to its theoretical value than to the absolute one. In addition, the highest possible FEV1 will be chosen using the available therapeutic arsenal (smoking cessation, pulmonary rehabilitation or drug treatment with bronchodilators or corticosteroids). Finally, we could say that for thoracic surgery the advisable value of FEV1 is greater than or equal to 80%.

Variables	Complications (n = 19)	No Complications (n = 38)	p Value
FEV <sub>1</sub> , L	2.15 ± 0.50	2.69 ± 0.66	< 0.01
FVC, L	3.39 ± 0.82	3.73 ± 0.79	ns
FEV <sub>1</sub> % predicted	72 ± 14	89 ± 19	< 0.001
FVC% predicted	87 ± 16	97 ± 15	< 0.05
FEV <sub>1</sub> /FVC, %	64 ± 11	72 ± 11	< 0.05
RV/TLC, %	40 ± 8 (n = 17)	36 ± 9 (n = 30)	ns
DL <sub>CO</sub> , ml/min/mm Hg	15.31 ± 3.72 (n = 17)	21.98 ± 5.92 (n = 30)	< 0.001
DL <sub>CO</sub> % predicted	62 ± 13 (n = 17)	87 ± 15 (n = 30)	< 0.001
DL <sub>CO</sub> /VA, ml/min/mm Hg/L	3.05 ± 0.91 (n = 17)	4.03 ± 0.97 (n = 30)	< 0.01
DL <sub>CO</sub> /VA% predicted	74 ± 23 (n = 17)	91 ± 17 (n = 30)	< 0.05

Table 4. Preoperative lung function variables in relation to complications. FEV1: Forced expiratory volume in 1 second. FVC: Forced vital capacity. RV: Residual volume. TLC: Total lung capacity. DLCO: Diffusion capacity of the lung for carbon monoxide. VA: Alveolar volume. ns: not significant (Wang et al., 2000).

In the algorithms used for the functional assessment of candidates for lung resection, the value of postoperative FEV1 (ppo-FEV1) plays an important role in the alternative to perform further tests or exclude patients from surgery without performing these tests (Wyser et al., 1999) (figure 1). In this sense, a value of ppo-FEV1 less than 40% of predicted increases the risk of perioperative complications and mortality by 16-50% (Pierce et al., 1994), being higher (60%) when ppo-FEV1 is less than 30% (Nakahara et al., 1985).

Even today there is a disagreement about whether ppo-FEV1 is a good predictor of perioperative complications or not. It has been seen that ppo-FEV1 is not a good predictor of

complications in patients with preoperative FEV1 greater than 70%. In addition, among these patients, who also have ppo-FEV1 less than 40%, the mortality is 4.8%. These findings explain the so-called "lung volume reduction effect", which shows a reduction of functional loss in patients with airflow limitations, such as, for example, in patients with chronic obstructive lung disease (COPD) (Sekine et al., 2003).

A ppo-FEV1 value of 40% is currently being used to distinguish between normal and high risk of complications in thoracic surgery. However, due to improvements in surgical techniques and perioperative management, the value of ppo-FEV1 could fall to 30%.

Although the ppo-FEV1 is fairly accurate in predicting the final residual value of FEV1 within 3-6 months after thoracic surgery, the real value of FEV1 is overestimated in the first postoperative days, when most of the complications occur. In this regard, it has been shown that the first postoperative day and after a lobectomy the real value of FEV1 was 30% lower than expected. Therefore, it would be a better predictor of complications than the ppo-FEV1 was (Varela et al., 2007).

The current recommendations of the ERS / ESTS Task Force are that the ppo-FEV1 should not only be used to select patients with pulmonary cancer for lung resection, especially in patients with moderate or severe COPD. It is known that in patients with COPD it is likely to overestimate the loss of lung function in the early postoperative stages and ppo-FEV1 does not seem to be a reliable predictor of complications. Finally, a value of ppo-FEV1 less than 30% predicted would be a high risk parameter when included in an algorithm for assessing pulmonary reserve before thoracic surgery (Brunelli et al., 2009).

### 3.2 Diffusing capacity of the lung for carbon monoxide

The DLCO represents the amount of carbon monoxide trapped by the lungs after inspiration of a small amount of this gas. This test provides us with information about the alveolo-capillary membrane, which is responsible for alveolar oxygen exchange. Thus, the DLCO is used to evaluate the surgical risk in patients scheduled for thoracic surgery.

Although DLCO is a technique which allows to estimate the risk of postoperative complications, it is not as well studied as FEV1. Several studies have shown that a preoperative DLCO less than 60% predicted was associated with increased mortality and postoperative complications were increased when the DLCO was less than 80% of predicted value (Ferguson et al., 1998). It has also been observed that patients with decreased DLCO ( $65.3 \pm 5.0\%$ ) had more respiratory complications than those with normal DLCO ( $90.1 \pm 5.9\%$ ) (Wang et al., 1999). In addition, decreased DLCO is related to an increase in the frequency of hospital readmissions and poor quality of life for the long term.

Therefore, the DLCO is an additional test to spirometry in which if a patient's preoperative functional evaluation has a FEV1 and DLCO greater than or equal to 80%, no additional testings are required. But if a patient has a DLCO lower than 80% despite a FEV1 greater than or equal to 80%, additional tests should be performed to make sure that it is a good candidate for thoracic surgery. This indicates that the DLCO is an important test to predict postoperative complications both in patients without COPD as well as in patients suffering from this pathology (Ferguson et al., 2008).

On the other hand, a value of postoperative DLCO (ppo-DLCO) of 40% is currently being used to distinguish between normal and high risk of complications in patients undergoing lung resection (Wyser et al., 1999) (figure 1). However, taking into account advances in perioperative care and surgical techniques, the allowed limit of ppo-DLCO should be lowered to 30%.

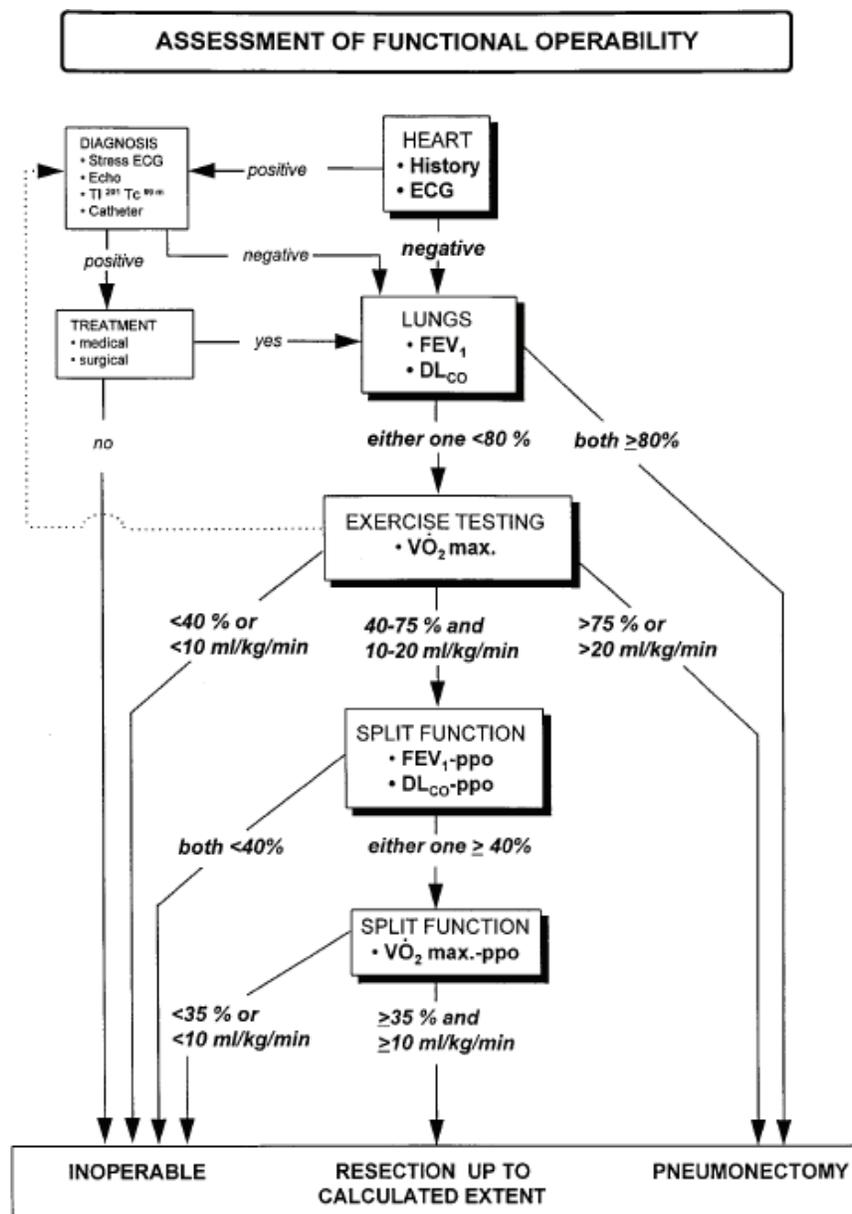


Fig. 1. Proposed algorithm for the assessment of the cardio-respiratory reserves of lung resection candidates. Tl 5 thallium; Tc 5 technetium. ECG: electrocardiogram. FEV1: Forced expiratory volume in 1 second. DLCO: Diffusion capacity of the lung for carbon monoxide. ppo: postoperative. VO2: Oxygen uptake. (Wyser et al., 1999).

The current recommendations of the ERS / ESTS Task Force indicate that the DLCO should be a routine measurement of functional evaluation of candidates for lung resection, especially if the spirometry is altered. The threshold value of ppo-DLCO of 30% is high risk when included in an algorithm for the assessment of pulmonary reserve before thoracic surgery (Brunelli et al., 2009).

### 3.3 Measurement of gas exchange

Arterial gasometry, is a test that is requested routinely in patients about to undergo thoracic surgery. Unlike spirometry, arterial blood gases values provide some more direct information about the problem with the gas exchange that is often present in this type of

surgery. However, they do not provide as useful measurement as FEV1 or DLCO in the perioperative functional assessment.

In relation to arterial oxygen pressure (PaO<sub>2</sub>), few studies describe the exact role of this parameter in the assessment of perioperative risk. In some of them it has been shown that PaO<sub>2</sub> below 50 mmHg is associated with postoperative complications (Mittman & Bruderman., 1977). Furthermore, sometimes hypoxemia in patients with bronchial carcinoma may be due to a shunt secondary to pulmonary atelectasis that is improved after the lung resection.

With regard to the blood pressure of CO<sub>2</sub> (PaCO<sub>2</sub>), it has been postulated that hypercapnia (PaCO<sub>2</sub> greater than 45 mmHg) involves an increase in postoperative complications (Meyer-Erkelenz et al., 1980). However, one study has demonstrated that patients with severe airflow obstruction (FEV1 40 ± 6%) and PaCO<sub>2</sub> of 44 ± 4 mmHg, did not have any complications after lobectomy (Morice et al., 1992) (table 5). In this sense, other authors have also come to the conclusion that hypercapnia is not a risk factor for the presence of postoperative pulmonary complications (Miller et al., 1981). Therefore, although there is no consensus about the usefulness of the arterial gasometry in the perioperative functional assessment, it seems clear that hypercapnia should not exclude patients who are candidates for lung resection.

Subject No./ Age, yr/Sex	Height, cm	Weight, kg	FVC, %	FEV <sub>1</sub> , L	FEV <sub>1</sub> , %	FEV <sub>1</sub> /FVC	Dco, %	TLC, %	PO <sub>2</sub> , mm Hg	PcO <sub>2</sub> , mm Hg	<sup>133</sup> Xe FEV <sub>1</sub> , %	$\dot{V}O_{2peak}$ , ml/kg/min	Concomitant Heart Disease*
1/65/M	172.5	71	65	1.04	30	36	43	137	71	52	24	20.1	Cor pulmonale
2/76/M	170	65	49	1.05	39	60	50	185	74	36	26	15.1	None
3/75/M	175	61	61	1.37	45	58	66	85	89	43	32	19.2	RV enlargement
4/63/F	152.5	48	89	.95	44	40	62	140	86	42	32	16.2	None
5/70/M	170	60	78	1.27	47	52	49	107	69	49	37	16.1	Atrial fibrillation
6/72/M	167.5	66	68	1.14	41	55	56	169	76	48	31	15.2	RV enlargement
7/60/M	170	49	87	1.46	47	42	65	111	80	35	32	15.4	Cor pulmonale
8/64/M	180	96	72	1.14	33	35	40	133	65	43	31	16.5	RV enlargement
Mean	68	170	64	1.18	40	47	53	133	76	44	31	16.7	
SD	6	7.5	15	0.17	6	10	10	32	8	6	4	1.9	

Table 5. Relationship among spirometry, arterial blood gases and exercise testing in patients undergoing lung resection. FVC: Forced vital capacity. FEV1: Forced expiratory volume in 1 s. DCO: Diffusion capacity of the lung for carbon monoxide. TLC: Total lung capacity. PO<sub>2</sub>: Oxygen partial pressure of artery. PCO<sub>2</sub>: Carbon dioxide partial pressure of artery. VO<sub>2</sub>: Oxygen uptake. RV: Right ventricle. (Morice et al., 1992).

### 3.4 Quantitative ventilation/perfusion scintigraphy

The quantitative perfusion scintigraphy is based on the radiation emitted by an isotope that is taken up by the lungs after being injected intravenously. The percentage of radioactivity is associated with lung function, the right lung being the largest (55% of the total radiation). The left lung is responsible for the remaining 45% (figure 2).

The calculation of ppo-FEV1 in patients scheduled for pneumonectomy, from preoperative FEV1 and lung perfusion scintigraphy, is performed as follows (Kristersson et al., 1972):

$$ppo - FEV1 = \text{preoperative FEV1} \times \% \text{ of perfusion of the undisturbed lung}$$

Therefore, if such a patient is a candidate for left pneumonectomy and has a 3-liter preoperative FEV1 and the scintigraphy shows 30% perfusion in the left lung and 70% in the right, the value of FEV1 postpneumonectomy is:

$$\text{ppo-FEV1} = 3 \text{ liters} \times 0,7 = 2,1 \text{ liters}$$

It has been shown that there is a good relationship between the ppo-FEV1 and real postoperative FEV1, while the ppo-FEV1 can be 10% lower than the measured FEV1 3 months after the surgery.

Wernley et al. applied the method of lung perfusion scintigraphy to calculate the FEV1 after lobectomy with the following formula (Wernley et al., 1980):

$$\text{Estimate of the FEV1 loss} = \text{preoperative FEV1} \times \% \text{ affected lung perfusion} \times (\text{number of segments in the lobe to be resected} / \text{number of segments in the lung})$$

Perfusion scintigraphy has also been used to calculate ppo-DLCO, using the same formulas for estimating the ppo-FEV1. Therefore, the ppo-DLCO is calculated using the following formula:

$$\text{ppo-DLCO} = \text{preoperative DLCO} \times \% \text{ de perfusion of the unresected lung}$$

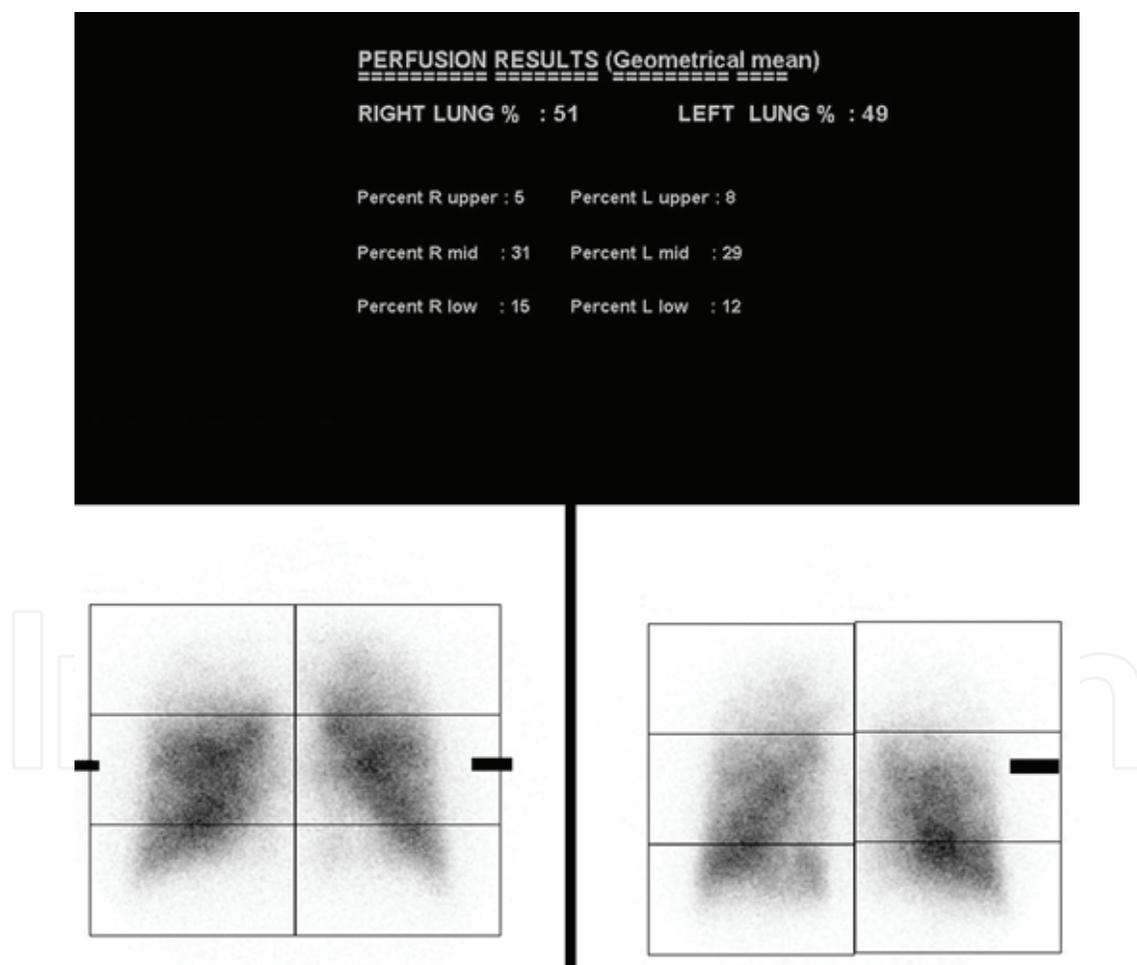


Fig. 2. Anterior and posterior images from perfusion scintigram. Three equally sized regions of interest over lungs are shown. Counts in each zone are measured. Geometric means of anterior and posterior images are then used to calculate relative perfusion and ventilation for each zone for each lung. By this method, percentages are obtained for upper, middle, and lower zones of right and left lungs for both perfusion and ventilation. (Win et al., 2006).

It is difficult to establish a definitive cut-off of ppo-FEV1 or ppo-DLCO above which resection of lung parenchyma will be safe. Some authors have estimated 0.8 liters as the limit below which it is unreasonable to perform the resection of the pulmonary parenchyma (Olsen et al., 1974). As an absolute value it can lead to errors, which is why it is better to use the percentage with respect to the theoretical value.

Several studies have shown that in candidates for lung resection, when ppo-FEV1 is greater than 40%, postoperative mortality is reduced (Markos et al., 1989), but other authors did not observe its increase when ppo-FEV1 is less than 40% (Morice et al., 1992). In relation to the ppo-DLCO it has also been noticed that the risk of postoperative complications is greater when the ppo-DLCO is less than 40% (Markos et al., 1989), and even one study estimates that this parameter is the best assessment of mortality and postoperative complications (Ferguson et al., 2008).

In practice, the scintigraphy has not been widely used in the functional assessment of patients about to undergo a lobectomy because of the difficulty in interpreting the individual contribution of each of the lobes to the whole of ventilation and perfusion. This could explain why several researchers consider that the simple calculation of the lung segments can predict the ppo-FEV1 as accurately as the ventilation perfusion scintigraphy does (Win et al., 2004). The ventilation scintigraphy has been widely used to predict postoperative lung function in patients with lung cancer who are scheduled for pneumonectomy (Colice et al., 2007).

The correlation between current and predicted ppo-FEV1 using the ventilation/perfusion scintigraphy has been variable with  $r$  between 0.67 and 0.9 (Win et al., 2006a). Both the ventilation and perfusion scintigraphies offer a good prediction of postoperative lung function individually, but it seems that there is no additional benefit in the performance of both (Win et al., 2006). However, the interpretation of the results should take into account that these techniques may underestimate the actual postoperative value (Zeiber et al., 1995).

### 3.5 Exercise test

During the exercise the patient is subjected to physical stress so that the whole system that regulates the uptake, transport and use of oxygen can be studied through the exercise test. When the latter is started, the lung increases the ventilation, oxygen uptake ( $VO_2$ ),  $CO_2$  production and blood flow similar to that which occurs during the postoperative period following the lung resection.

Among all the variables mentioned above, the most important is the peak oxygen uptake ( $VO_2$  peak), which gives us an idea of the global response to the effort and is defined as the maximum amount of oxygen a subject can capture, transport and use during the exercise. In addition, during the preoperative evaluation process the  $VO_2$  peak is the parameter that estimates the probability of complications best of all. Despite this, the exercise test should be performed only in selected cases (decrease in FEV1 and/or in DLCO below 80%) (Wayser et al., 1999).

#### 3.5.1 Low-technology exercise; stair climbing, shuttle walk, and 6-min walk tests

Six-minute walk, stair climbing and shuttle walk tests have proved to be useful for preoperative risk stratification. In this sense, the 6-min walk test has a high reliability in the estimation of  $VO_2$  peak in healthy subjects and patients with COPD or those who are about to undergo lung transplantation and, therefore, in assessing the postoperative risk after thoracic surgery (Brunelli et al., 2009).

The shuttle walk test appears more reproducible and highly correlated with VO<sub>2</sub> peak, estimating that 25 routes in this test are equivalent to a VO<sub>2</sub> peak of 10 mL/kg/min (Singh et al, 1994). This cutoff point has been included in the algorithm proposed by the British Thoracic Society (BTS, 2001). However, no statistically significant differences have been found in the shuttle walk test among patients with and without complications after lung resection (Win et al., 2006b). This test tends to overestimate the exercise capacity in its range of lower values compared to VO<sub>2</sub> peak, concluding that it should not be used alone to exclude patients from surgery (BTS, 2001). It has also been observed that patients who walk more than 400 meters in the shuttle walk test have a VO<sub>2</sub> peak higher than 15 mL/kg/min (BTS, 2001).

The effectiveness of stair climbing test to predict serious cardiopulmonary complications following the lung resection surgery has already been demonstrated (Olsen et al., 1991). Against this background, the patients who climb less than 12 meters have a 2-fold higher rate of complications and mortality 23 times higher when compared with those who climb more than 22 meters, with a mortality rate of less than 1% (Brunelli et al., 2008). It has also been noticed that in patients with ppo-FEV1 or ppo-DLCO less than 40%, who climbed more than 22 meters, the mortality rate is nonexistent (Brunelli et al., 2008).

Oximetry during the exercise has been proposed as a useful test in the preoperative assessment of candidates for lung resection (Colice et al., 2007). The role of oxygen desaturation during the exercise in postoperative risk stratification has not been defined in relation to early complications after the resection. In addition, it has been seen that oxygen desaturation during the exercise is a good predictor of postoperative respiratory failure, need for admission to an Intensive Care Unit (ICU), prolonged hospital stays and home treatment with oxygen (Ninan et al., 1997). On the other hand, oxygen saturation below 90% during the exercise test with incremental protocol is not a good predictor of postoperative cardiopulmonary morbidity (Varela et al., 2001).

### 3.5.2 High-technology exercise; cardiopulmonary exercise testing

There are 2 types of exercise protocol that have been used to evaluate the surgical risk: incremental or submaximal. They are usually carried out on a bicycle or a treadmill. The incremental protocol is the most used and consists in increasing the work to be performed by each patient to the limit of his tolerance. The exercise ends when the symptoms do not allow the patient to continue performing the exercise or when the registered variables do not permit to continue the test (ATS, 2003) (table 6).

Chest pain suggestive of ischemia Ischemic ECG changes Complex ectopy Second or third degree heart block Fall in systolic pressure > 20 mm Hg from the highest value during the test Hypertension (> 250 mm Hg systolic; > 120 mm Hg diastolic) Severe desaturation: Sp <sub>O<sub>2</sub></sub> ≤ 80% when accompanied by symptoms and signs of severe hypoxemia Sudden pallor Loss of coordination Mental confusion Dizziness or faintness Signs of respiratory failure
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Table 6. Indications for exercise terminations. ECG: electrocardiogram. SpO<sub>2</sub>: arterial oxygen saturation. (ATS, 2003).

The reliability of the exercise test with incremental protocol has been confirmed by numerous studies. In 1982 it was already proved that the complication rate decreased in patients with VO<sub>2</sub> peak more than 1 liter (Eugene et al., 1982). In 1984 it was observed that the rate of postoperative complications was 100% when the VO<sub>2</sub> peak was less than 15 mL/kg/min, but if this parameter was greater than 20 mL/kg/min, the risk of complications was 10% (Smith et al., 1984).

In 1992 it was found that among the patients with preoperative FEV<sub>1</sub> less than or equal to 40%, ppo-FEV<sub>1</sub> less than or equal to 33% or PaCO<sub>2</sub> more than or equal to 45 mmHg, those who did not undergo an exercise test and had a VO<sub>2</sub> peak above 15 mL/kg/min were considered suitable for lung resection with less postoperative complications (Morice et al., 1992).

In 1995 with a larger group of patients, it was already found that the VO<sub>2</sub> peak, expressed as a percentage of predicted, estimated better postoperative complications, and that the patients with a VO<sub>2</sub> peak more than 75% had 10% probability of complications. In contrast, in patients with VO<sub>2</sub> peak less than 43% this probability increased to 90%, using as the cutoff point the VO<sub>2</sub> peak of 60% (Bolliger et al. 1995a). At the same time, it was observed that patients with complications had a VO<sub>2</sub> peak lower than 62.8% and if postoperative VO<sub>2</sub> peak (ppo-VO<sub>2</sub> peak) was less than 10 mL/kg/min, the risk of complications was very high (Bolliger et al., 1995b).

Recently it has been noticed that patients with complications have a VO<sub>2</sub> peak of 15 mL/kg/min, while those without complications, have a VO<sub>2</sub> peak of 19.2 mL/kg/min (Wang et al., 1999). Therefore, we can say that patients with a VO<sub>2</sub> peak less than 10 mL/kg/min are not candidates for lung resection surgery. On the contrary, they are candidates if the VO<sub>2</sub> peak is more than 15 mL/kg/min. Furthermore, in connection with the completion of pneumonectomy, VO<sub>2</sub> peak values above 20 mL/kg/min or 75% of predicted value indicate a low risk of postoperative complications, while values below 10 mL/kg/min or 40% of predicted indicate a high risk (Bolliger et al., 1995b).

Trying to get a better tolerance for exercise testing, especially in patients with dyspnoea who were not able to reach their VO<sub>2</sub> peak, the submaximal protocol was proposed. In it the patient performs a pre-defined level of work (ATS, 2003).

After studying the exercise test with submaximal protocol in candidates for lung resection surgery, it has been observed that the VO<sub>2</sub> reached allowed to predict the risk of postoperative complications (Miyoshi et al., 1989). However, this type of protocol usually requires invasive techniques which are not tolerated so well, therefore, this type of protocol is usually replaced by the incremental one.

The current recommendations of the ERS / ESTS Task Force is that the cardiopulmonary exercise test is sure, reproducible and should be performed in a controlled environment. In addition, the VO<sub>2</sub> peak measured during the test with incremental protocol should be considered as the most important parameter to assess, as a measure of exercise capacity and as a good predictor of postoperative complications after thoracic surgery. Finally, to perform pneumonectomy the value of 75% of predicted or more than 20 mL/kg/min should be considered as cutoff point. The risk of postoperative complications is high if the VO<sub>2</sub> peak is less than 35% of predicted or less than 10 mL/kg/min for any resection. Instead, there is insufficient evidence to recommend cutoff points for lobectomy (Brunelli et al., 2009).

### 3.6 Other tests

Thoracic computed tomography (CT) has efficacy comparable to that of perfusion scintigraphy in the calculation of ppo-FEV<sub>1</sub> (Wu et al., 2002). In one study that compared

the usefulness of thoracic CT (figure 3), single photon emission computed tomography (SPECT) and magnetic resonance imaging (MRI) in patients with bronchogenic carcinoma who are candidates for lung resection, MRI proved to be more accurate than the other two techniques in the measurement of ppo-FEV1 (Ohno et al., 2007).

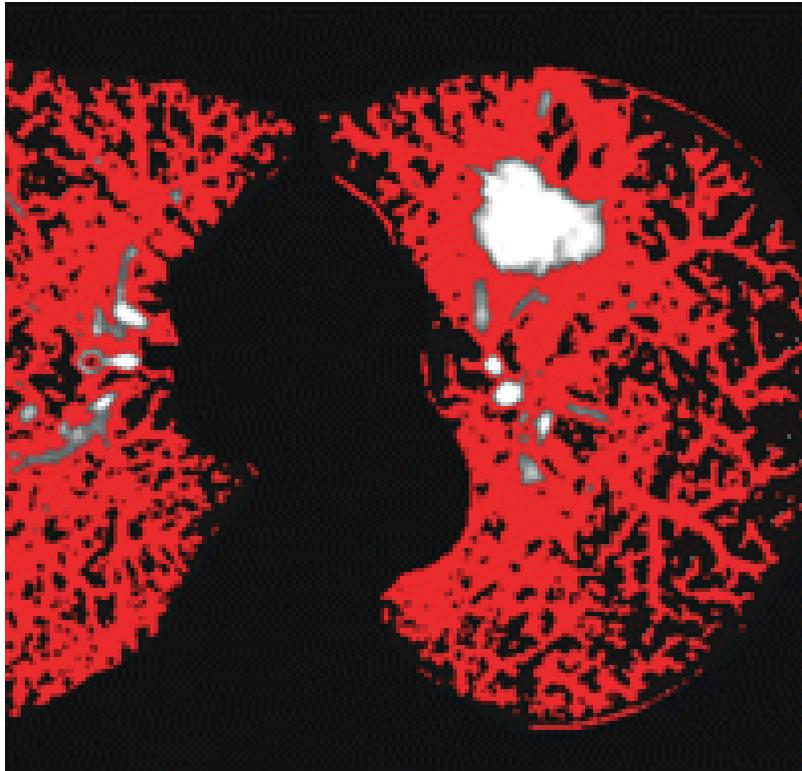


Fig. 3. Quantitative CT scan shows functional lung (*red*), pulmonary emphysema (*black*), and lung cancer (*white*). (Ohno et al., 2007).

The anatomical method is the calculation of postoperative lung function with the help of a formula that uses the preoperative FEV1 or FVC and the number of segments planned for resection (Zeiber et al., 1995). In case of lobectomy this formula estimates accurately the FEV1 postoperative and FVC which is not true in the case of pneumonectomy. That is why the latter is considered as inaccurate anatomical method.

The studies of pulmonary hemodynamics have also been used in the research of respiratory function in lung resection candidates. Perioperative risk is estimated by measuring the pulmonary arterial pressure and PaO<sub>2</sub> during temporary occlusion of the pulmonary artery. This technique simulates the "physiological pneumonectomy" and is performed both at rest and during the exercise. It has been observed that growth in pressure in the pulmonary artery during the occlusion period increases the postoperative risk and complications (Gass & Olsen 1986). In addition, it has been observed that if the pulmonary arterial pressure is higher than 35 mmHg and PaO<sub>2</sub> less than 45 mmHg, the patient is inoperable (Olsen et al., 1975). Another hemodynamic parameter used in the postoperative pulmonary assessment is the measurement of pulmonary vascular resistance (Schuurmans et al., 2002).

The main drawbacks of the use of pulmonary hemodynamics are the complexity of these techniques and the fact that they are invasive. Currently and in practice pulmonary hemodynamics is rarely used in respiratory assessing of candidates for thoracic surgery because the noninvasive tests have proved to have equal or superior efficacy.

#### 4. Algorithms in the preoperative functional assessment

The use of algorithms in the evaluation of lung function in patients scheduled for thoracic surgery has as the main objective the step standardization of a series of diagnostic tests. These procedures avoid unnecessary costs, save time and allow you to gain experience in a more regulated way. This rationalization process contributes to improved patients care and decreased postoperative morbidity and mortality (Juliá Serdá et al., 2010).

Although several algorithms have been proposed to assess respiratory function in patients undergoing thoracic surgery, there are few validations of them. In addition, they depend on the patients population being served and the technical possibilities of each hospital or center where they are performed (Juliá Serdá et al., 2010).

One of the most widely accepted algorithms was proposed by Bolliger et al. and performed in 80 patients scheduled for resection of lung parenchyma (Bolliger et al. 1995a). This algorithm was validated later by Wyser et al. in 137 patients (figure 1), demonstrating a low postoperative complication rate (11%) and mortality (1.5%) (Wyser et al., 1999).

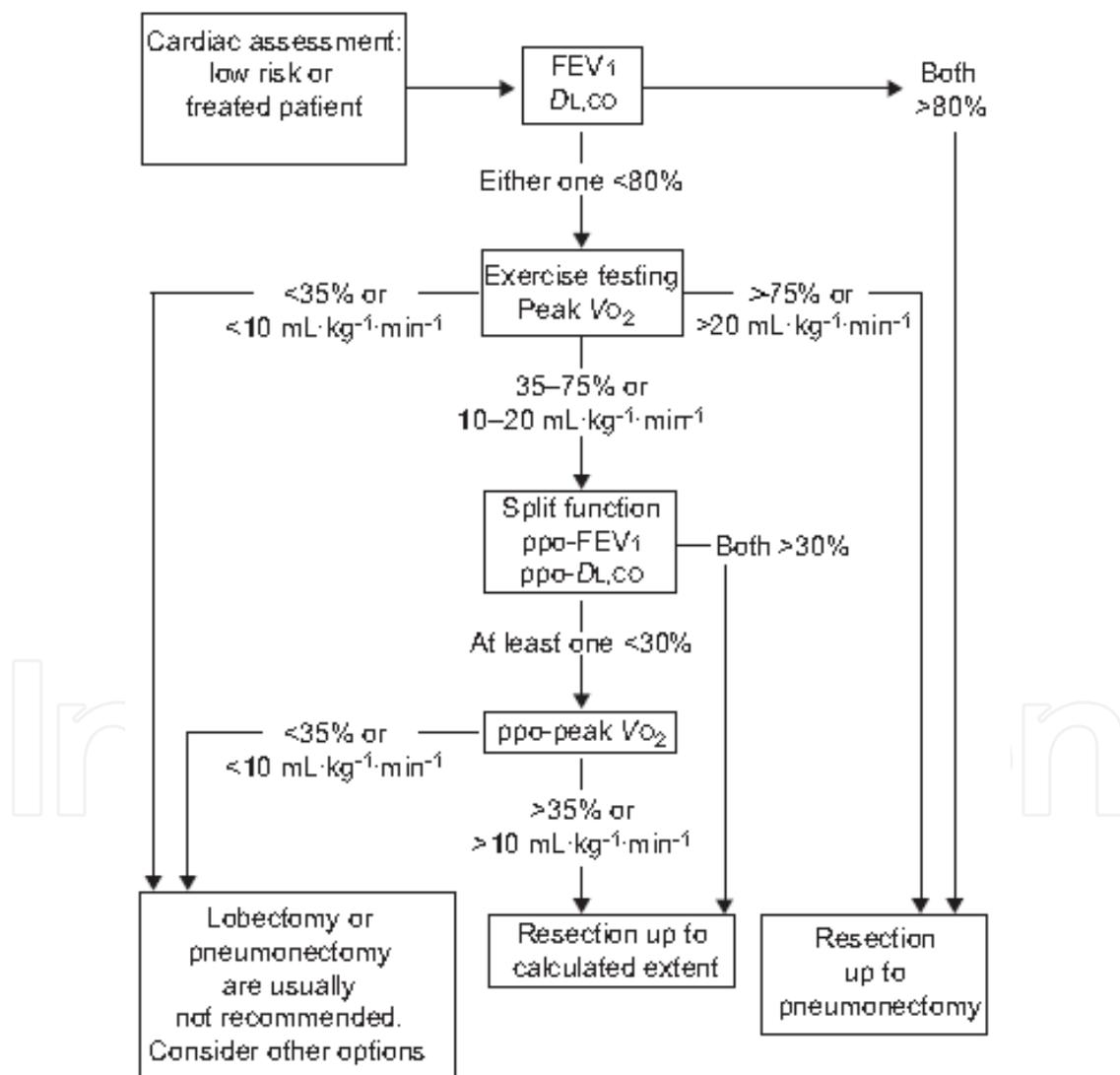


Fig. 4. Algorithm for assessment of cardiopulmonary reserve before lung resection in lung cancer patients. FEV1: Forced expiratory volume in 1 s. DLCO: Diffusion capacity of the lung for carbon monoxide. ppo: postoperative. VO2: Oxygen uptake. (Brunelli et al., 2009)

Taking into account these issues the ERS / ESTS Task Force has recently published its algorithm based fundamentally on the performance of exercise tests when preoperative FEV1 or DLCO is less than 80%. If in the exercise test VO2 peak is less than 35% or 10 mL/kg/min, it should not be recommendable to perform pneumonectomy or lobectomy, but if it is higher than 75% or 20 mL/kg/min, any resection (including pneumonectomy) would be indicated. If the VO2 peak is between these cutoff values, it would be advisable to calculate ppo-FEV1 and ppo-DLCO. If these are greater than 30%, lung resection would be indicated according to the calculated extension, and if, at least, one of these parameters is less than 30% it would be necessary to calculate the ppo-VO2 peak. After its calculation and if it is greater than 35% or 10 mL/kg/min, resection would be indicated depending on the calculated extension, and if its value is less than this cutoff, neither pneumonectomy nor lobectomy would be recommended. Finally, if it is impossible to perform cardiopulmonary exercise test and calculate the VO2 peak, it is recommendable to carry out the stair climbing test, but if the reached altitude is less than 22 meters, its calculation would be advisable (Brunelli et al., 2009) (figure 4).

One limitation in this type of algorithms, focusing on the completion of cardiopulmonary exercise testing, is that some candidates for lung resection are unable to execute any kind of exercise test due to the burden of concomitant comorbidities. These patients have demonstrated increased mortality after lung resection (Brunelli et al., 2005) and, after careful selection based on cardiopulmonary parameters they should be considered as high-risk patients and candidates to be perioperatively monitored.

## **5. Patient care management**

The use of bronchodilators, corticosteroids or a combination of both, as well as pulmonary rehabilitation and smoking cessation can help reduce postoperative complications occurring after thoracic surgery, especially in patients with comorbidities who present declining values of FEV1 or DLCO.

### **5.1 Smoking cessation**

Smokers have significantly higher risk of postoperative complications, so an intervention for smoking cessation during the preoperative period may be effective to reduce the incidences of complications. Moreover, the time of surgery may be a unique opportunity for smoking cessation attempts to succeed (Moller & Villebro, 2005).

There is evidence that interventions for smoking cessation, which include nicotine replacement therapy (NRT), increase for a short term the rate of smoking cessation and decrease postoperative morbidity. In this process it remains unclear which treatment intensity is optimal. Derived from indirect comparisons, the interventions that begin from 4 to 8 weeks before surgery, based on weekly counselling and the NRT are the most effective to quit smoking and to prevent long-term postoperative complications (Moller & Villebro, 2005).

### **5.2 Pulmonary rehabilitation**

Pulmonary rehabilitation, that includes exercise and education, is effective in candidates for lung volume reduction and in the pre-and postoperative period of lung transplantation (Nici et al., 2006). However, this effectiveness is not clearly demonstrated in surgical patients with lung cancer.

Before the surgery, the preoperative VO<sub>2</sub> is inversely proportional to the probability of the presence of complications after lung resection (Wu et al., 2002), which, in turn, is associated with postoperative loss of lung function (Nagamatsu et al., 2007). In addition, pulmonary rehabilitation improves VO<sub>2</sub> before the surgery in patients with COPD with low VO<sub>2</sub> (less than 15 mL/kg/min), which reduces late complications without affecting the operability or the prognosis (Bobbio et al., 2008).

Preoperative training programs lead to a reduction of hospital stay and of complications in patients with COPD and lung cancer (Sekine et al., 2005). However, improved accessibility to intervention has been observed only in patients with “quasi normal” lung function (Lovin et al., 2006). Pulmonary rehabilitation in inpatients has shown benefits in exercise capacity and lung volumes (Cesario et al., 2007).

Therefore, in the light of the data presented, it seems logical that pulmonary rehabilitation may decrease the complication rate in candidates for lung resection, which is why future researches on the content and duration of rehabilitation programs are priorities.

### 5.3 Pharmacologic therapy

The diagnosis of COPD is often established during the preoperative functional assessment in patients scheduled for lung resection after the diagnosis of lung cancer. These patients, with a high percentage of respiratory complications, may be excluded from surgery if we fail to achieve, with proper treatment, a sufficient pulmonary function value.

The main guidelines for the management of COPD patients who are to undergo lung resection indicate that it is necessary that the patient quit smoking, do exercises in pulmonary rehabilitation and optimize proper treatment to improve lung function and reduce postoperative complications (Brunelli et al., 2009). However, the treatments indicated for patients with COPD and lung cancer do not differ from those which are recommended to patients who have only COPD, in which a short-term therapeutic effect is not expected.

In the scientific literature we have found only few studies that evaluate the short and long term effect of initiation of therapy in patients with COPD and lung cancer. Several of them value the effect of tiotropium on lung function, establishing its improvement up to 226ml in FEV<sub>1</sub> (Kobayashi et al., 2009), but without any effect on post surgery complications (Ueda et al. 2010). In a recent study, the treatment with formoterol and budesonide added to tiotropium improved the FEV<sub>1</sub> in 310ml and decreased the number of postoperative pulmonary complications (Bölükbas et al., 2011). One of the keys to these results is the improvement in lung function that occurs when adding corticosteroids to long-acting bronchodilators. Another key is the improvement in FEV<sub>1</sub> due to these drugs, since its value, both pre-and postoperative, is associated with mortality and morbidity after the surgery. Therefore, an elevation of FEV<sub>1</sub> can increase the number of candidates for surgical resection, thus optimizing the treatment of cancer and improve the prognosis of these patients.

## 6. Conclusion

A lot of scientific literature dedicated to pre-operative evaluation before surgical treatment of lung diseases has been published. The search for the ideal preoperative test to predict major perioperative risk of patients began with the use of spirometry in 1955. Since then, scientific evidence allowing the stratification of perioperative risk based in different preoperative pulmonary function tests, estimations of postoperative lung function,

pulmonary circulation hemodynamics, arterial blood gases or exercise testing has been given. Therefore, the functional assessment has undergone major changes; apart from preoperative measurement of pulmonary function (FEV1, DLCO or VO2 peak) is getting more and more importance.

In the last few years, a number of decision-making algorithms interpreting the abundant literature on the issue have been described. These algorithms are mainly based on that postoperative FEV1 should not to be used alone to select patients for lung resection. DLCO should be routinely measured during pre-operative evaluation of lung resection candidates (regardless of whether the spirometric evaluation is abnormal or not). A postoperative FEV1 and DLCO values of 30% predicted is suggested to be a high risk threshold for this parameter when included in an algorithm for assessment of pulmonary reserve before surgery, exercise tests should be indicated for all the patients undergoing surgery with FEV1 or a DLCO < 80% of normal values and either ventilation scintigraphy or perfusion scintigraphy offer good prediction of post-operative lung function.

Finally, the main recommendation to the patients on which lung resection will be performed is to give up smoking for sufficient spell (at least 2–4 weeks) before the surgery, since it may decrease post-operative complications. Moreover, early pre- and post-operative rehabilitation should also be recommended, since it may produce functional benefits in patients with resected lung.

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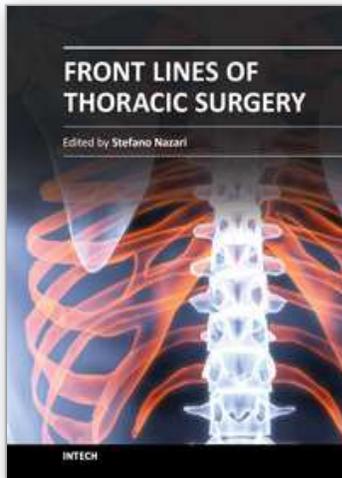
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Front Lines of Thoracic Surgery collects up-to-date contributions on some of the most debated topics in today's clinical practice of cardiac, aortic, and general thoracic surgery, and anesthesia as viewed by authors personally involved in their evolution. The strong and genuine enthusiasm of the authors was clearly perceptible in all their contributions and I'm sure that will further stimulate the reader to understand their messages. Moreover, the strict adhesion of the authors' original observations and findings to the evidence base proves that facts are the best guarantee of scientific value. This is not a standard textbook where the whole discipline is organically presented, but authors' contributions are simply listed in their pertaining subclasses of Thoracic Surgery. I'm sure that this original and very promising editorial format which has and free availability at its core further increases this book's value and it will be of interest to healthcare professionals and scientists dedicated to this field.

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