

## REVIEW

# Functional evaluation of the lung resection candidate

C.T. Bolliger, A.P. Perruchoud

*Functional evaluation of the lung resection candidate. C.T. Bolliger, A.P. Perruchoud. ©ERS Journals Ltd 1998.*

**ABSTRACT:** Advances in operative technique and perioperative care have considerably reduced surgical morbidity and mortality after pulmonary resections. Various single and combined parameters of functional operability have been proposed to assess the surgical risk. Pulmonary function tests adequately assess the pulmonary risk, and baseline or stress electrocardiography, echocardiography and nuclear cardiac studies assess the cardiac risk.

Patients with normal or only slightly impaired pulmonary function (forced expiratory volume in one second (FEV<sub>1</sub>) and transfer factor of the lung for carbon monoxide (TL<sub>CO</sub>) ≥80% of predicted) and no cardiovascular risk factors can undergo pulmonary resections up to a pneumonectomy without further investigation. For others, exercise testing, pulmonary split-function studies, or a combination of these two methods are recommended. Exercise testing, most frequently performed as a symptom-limited test with the measurement of maximal oxygen uptake (V'O<sub>2,max</sub>), assesses both the pulmonary and cardiovascular reserves. A V'O<sub>2,max</sub> of <10 mL·kg<sup>-1</sup>·min<sup>-1</sup> is generally considered prohibitive for any resection, a value of >20 mL·kg<sup>-1</sup>·min<sup>-1</sup> or >75% of predicted normal, safe for major resections. Split-function studies are radionuclide-based estimations of the predicted postoperative (ppo) values of various parameters. The currently used ppo-parameters are FEV<sub>1</sub>-ppo, TL<sub>CO</sub>-ppo and, most recently, V'O<sub>2,max</sub>-ppo. Suggested cut-off values for safe resection are: for FEV<sub>1</sub>-ppo and TL<sub>CO</sub>-ppo ≥40% pred; and for V'O<sub>2,max</sub> ≥35% pred, combined with an absolute value of ≥10 mL·kg<sup>-1</sup>·min<sup>-1</sup>. The lowest acceptable ppo-values will still have to be established by additional prospective studies.

In the long-term, resections involving not more than one lobe usually lead to an early functional deficit followed by later recovery. The permanent functional loss in pulmonary function is small (≤10%) and exercise capacity is only slightly reduced or not at all. Pneumonectomy, on the other hand, leads to an early permanent loss of about 33% in pulmonary function and 20% in exercise capacity. Thus, pulmonary function tests alone overestimate the functional loss after lung resection.

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The dramatic increase in the incidence of bronchogenic carcinoma has made this disease the most frequent malignancy worldwide. In industrialized nations, the majority of lung resection candidates suffer from bronchogenic carcinoma, whereas only some decades ago benign conditions, such as destroyed lung parenchyma after tuberculosis, had to be removed. The prognosis of bronchogenic carcinoma remains sombre as about 75–85% are inoperable at the time of diagnosis [1], and despite recent advances in chemo- and radiotherapy regimens, surgical resection remains the only curative form of treatment [2].

Depending on their extent, pulmonary resections lead to permanent loss of pulmonary function. In healthy people, resections up to a pneumonectomy are tolerated remarkably well. Lung cancer patients, however, are mainly smokers or exsmokers who suffer not only from their neoplasm, which should be resected, but also from varying degrees of chronic obstructive pulmonary disease (COPD) or ischaemic heart disease. This puts them

at increased risk for postoperative complications and permanent respiratory disability. Apart from the stage and histology of the tumour, the cardiopulmonary reserves, thus, play an important role in the assessment of the surgical risk in lung cancer patients. As recently discussed by BECHARD [3], two critical issues have to be addressed in this context: the ability of the patient to survive the physical stress of the operation itself (*i.e.* operability) and the amount of lung tissue that can be removed without making the patient a "pulmonary cripple" (*i.e.* resectability). The term "resectability", as described by BECHARD [3], is used as a functional entity in this article, whereas it usually stands for the anatomical resectability of a tumour. Many single and combined parameters have been used to assess the functional reserves prior to pulmonary resection.

Apart from pulmonary function tests (forced expiratory volume in one second (FEV<sub>1</sub>), forced vital capacity (FVC), FEV<sub>1</sub>/FVC), the transfer factor of the lung for carbon monoxide (TL<sub>CO</sub>) the carbon monoxide transfer

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coefficient ( $K_{CO}$ ) and the measurement of pulmonary haemodynamics (pulmonary artery pressure, pulmonary vascular resistance) have traditionally been used in the past. Exercise testing has become increasingly popular since a report by EUGENE *et al.* [4] in 1982, who found that the maximal oxygen uptake ( $V'O_{2,max}$ ) during symptom-limited exercise was a much better predictor of operative mortality than tests of ventilatory mechanics ( $FEV_1$  and  $FEV_1/FVC$ ). When analysing the literature on functional evaluation of lung resection candidates, one must keep in mind that, since the early reports in the 1950s [5, 6], extensive development has taken place; modern anaesthetic techniques, readily available intensive care unit (ICU) facilities, and, more recently, minimally invasive surgical procedures allow pulmonary resections in patients who would have been deemed in-operable some years ago.

In this overview, we would like to discuss the development and the current state of the art of the preoperative functional evaluation before lung resection, with emphasis on the most important tests. It is of utmost importance to measure all functional parameters when the patient is at his or her best. Quite often, pulmonary function and exercise capacity can be improved with an intensive course of antiobstructive therapy, which necessitates postponement or repeat assessment of the functional measurements.

### Pulmonary function tests (PFTs)

#### *Spirometry*

Various lung function parameters have been recommended. As early as 1955, GAENSLER *et al.* [6] suggested the use of the vital capacity (VC), which should be >2 L before pulmonary resection, without mentioning the extent. Although other authors have also reported the use of the VC, either in absolute values [7] or in percentage of predicted normal values [8–13], it has practically been abandoned in favour of the  $FEV_1$ .

Early recommendations of  $FEV_1$  values for safe resections were >2 L for pneumonectomy by BOUSHY *et al.* [14] and >1.5 L for lobectomy by WERNLY *et al.* [15]. LODDENKEMPER *et al.* [16] suggested clearly more conservative values of >2.5 L for a pneumonectomy, >1.75 L for lobectomy, and >1.5 L for segmentectomy. WERNLY *et al.* [15] also suggested an  $FEV_1$  >2 L for pneumonectomy, with the rationale that with a 50% left-right functional distribution the postresectional  $FEV_1$  would be 1 L, which they deemed to be the lower limit for adequate pulmonary reserve. In a recent paper by MILLER [17], reporting on 2,340 patients, the suggested  $FEV_1$  values were >2 L for pneumonectomy, >1 L for lobectomy, and >0.6 L for wedge or segmental resections. Three reports used the  $FEV_1$  in percentage predicted: MITTMAN [18] suggesting >70%, NAGASAKI *et al.* [19] and, most recently, PATE *et al.* [20], >40%; however, none of the three studies mentioned the extent of resection possible with these values. PATE *et al.* [20] suggested >1.6 L for absolute  $FEV_1$  values. The recent emphasis on predicted postoperative (ppo) values for  $FEV_1$  ( $FEV_1$ -ppo) will be discussed in the split-function section.

Other parameters, such as the maximal voluntary ventilation [6], peak flow [21], and maximal midexpiratory flow (MEF50) [10, 22], have not been widely used. Static lung volumes measured by helium diffusion or body plethysmography have been suggested to appreciate the extent of overinflation as a potential risk factor. Recommendations for the residual volume (RV) vary, SCHAEFER *et al.* [23] recommending <2 L and BAGG *et al.* [24] <2.5 L. For the ratio between RV and total lung capacity (TLC) (RV/TLC), recommendations are <40% [25, 26] and <50% [18, 27–29]. The plethysmographically determined airway resistance for a pneumonectomy should be <0.5–0.8 kPa (<5–8 mbar·L<sup>-1</sup>·s) according to certain authors [13, 26, 30, 31]. All of these measurements of maximal flows, static lung volumes and airway resistance have been abandoned over time.

#### *Transfer factor*

The transfer factor for carbon monoxide ( $TL_{CO}$ ) measured with the single-breath technique was suggested as early as 1963 by CANDER [32], who considered a value of <50% of predicted as a clear contra-indication for pulmonary resections. NAGASAKI *et al.* [19] estimated that a  $TL_{CO}$  of <50% pred was insufficient for a pneumonectomy, but FERGUSON *et al.* [33] found a more conservative estimate of <60% pred insufficient for "major pulmonary resections". Only recently, MARKOS *et al.* [34] brought in the concept of the predicted postoperative  $TL_{CO}$  which will be discussed in the split-function section.

#### *Blood gas measurements*

Arterial blood gas measurements have been part of the routine preoperative evaluation for a long time. However, their predictive value for functional operability is less than certain. For the arterial oxygen tension ( $P_{a,O_2}$ ) some authors estimate a value of <6.7 kPa (50 mmHg) as a clearly increased risk [31, 35]. For NAGASAKI *et al.* [19] a value of <8.0 kPa (60 mmHg) was associated with a high risk for pulmonary resections, and for OLSEN *et al.* [28] a value of <6.0 kPa (45 mmHg) on moderate exercise with simultaneous balloon occlusion of the pulmonary artery of the lung to be resected.

More importance has been attached to the arterial carbon dioxide tension ( $P_{a,CO_2}$ ), where considerable agreement exists that a raised value of >6.0 kPa (45 mmHg) represents a high risk for pulmonary resections [8, 31, 36–39]. This value was also mentioned in a recent statement by the American College of Chest Physicians [40]. For NAGASAKI *et al.* [19], only values exceeding 6.7 kPa (50 mmHg) represented high risk. On the other hand, in a prospective study, recently published by KEARNEY *et al.* [41], a  $P_{a,CO_2}$  of >6.0 kPa (45 mmHg) was not a risk factor for postoperative complications. Similarly, MORICE *et al.* [39] found that in high-risk patients a good exercise capacity allowed safe lobectomy in patients with a  $P_{a,CO_2}$  value of >6.0 kPa (45 mmHg). At our institution, BOLLIGER *et al.* [42] were able to confirm the findings of MORICE *et al.* [39] in a series of five patients of comparable high risk. All five patients had

Table 1. – Historical synopsis of various single criteria of operability (extent of possible resection indicated where specified)

Parameter	Extent of resection	[Ref.]
<b>Spirometry</b>		
VC	≥50%	Lobec [13]
	≥80%	Pneum [13]
VC-ppo	>40%	[43]
FEV <sub>1</sub>	>1.5 L	Lobec [15]
	>2.0 L	Pneum [14, 15]
FEV <sub>1</sub> % pred	>40%	[19, 20]
MVV	>50%	[6]
RV/TLC	<50%	[18, 27–29]
FEV <sub>1</sub> -ppo	>700 mL	[20]
	>800 mL	[28]
	>1000 mL	[15, 44]
	>30%	[34, 45]
	>40%	[34, 46]
PPP	>1650	[47]
<b>Transfer factor</b>		
TL <sub>CO</sub>	>50%	[19, 32]
	>60%	[33]
TL <sub>CO</sub> -ppo	>40%	[34, 48]
PPP	>1650	[47]
<b>Arterial blood gas measurements</b>		
P <sub>a,O<sub>2</sub></sub>	>6.7 kPa (50 mmHg) at rest or on exercise	[31, 35]
P <sub>a,CO<sub>2</sub></sub>	<6.0 kPa (45 mmHg) at rest or on exercise	[8, 31, 36–39]
<b>Cardiovascular</b>		
No ECG changes:		[18, 49–53]
P <sub>pa</sub>	<35 mmHg on TUPAO/50 W	[28, 45]
	<40 mmHg on 40–50 W	Lobec [54]
	<35 mmHg on 40–50 W	Pneum [54]
	<30 mmHg on 40–50 W	Pneum [55]
PVR	<190 dyn·s·cm <sup>-5</sup> at rest or on exercise	[56]
<b>Cardiopulmonary</b>		
V'O <sub>2,max</sub>	>1000 mL	[4]
	>20 mL·kg <sup>-1</sup> ·min <sup>-1</sup>	Pneum [57, 58]
	≥15 mL·kg <sup>-1</sup> ·min <sup>-1</sup>	Lobec [39]
	≥10 mL·kg <sup>-1</sup> ·min <sup>-1</sup>	[58]
	>75%	Pneum [59]
	≥50%	[60]
	≥40%	Lobec [59]
V'O <sub>2,max</sub> -ppo	≥40%	[48]
	≥10 mL·kg <sup>-1</sup> ·min <sup>-1</sup>	[48]
Stair climb	5 flights	Pneum [61, 62]
	3 flights	Lobec [61, 62]
Walk tests	6 min >1000 ft	[46]

VC: vital capacity; ppo: predicted postoperative; FEV<sub>1</sub>: forced expiratory volume in one second; % pred: percentage of predicted value; MVV: maximal voluntary ventilation; RV: residual volume; TLC: total lung capacity; P<sub>a,O<sub>2</sub></sub>: arterial oxygen tension; P<sub>a,CO<sub>2</sub></sub>: arterial carbon dioxide tension; TL<sub>CO</sub>: transfer factor of the lung for carbon monoxide; PPP: predicted postoperative product (FEV<sub>1</sub>-ppo × TL<sub>CO</sub>-ppo); P<sub>pa</sub>: mean pulmonary artery pressure, TUPAO: temporary unilateral occlusion of the pulmonary artery; PVR: pulmonary vascular resistance; V'O<sub>2,max</sub>: maximal oxygen uptake on exercise; ECG: electrocardiograph; Pneum: pneumonectomy; Lobec: lobectomy.

good exercise capacity (V'O<sub>2,max</sub> ≥69% pred), although in three of the five the P<sub>a,CO<sub>2</sub></sub> was >6.0 kPa (45 mmHg) at rest with a further increase on exercise. Overall, there is agreement that the determination of arterial blood gas values, primarily the P<sub>a,CO<sub>2</sub></sub> as a parameter of alveolar ventilation, is useful, and that the old established cut-off values are markers for increased operative risk, but should not in themselves exclude patients from surgery (table 1).

### Age

Increasing age is associated with complications after pulmonary resections. In 1955, KROSNIK and WASSERMAN [63] found postoperative arrhythmias after thoracotomies, which were accentuated in the elderly. BATES [64] found a high mortality in patients >70 yrs of age after pneumonectomy but not after lobectomy. Various other authors have confirmed that the age limit of 70 yrs represented an independent risk factor for lung resections [19, 49, 50]. On the other hand, reports by KIRSH *et al.* [65], BREYER *et al.* [66] and BERGGREN *et al.* [67], looking more specifically at elderly patients, came to the conclusion that in malignant disease, in particular, pulmonary resections were beneficial. In a study of 100 patients >65 yrs old, GERSON *et al.* [68] found that those with good exercise capacity did not suffer postoperative complications. Based on the majority of reports, age >70 yrs represents an independent risk factor for lung resection, but this increased risk is mainly due to co-morbidity in this age group. Elderly patients in a good state of health do not have increased postoperative complications and should not be excluded from surgery solely on the basis of their age [69].

### Pulmonary haemodynamics

Early investigators found that after major pulmonary resection, exercise capacity was decreased due to a reduced maximal cardiac output [70]. It was thought that the marked reduction of the pulmonary vascular bed led to pulmonary artery hypertension and subsequently to right heart failure. Therefore, certain investigators assessed preoperative right ventricular and pulmonary vascular reserve with the use of temporary unilateral occlusion of the pulmonary artery (TUPAO). With this technique, the pulmonary artery pressure (P<sub>pa</sub>) and the P<sub>a,O<sub>2</sub></sub> at rest and during exercise were measured while the pulmonary artery of the lung to be resected was occluded by a balloon-tipped catheter. Various authors found that an increased P<sub>pa</sub> on TUPAO was associated with increased operative risk [32, 51, 71]. UGGLA [9] found a fall in the P<sub>a,O<sub>2</sub></sub> on TUPAO and exercise to be the best risk predictor. Patients with a P<sub>pa</sub> of ≥35 mmHg on TUPAO and exercise combined with arterial hypoxaemia (P<sub>a,O<sub>2</sub></sub> <6.0 kPa (45 mmHg)) were generally deemed to be functionally inoperable by OLSEN and co-workers [28, 45]. Due to its invasiveness, a high failure rate and complications TUPAO has been totally abandoned.

However, P<sub>pa</sub> measurements at rest and on usually moderate exercise (40–50 W steady-state) without TUPAO are still used. KELLER *et al.* [55] found that patients with a preoperative P<sub>pa</sub> >30 mmHg on 40 W steady-state exercise developed pulmonary artery hypertension (PAH)

limiting exercise 1 yr after pneumonectomy. TAUBE and KONIETZKO [72], on the other hand, did not find significant PAH 6 months postoperatively, independent of the extent of resection. According to GOERG *et al.* [54]  $P_{pa}$  on moderate exercise should be <35 mmHg for a pneumonectomy and <40 mmHg for a lobectomy. LODDENKEMPER *et al.* [16] did not find the  $P_{pa}$  on exercise predictive up to a value of 45 mmHg. OLSEN *et al.* [73] found neither  $P_{pa}$  nor the calculated pulmonary vascular resistance (PVR) on submaximal exercise predictive of postoperative complications. The latter finding is in contrast to an early, often cited report by FEE *et al.* [56], who found a PVR of <190 dyn·s·cm<sup>-5</sup> at rest or on exercise a criterion of operability (table 1). At our institution, BRÜNDLER *et al.* [74] reported on 637 patients in whom right heart catheterization was performed. They found a formula incorporating FEV<sub>1</sub>, TLCO and  $P_{a,O_2}$  to predict PAH. Surprisingly, in 276 (43%) of these patients, PAH on moderate exercise was due to left ventricular dysfunction. More recently, the right ventricular ejection fraction was suggested as a further useful parameter for risk prediction [75, 76].

Although these recent investigations show continued interest in pulmonary haemodynamics, the conflicting results and the widely differing cut-off values of  $P_{pa}$  make their use questionable. The routine measurement of pulmonary haemodynamics in patients with impaired pulmonary function has, therefore, been abandoned in many institutions in favour of split-function studies and exercise testing.

### Cardiac risk

In comparison to the abundant literature on pulmonary function evaluation before pulmonary resection, the assessment of the cardiac risk in pulmonary resections has received less attention. As early as 1961, MITTMAN [18] showed that an abnormal electrocardiograph (ECG) was associated with an increased risk of suffering an intraoperative or postoperative cardiac event, defined as heart failure, arrhythmias or myocardial infarction. In patients with bronchogenic carcinoma, DIDOLKAR *et al.* [49] found a postoperative mortality of 9.1% when the ECG was normal but 21.9% when it was pathological. The reports of many authors have shown similar findings [51–53, 77, 78]. The multifactorial cardiac risk index published in 1977 by GOLDMAN *et al.* [50] has since been confirmed by many other reports [79–86]. One of Goldman's risk factors for an operation was a myocardial infarction within the previous 6 months. STEEN *et al.* [87] found that this risk is especially high with an infarction within the previous 3 months. FOSTER *et al.* [88] recommended coronary artery bypass surgery before patients with coronary artery disease undergo any other planned surgery. In an interesting study, of 100 patients >65 yrs of age before elective abdominal or thoracic surgery, GERSON *et al.* [68] found that the inability to sustain a cardiac frequency of >99 beats·min<sup>-1</sup> over 2 min on supine cycle ergometry was more predictive of perioperative complications than radionuclide heart studies.

The problem of postoperative arrhythmias after lung resections was first mentioned by BAILEY and BETTS [89] and CURRENS *et al.* [90] in 1943, and has been described by various authors since [63, 90–93]. Prophylactic dig-

italization was advocated by many authors in the 1960s and 1970s [94–96]. However, these early studies were not randomized, and a recent report by RITCHIE *et al.* [97] in a prospective randomized trial found no beneficial effect of perioperative digitalization. The benefit of this practice is, therefore, questionable.

### Extent of resection

There is a clear correlation between the extent of resection and postoperative morbidity and mortality. Segmental or wedge resections have the lowest and pneumonectomies the highest risk [69, 98]. By international standards, an overall 30 day mortality rate of ±5% can be considered a very good result. The mortality after pneumonectomy is usually twice or more that after lobectomy. In a large series by LODDENKEMPER [99] comprising 433 patients, the rates were 9.4 and 5.0%, respectively. In the study by MARKOS *et al.* [34] the rates were 16.7 and 0%, respectively. At our own institution, HASSE [100] found rates of 7 and 4%, respectively, for the years 1972–1978, and recently the figures from 1991–1992, were 10 and 2.2%, respectively [59]. The best results so far were published by MILLER [17] in 1993. In his impressive series of 2,340 patients, the overall mortality was 0.64%, for exploratory thoracotomy 0.59%, for wedge resections 0.13%, for lobectomies 0.39%, and for pneumonectomies 4.97%. These excellent results may have been achieved, in part, through fairly rigorous patient selection; as for a pneumonectomy, the FEV<sub>1</sub> had to be >2 L and FEV<sub>1</sub>-ppo >1 L.

The estimation of the amount of lung tissue which can safely be removed is very important in the preoperative evaluation. The development of split-function studies has made it possible to calculate the relative function of the tissue to be removed to the total function of both lungs, and thereby to predict postoperative function.

### Split-function studies

Patients with normal pulmonary function tolerate removal of an entire lung without respiratory problems. In patients with impaired pulmonary function, however, knowledge of the postresectional function is of importance for the assessment of surgical risk. This necessitates the ability to measure the relative contribution of the parenchyma to be resected to the total lung function. The simplest approach is the separate functional analysis of the right and left lung. In 1932, JACOBÆUS *et al.* [101] introduced bronchspirometry, which was used more extensively after the development of the double-lumen catheter by CARLENS [102] in 1949, which allowed separate analysis of the ventilation of the left and right lung. Various authors [5, 103–107] have used the method, which was invasive (separate intubation of the right and left lung) and has been abandoned in favour of scintigraphic techniques.

Another early test introduced by BERGAN [108] in 1960 was the lateral position test, whereby the relative function of the right and left lung could be determined by changes in the functional residual capacity (FRC) when the patient switched from a supine to a left and right decubital position. The accuracy of this test has

since been criticized [109–111], and it has also been replaced by scintigraphic investigations.

Radiospirometry with xenon-133 [112] has been used for the regional analysis of ventilation. In the early 1970s, KRISTERSSON *et al.* [44] were able to accurately predict the functional loss after pneumonectomy and lobectomy [113], TØNNESEN *et al.* [114] and subsequently ALI *et al.* [115] have confirmed these findings, the latter as long as the resection involved more than three segments. Since then, radiospirometry has been replaced by split perfusion scans using intravenous technetium-99 macro-aggregate. The breakthrough of this method came with an article by OLSEN *et al.* [116] in 1974, which reported a good correlation in 13 pneumonectomy patients, between the FEV<sub>1</sub>-ppo and the value measured 3 months postoperatively. Many authors have since confirmed the feasibility of estimating ventilatory function by perfusion scans, which, because of their general availability and easy performance, have replaced the ventilation studies [15–17, 28, 34, 48, 72, 117, 118]. The scintigraphic formula generally used is: FEV<sub>1</sub>-ppo = preoperative FEV<sub>1</sub> × (1 - functional contribution of the parenchyma to be resected).

Only LADURIE and RANSON-BITKER [119] could not find good correlations between the predicted and measured postoperative FEV<sub>1</sub> 1 yr after pneumonectomy. To this date, there is no consensus on the minimum FEV<sub>1</sub>-ppo value required for safe resection. OLSEN *et al.* [28] suggested 800 mL because of an early publication by SEGAL and BUTTERWORTH [120], who showed that COPD patients with lower values generally had carbon dioxide retention. Other authors [15, 44] have suggested a higher value of 1,000 mL, whereas, most recently, PATE *et al.* [20] found that even 700 mL based on pneumonectomy was sufficient, as long as the patient could climb at least three flights of stairs or had a maximal oxygen consumption of >10 mL·kg<sup>-1</sup>·min<sup>-1</sup>. The value of FEV<sub>1</sub>-ppo to predict postoperative complications has received increasing attention in recent publications. OLSEN *et al.* [73] did not find it predictive, whereas KEARNEY *et al.* [41], in a large prospective study involving 331 patients, found the FEV<sub>1</sub>-ppo the only independent predictor of postoperative complications.

In the interesting study by MARKOS *et al.* [34] the formula used to estimate FEV<sub>1</sub>-ppo also proved to be accurate in calculating the predicted postoperative transfer factor (TL,CO-ppo). They found that both a FEV<sub>1</sub>-ppo and a TL,CO-ppo of <40% pred were good predictors for postoperative complications, but not baseline pulmonary function. They suggested that an FEV<sub>1</sub>-ppo of <30% pred as well as the combination of an FEV<sub>1</sub>-ppo with a TL,CO-ppo of <35% pred represented inoperability. The approach of MARKOS *et al.* [34] to use percentage of predicted rather than absolute values is probably superior to arbitrary absolute values. This might be especially important in the light of the increasing number of females with bronchogenic carcinoma, who should not be denied surgery on the grounds of values established mainly in males. In a small study of 16 patients, HOLDEN *et al.* [46] found neither FEV<sub>1</sub>-ppo nor TL,CO-ppo predictive of complications, but all five patients who died within 90 days of surgery had an FEV<sub>1</sub>-ppo <40% pred. On the other hand, the TL,CO-ppo in all non-survivors was >40% pred. PIERCE *et al.* [47], in 54 patients,

looked at the product of FEV<sub>1</sub>-ppo × TL,CO-ppo in percentage predicted (predicted postoperative product) and found values of <1,650 highly predictive of complications, whereas baseline PFTs were not. In this paper, the predicted postoperative function was scintigraphically estimated in patients with an FEV<sub>1</sub> of <55% pred; in the other patients the formula used was: FEV<sub>1</sub>-ppo = preoperative FEV<sub>1</sub> × (1-y/19) (where y is the number of segments to be removed and 19 the total number of segments).

This formula obviates the need for a perfusion scan but has the disadvantage of not taking into account the function of the segments to be removed. This might lead to overestimation of functional loss and possibly the denial of surgery to patients with borderline pulmonary function. ZEIHNER *et al.* [121] found this overestimation to be approximately 250 mL after lobectomy and 500 mL after pneumonectomy. This aspect was taken into account by NAKAHARA *et al.* [122], who also estimated the FEV<sub>1</sub>-ppo nonscintigraphically, but made a distinction between obstructed and normal subsegments; their formula was: FEV<sub>1</sub>-ppo = (1-(b-n)/(42-n)) × preoperative FEV<sub>1</sub> (where n and b are the number of obstructed subsegments and total subsegments, respectively, of the parenchyma to be resected, and 42 the total number of subsegments). In this study, FEV<sub>1</sub>-ppo was also predictive of postoperative complications.

A brand new approach to predict postoperative pulmonary function is the use of quantitative computed tomography (CT) of the chest, which was described by WU *et al.* [123] in 1994. They found excellent correlations between predicted and postoperatively measured values for FEV<sub>1</sub> (r=0.93) and FVC (r=0.86) in a group of 38 patients. These results will have to be validated in prospective studies comparing ppo-values estimated by scintigraphy *versus* quantitative CT. If CT-based calculations should prove to be equivalent or superior to scintigraphic estimations, the former investigation might become obsolete, as many patients undergo CT scanning of the chest anyway as part of their routine preoperative work-up.

In 1987, CORRIS *et al.* [124] and, recently, PUENTE-MAESTU *et al.* [125], showed that using Olsen's perfusion scan formula they were able to predict postoperative exercise capacity (V'O<sub>2,max</sub>-ppo). At our institution, BOLLIGER *et al.* [48] recently studied a group of 25 patients with impaired pulmonary function using this formula to predict V'O<sub>2,max</sub>-ppo; and very good correlations were found between predicted and measured postoperative values. Furthermore, V'O<sub>2,max</sub>-ppo was significantly lower in patients with postoperative complications (10.6±3.6 vs 14.8±3.5 mL·kg<sup>-1</sup>·min<sup>-1</sup>), with a value of <10 mL·kg<sup>-1</sup>·min<sup>-1</sup> being associated with 100% mortality (three out of three). Baseline pulmonary function, FEV<sub>1</sub>-ppo and TL,CO-ppo were not significantly different between the two groups, but TL,CO-ppo was significantly lower in the three patients who died than in the 22 survivors. On the other hand, all three variables FEV<sub>1</sub>-ppo, TL,CO-ppo and V'O<sub>2,max</sub>-ppo were associated with a 50% mortality (two out of four patients) if their value was <40% pred.

Currently, split-function studies for the predicted postoperative function in the evaluation of lung resection candidates are firmly established, especially in patients

with impaired pulmonary function (table 1). The value of the new parameter,  $V'O_{2,max-ppo}$ , proposed by BOLLIGER *et al.* [48] warrants prospective evaluation.

### Exercise testing

All parameters discussed so far look at certain specific aspects of a patient's functional reserves. For decades, the desire was to find an overall parameter for the assessment of the cardiopulmonary reserves encompassing all the others. With this concept, exercise testing seems an ideal tool as it looks at the fitness of a patient, which is an equivalent of the cardiopulmonary reserves. During exercise, oxygen consumption, carbon dioxide production and cardiac output all increase, and the level of work achieved reflects how well the lung, the heart and the vasculature interact to deliver oxygen to the tissue. A thoracotomy with pulmonary resection imitates the stress of exercise to a certain extent.

Exercise testing in the preoperative evaluation before pulmonary resection has attracted interest for some time, and many different protocols have been proposed in the past. Basically, they can be grouped according to the effort demanded from the patient. Three different types of exercise intensity are used: minimal achievement, submaximal; and maximal or symptom-limited tests. The bulk of the literature concerns maximal tests, which are more easily standardized than the two other forms (table 1).

#### Minimal achievement

With these tests, a minimal effort has to be achieved, such as climbing a certain number of stairs [51] or maintaining a certain workload for a given amount of time [67]. Walking and stair-climbing tests have been used. For the 12 min walking test, BAGG [126] found no difference between patients with and without postoperative ventilatory complications. In 16 patients at increased operative risk ( $FEV_1 \leq 1.6$  L), HOLDEN *et al.* [46] found a 6 min walking test of >1,000 ft or >44 steps of stair-climbing predictive of successful surgical outcome. Other reports on stair-climbing by OLSEN and co-workers [61, 62] indicate that three flights of stairs permit a lobectomy and five flights pneumonectomy. In a recent study by POLLOCK *et al.* [127], stair-climbing was standardized (height and width of steps, number of steps per floor), and it was concluded that an achievement of 4.6 flights (83 steps) corresponded to a  $V'O_2$  of 20 mL·kg<sup>-1</sup>·min<sup>-1</sup>, which is generally considered a safe limit for a pneumonectomy. All these studies have the advantage of being simple and cheap. On the other hand, they generally suffer the disadvantage of poor standardization. For stair-climbing, for example, the speed of ascent is important, and an insufficient number of floors in a hospital could very simply preclude the feasibility of the test. Furthermore, in the available literature, on-line ECG readings for the assessment of exercise-induced cardiac events, such as arrhythmias or ischaemias, are not usually reported. OLDER *et al.* [128] showed, in a group of 187 elderly patients undergoing major abdominal surgery, that a low anaerobic threshold ( $V'O_{2,max} < 11$  mL·kg<sup>-1</sup>·min<sup>-1</sup>) and ischaemia on maximal exercise testing were independent risk factors for perioperative

mortality, and the combination of the two resulted in a mortality rate of 42%. In summary, the minimal achievement exercise tests lack standardization and inadequately assess cardiac events. In the absence of cardiopulmonary exercise units, a set-up like the one described by POLLOCK *et al.* [127] is certainly acceptable provided the patient does not have ischaemic heart disease.

#### Submaximal tests

The rationale behind submaximal testing is the better tolerance of the exercise stress in lung resection candidates who are usually elderly, suffer from COPD and might, therefore, not be motivated to perform exercise to exhaustion. MIYOSHI *et al.* [129] (in 1987), NAKAHARA *et al.* [43] and NAKAGAWA *et al.* [130] (in 1992), who were all from the same Japanese group, reported on their protocol in which patients with a VC-ppo of >40% pred were exercised with a 25 W increase every 3 min until the cardiac frequency reached 140 beats·min<sup>-1</sup> or the respiratory exchange ratio (R) exceeded 1.0. All patients had catheters in the pulmonary and radial arteries. They found that age and resting pulmonary function were predictive of postoperative morbidity but not mortality. Good predictors of mortality were two calculated parameters: the  $V'O_2$ /body surface area (BSA) and the oxygen delivery ( $O_2D$ )/BSA measured at a blood lactate level of 20 mg·dL<sup>-1</sup> (LA20), which they termed the "empirical anaerobic threshold".  $V'O_2/BSA_{LA20}$  should be >400 mL·min<sup>-1</sup>·m<sup>-2</sup> and  $O_2D/BSA_{LA20}$  >500 mL·min<sup>-1</sup>·m<sup>-2</sup> for thoracotomy. They proposed an algorithm for the preoperative functional evaluation [43] incorporating these parameters together with the VC-ppo, which should be ≥40% pred, and FEV<sub>1</sub>-ppo, >30% pred.

OLSEN *et al.* [73] studied 29 patients with pulmonary artery catheters on cycle ergometry at workloads of 25 and 40 W during 2–4 min. The 22 survivors were best separated from the seven nonsurvivors by the cardiac index ( $5.5 \pm 1.3$  vs  $3.9 \pm 0.3$  L·min<sup>-1</sup>·m<sup>-2</sup>),  $O_2$  delivery ( $1,630 \pm 462$  vs  $1,070 \pm 95$  mL·min<sup>-1</sup>·m<sup>-2</sup>) and calculated  $V'O_2$  ( $11.3 \pm 2.1$  vs  $7.8 \pm 1.5$  mL·kg<sup>-1</sup>·min<sup>-1</sup>). In a study by PIERCE *et al.* [131], patients exercised on a bicycle, and the lobe to be resected was occluded through a fibre-optically introduced balloon catheter. If the patient could maintain moderate exercise, he was sent to surgery and progressed well. RAO *et al.* [132] found that desaturation to <90% on pulse oximetry, at rest, while walking on level ground or climbing two flights of stairs identified high-risk lung resection candidates.

Although submaximal exercise protocols are less strenuous than maximal tests, they have the clear disadvantage of being invasive and causing discomfort to the patient. The current trend in exercise testing is, therefore, towards less invasiveness but maximal effort.

#### Maximal tests

As early as 1955, TAYLOR *et al.* [133] showed  $V'O_{2,max}$  to be an objective parameter of the cardiorespiratory reserves. Later it was shown, mainly by cardiologists [134–136], that  $V'O_{2,max}$  was more reproducible than duration of exercise. Most recently, CAHALIN *et al.* [137] showed the distance ambulated in a 6 min walk test to

be predictive of  $V'O_{2,max}$  and short-term event-free survival in patients with advanced heart failure.

Although known of for some time, the assessment of  $V'O_2$  in lung resection candidates has only gained interest after a report by EUGENE *et al.* [4] in 1982, who found that 15 out of 19 patients with a  $V'O_{2,max}$  of  $>1$  L had no postoperative complications, whereas three out of four patients with  $<1$  L died of cardiopulmonary failure. In that study, FEV<sub>1</sub> and VC had no predictive value. In the same year, COLMAN *et al.* [138] published a study with a larger number of 59 patients, in which  $V'O_{2,max}$  was not found to be predictive of postoperative complications. This study is continuously cited as a negative study. But it is difficult to compare it to other reports because the definition of complications included surgical parameters, such as excess blood loss, prolonged air leak, empyema, wound infection and gastric haemorrhage, which are not likely to be predictable by exercise testing.

SMITH *et al.* [57], studying 22 patients, did not find baseline pulmonary function or FEV<sub>1</sub>-ppo predictive of surgical outcome.  $V'O_{2,max}$ , on the other hand, was significantly higher in patients without than in patients with complications ( $22.4 \pm 1.4$  vs  $14.9 \pm 0.9$  mL·kg<sup>-1</sup>·min<sup>-1</sup>). Of 10 patients with a  $V'O_{2,max}$  of  $>20$  mL·kg<sup>-1</sup>·min<sup>-1</sup> only one suffered a complication, in contrast to all six patients with a  $V'O_{2,max}$  of  $<15$  mL·kg<sup>-1</sup>·min<sup>-1</sup>. In 1987, BECHARD and WETSTEIN [58] reported a study with 50 patients confirming the findings of SMITH *et al.* [57] of a safe upper cut-off value of 20 mL·kg<sup>-1</sup>·min<sup>-1</sup>: none of their patients with a  $V'O_{2,max}$   $>20$  mL·kg<sup>-1</sup>·min<sup>-1</sup> sustained any complications. On the other hand, five of the seven patients with a  $V'O_{2,max}$   $<10$  mL·kg<sup>-1</sup>·min<sup>-1</sup> had complications, including two deaths. The definition of complications was virtually identical to that in the study by SMITH *et al.* [57].

In the study by MARKOS *et al.* [34] mentioned above,  $V'O_{2,max}$ , either in absolute values (mL·kg<sup>-1</sup>·min<sup>-1</sup>) or expressed as a percentage of predicted, did not discriminate between the presence and the absence of complications. However, in lobectomy patients with complications,  $V'O_{2,max}$  was significantly lower and a fall in oxygen saturation at exercise  $>2\%$  was also predictive of complications. In the study by HOLDEN *et al.* [46],  $V'O_{2,max}$  on cycle ergometry was not a discriminator between patients without or with minor complications and those who died within 90 days of surgery. These results should be interpreted with caution, as seven out of the 16 patients did not exercise to exhaustion, making the remaining nine a very small sample size. Furthermore, postoperative mortality cannot be compared to most other studies, where it is limited to 30 days.

A very valuable study, published by MORICE *et al.* [39] and discussed in a editorial by OLSEN [139], investigated 37 patients with resectable bronchogenic carcinoma, who were at high operative risk because of at least one of the following parameters: FEV<sub>1</sub>  $\leq 40\%$  pred; radionuclide calculated FEV<sub>1</sub>-ppo  $\leq 33\%$  pred; or  $P_{a,CO_2}$   $\geq 6.0$  kPa (45 mmHg). Eight of these patients underwent lobectomy because their  $V'O_{2,max}$  was  $>15$  mL·kg<sup>-1</sup>·min<sup>-1</sup>. Only two of the eight patients had nonfatal postoperative complications, and all eight were discharged from hospital by day 22. Similar results were reported by PATE *et al.* [20].

In a small series of five lung cancer patients, BOLLIGER *et al.* [42] recently confirmed that good exercise capacity, defined as a  $V'O_{2,max}$  of  $\geq 69\%$  pred on cycle ergometry, allowed safe lobectomy, although all five patients had at least one criterion of high surgical risk (FEV<sub>1</sub>-ppo  $<30\%$  pred, TLCO  $<60\%$  pred combined with a fall in  $P_{a,O_2}$  at peak exercise  $>0.67$  kPa (5 mmHg), and  $P_{a,CO_2}$   $>6.0$  kPa (45 mmHg)).

In 1993, DALES *et al.* [140] reported on 117 consecutive patients undergoing thoracotomy for possible or definite lung cancer. One hundred and fifteen underwent PFT but only 46 had treadmill exercise testing. The reasons given for not exercising everybody were lack of time or money. Outcome parameters were separated into all complications and respiratory complications only. The definition of all complications included purely surgical problems such as air leak, bronchopleural fistula and haemothorax, as in the study by COLMAN *et al.* [138]. When the analysis was restricted to respiratory complications only, a twofold or greater risk was associated with current smoking, cancer as the final pathological condition, at least moderate dyspnoea, FEV<sub>1</sub>  $<60\%$  pred, ventilatory reserve  $<25$  L and a  $V'O_{2,max}$   $<1.25$  L. The shortcomings of this study are the lack of explanation as to why the reported cut-off values were chosen, and the fact that only 39% (46 out of 117) patients underwent exercise testing, which could well reflect a selection bias.

EPSTEIN *et al.* [141] compared preoperative cycle ergometry to a multifactorial cardiopulmonary risk index (CPRI) in 42 lung cancer patients. The definition of postoperative complications was comparable to that in the paper by SMITH *et al.* [57]. There was no difference in  $V'O_{2,max}$  between the patients with and without complications ( $16.4 \pm 1.4$  vs  $16.7 \pm 0.8$  mL·kg<sup>-1</sup>·min<sup>-1</sup>), but based on a threshold value the risk for cardiopulmonary complications was six times greater in those with a  $V'O_{2,max}/BSA$  of  $<500$  mL·min<sup>-1</sup>·m<sup>-2</sup>. The CPRI was found to be superior to  $V'O_{2,max}$  as a predictor of complications. This CPRI consists of a cardiac part containing the time-honoured criteria established by GOLDMAN *et al.* [50] with a score of 0–4. The pulmonary part has a score of 0–6, one point for each of the following six variables: 1) obesity (body mass index (BMI)  $\geq 27$  kg·m<sup>-2</sup>); 2) cigarette smoking within 8 weeks of surgery; 3) productive cough within 5 days of surgery; 4) diffuse wheezing within 5 days of surgery; 5) FEV<sub>1</sub>/FVC  $<70\%$ , and 6) a  $P_{a,CO_2}$   $>6.0$  kPa (45 mmHg). The total CPRI score has, therefore, a range of 1–10. Patients with a score of  $\geq 4$  were 22 times more likely to develop a complication compared to a CPRI  $<4$ .

In a recent second report, EPSTEIN *et al.* [142] confirmed the value of the CPRI, but found that the inability to perform bicycle ergometry also independently predicted postoperative complications. The CPRI is an interesting and simple way of obtaining information concerning cardiopulmonary risk factors; nevertheless, the pulmonary part of this CPRI must be addressed critically: criteria 2 to 4 are observer-dependent, and an FEV<sub>1</sub>/FVC ratio  $<70\%$  is not a generally accepted parameter of increased operative risk. We therefore think that this CPRI needs further prospective evaluation and that, at this stage, a patient should not be denied surgery solely on the basis of such an index.

At our institution, BOLLIGER *et al.* [59] evaluated a consecutive series of 80 lung resection candidates and found that  $V'O_{2,max}$  was the best predictor of postoperative complications. A receiver operating characteristic (ROC)-curve analysis proved  $V'O_{2,max}$ , when expressed as a percentage of predicted, to be significantly more sensitive than when analysed in absolute values ( $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ). The estimated probability of suffering no complication was 90% with a  $V'O_{2,max}$  of  $>75\%$  pred, and 10% with a  $V'O_{2,max}$  of  $<43\%$  pred. A value of  $<60\%$  pred proved to be prohibitive for resections involving more than one lobe. A subgroup of 25 patients with impaired pulmonary function ( $\text{FEV}_1 < 2 \text{ L}$  or  $\text{TL,CO} < 50\%$  pred) underwent radionuclide split-function studies [48]. Again,  $V'O_{2,max}$  both expressed as a percentage of predicted and in absolute values ( $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) discriminated between patients suffering complications and those who did not.  $\text{FEV}_1\text{-ppo}$  and  $\text{TL,CO-ppo}$  were not predictive, but  $\text{TL,CO-ppo}$  was predictive of fatal complications. In their latest study in high-risk lung resection candidates, MORICE *et al.* [60] confirmed the usefulness of  $V'O_{2,max}$  expressed as a percentage of predicted normal values. They found that a  $V'O_{2,max}$  of  $\geq 50\%$  pred was a better predictor of operability than the absolute value of  $\geq 15 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  that they had used previously [39].

#### Algorithm for the functional evaluation of the lung resection candidate

Despite the increasing enthusiasm for split-function studies and exercise testing, one has to remember that many lung resection candidates can undergo resections up to a pneumonectomy without any sophisticated tests, which are costly and not universally available. This stresses the need for an algorithm for the preoperative functional evaluation. A modern approach should probably include PFT, ppo-function and exercise variables. In 1992, NAKAHARA *et al.* [43] reported their approach based on submaximal testing. Criteria of operability are a VC-ppo  $\geq 40\%$  pred, an  $\text{FEV}_1\text{-ppo} \geq 30\%$  pred,  $V'O_2/\text{BSALA}_{20} \geq 400 \text{ mL}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$ , and  $\text{O}_2\text{D}/\text{BSALA}_{20} \geq 500 \text{ mL}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$ . Similarly, BECHARD [3] recommends  $\text{FEV}_1\text{-ppo} \geq 30\%$  pred,  $\text{TL,CO-ppo} > 40\%$  pred and a  $V'O_{2,max} > 10 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  as limits of operability.

Based on the bulk of the recent literature and on our own investigations, we favour noninvasive maximal over invasive submaximal exercise testing. In the preoperative functional evaluation, we propose the following algorithm (fig. 1), which was slightly amended after prospective testing in 132 consecutive patients [143]. Adherence to this algorithm resulted in a postoperative complication rate of 11%, with a very low mortality of 1.5%. This meant a 50% reduction in complications in comparison to our previous series [59].

Patients who have a negative cardiac history (including a normal ECG) and whose  $\text{FEV}_1$  and  $\text{TL,CO}$  are both  $\geq 80\%$  pred can undergo lung resection up to a pneumonectomy without any further tests. The cut-off values of 80% pred were chosen because the respective postoperative values are usually  $>40\%$  pred - identified as safe [34, 47] - even after pneumonectomy as the diseased lung rarely contributes  $> 50\%$  of the total lung

function [144]. Any patient with active or suspected cardiac disease should first undergo a thorough cardiac work-up and, if necessary, even coronary bypass surgery in case of ischaemic heart disease [88]. Only patients whose cardiac condition is amenable to treatment can undergo further investigation for pulmonary resection.

If either  $\text{FEV}_1$  or  $\text{TL,CO}$  is  $<80\%$  pred, exercise testing with the measurement of  $V'O_{2,max}$  is performed. Rarely, exercise testing will pick up ischaemic heart disease in patients with a negative cardiac history and a normal ECG. This will also lead to a cardiac work-up (interrupted line in the algorithm). If  $V'O_{2,max}$  is  $>75\%$  pred or  $>20 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ , patients qualify for resection up to a pneumonectomy; if it is  $<40\%$  pred or  $10 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  they are inoperable. All patients with  $V'O_{2,max}$  values in between undergo split-function studies with the aid of a pulmonary perfusion scan to determine their predicted postoperative function (ppo-function). Firstly,  $\text{FEV}_1\text{-ppo}$  and  $\text{TL,CO-ppo}$  are analysed; if the values for both parameters are  $<40\%$  pred, patients are deemed inoperable. If either one is  $\geq 40\%$  pred, then  $V'O_{2,max}\text{-ppo}$  becomes the decisive factor. With a  $V'O_{2,max}\text{-ppo}$  of either  $<35\%$  pred or  $<10 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  patients are also deemed inoperable; whereas patients with a  $V'O_{2,max}\text{-ppo} \geq 35\%$  pred and  $\geq 10 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  are operable up to the extent which was used for the prediction of postoperative function. This algorithm integrates the functional parameters of operability and their respective cut-off values from the most recent literature.

The difference between our approach and those suggested by NAKAHARA *et al.* [43] and BECHARD [3] is that we perform exercise testing before split-function studies as we found it superior to them. In any case, both tests are complementary and their combined use allows excellent assessment of the surgical risk.

#### Effect of lung resection on postoperative pulmonary function and exercise capacity

Most of the above-mentioned tests have been used to assess operability and resectability in patients with impaired pulmonary function. The studies available indicate that a patient with an estimated  $\text{FEV}_1\text{-ppo}$  of  $>700\text{--}1,000 \text{ mL}$  or 30% pred will survive the operation, be discharged from hospital, and actually have the predicted postoperative  $\text{FEV}_1$ , which will be enough to avoid pulmonary incapacity. For patients with normal or only slightly abnormal pulmonary function, however, a lung resection up to a pneumonectomy is clearly feasible without split-function or exercise studies.

The relevant question for many lung resection candidates is, therefore, not whether they will tolerate pulmonary resection but rather whether they can lead a normal life as before, both in their private as well as in their professional environment. The answer depends mainly on the extent of resection. Various studies have looked at the functional loss after lung resection in terms of pulmonary function [16, 44, 113, 115–117, 145–147]. ALI *et al.* [115] and LODDENKEMPER *et al.* [16] have shown that resections involving not more than one lobe lead to an early loss in pulmonary function with later recovery and little permanent deficit. As for the preoperative assessment, exercise capacity reflects the



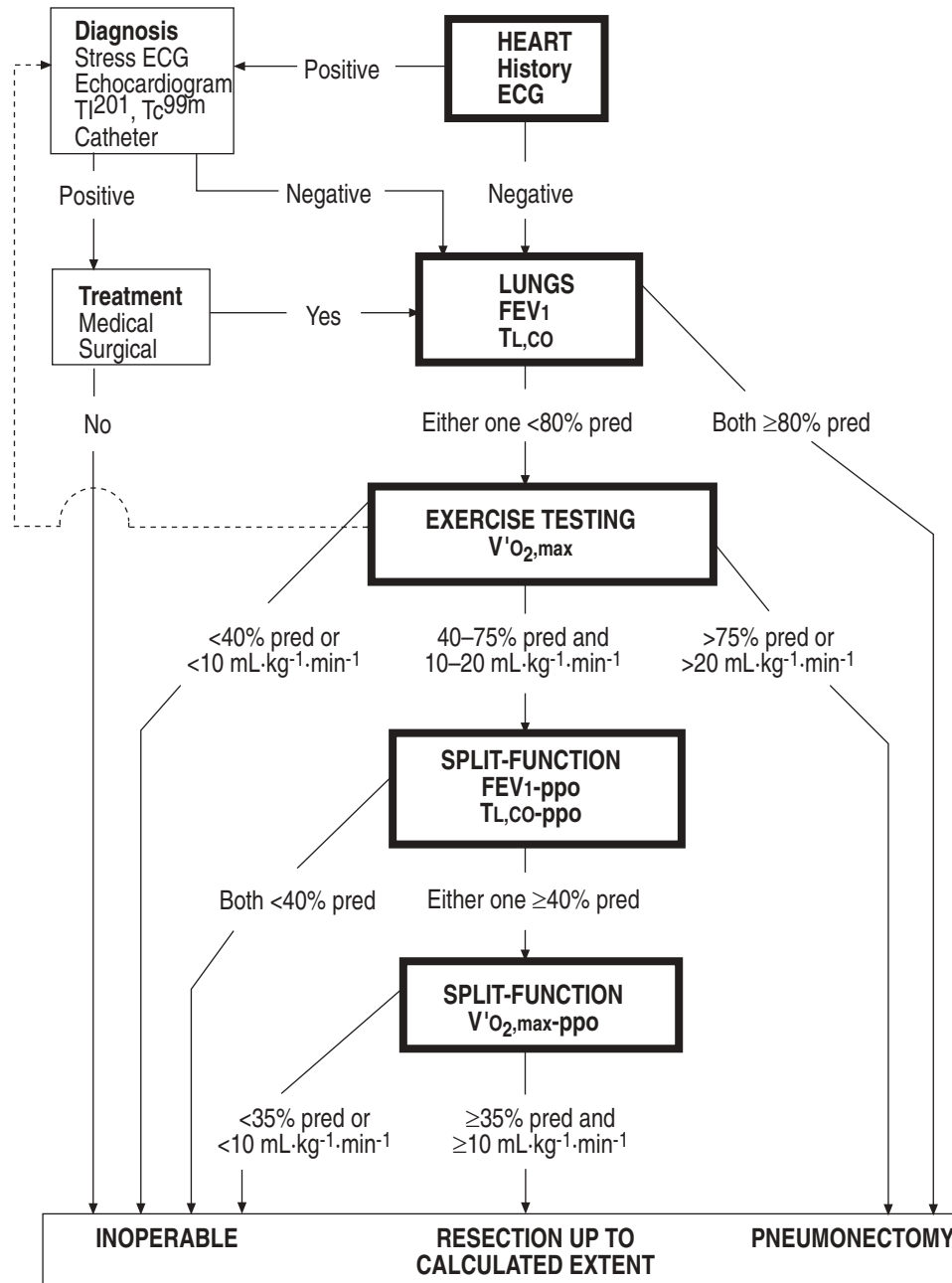


Fig. 1. – Algorithm for the assessment of the cardiorespiratory reserves (functional operability) of lung resection candidates. Patients undergo successive steps of functional investigation from top to bottom, until they qualify for varying extents of resection or are deemed inoperable. The "safety loop" for patients with cardiac problems is indicated in the upper left-hand corner; the cardiac work-up and treatment are only described qualitatively. The dashed line leading from exercise testing back to the cardiac work-up is for patients with a negative cardiac history and a normal ECG, who show symptoms or signs of ischaemia during exercise testing. TI: thallium; Tc: technetium;  $V'O_{2,max}$ : maximal oxygen uptake on exercise; ppo: predicted postoperative; ECG: electrocardiograph; FEV<sub>1</sub>: forced expiratory volume in one second; TL,CO: transfer factor of the lung for carbon monoxide.

functional postoperative reserves better than simple PFT, but has been investigated much less frequently than PFT [70, 124, 148, 149]. As early as 1965, DEGRAFF *et al.* [70] reported on exercise limitation after extensive pulmonary resection. CORRIS *et al.* [124] analysed a group of 28 patients 4 months after pneumonectomy, and found that the average reduction was 22% for the FEV<sub>1</sub>, 29% for VC, and 23% for  $V'O_{2,max}$ . VAN MIEGHEM and DEMEDTS [148] studied 28 patients (14 lobectomies and 14 pneumonectomies) 6 months after surgery, and found a decrease in VC of 15% after lobectomy and 37%

after pneumonectomy, the values for FEV<sub>1</sub> were 12 and 33%, respectively, and for  $V'O_{2,max}$  11 and 21%, respectively.

In a recent report, BOLLIGER *et al.* [150] analysed patients 3 and 6 months postoperatively. Lobectomy led to an early functional deficit followed by later recovery, with little permanent loss in pulmonary function ( $\leq 10\%$ ) and with no decrease in exercise capacity, whereas pneumonectomy led to an early permanent functional loss of about 33% in pulmonary function and 20% in exercise capacity. The findings of BOLLIGER *et al.* [150]

are similar to those of VAN MIEGHEM and DEMEDTS [148] for pneumonectomies, but show less permanent functional loss after lobectomy.

PELLETIER *et al.* [149] investigated 20 patients after pneumonectomy and 27 after lobectomy. The mean decrease in FEV<sub>1</sub> was 17% after lobectomy and 31% after pneumonectomy, and the respective values for the maximal work capacity were 12 and 26%. As the analysis was performed early after surgery (2 months), it is more difficult to compare to other reports, and probably overestimates the permanent functional loss after lobectomy. A further interesting finding of this study was a weak relationship between the decrease in FEV<sub>1</sub>, and in exercise capacity ( $r^2=0.30$ ). Subjectively, pneumonectomy but not lobectomy led to an appreciable increase in dyspnoea during exercise.

The study by BOLLIGER *et al.* [150] came to similar conclusions about the patient-rated factors limiting exercise; before the operation, the majority of patients indicated leg muscle fatigue as the factor limiting their exercise capacity. Three and 6 months after surgery, however, leg muscle fatigue remained the most important subjective factor only in lobectomy patients, whereas after pneumonectomy dyspnoea became the leading cause. Objectively, pneumonectomy led to a significantly smaller breathing reserve and  $P_{a,O_2}$  at peak exercise than lobectomy, which probably reflects a limited transfer capacity of the reduced alveolar surface. Most recently, NEZU *et al.* [151] reported similar results in a group of 82 patients.

There is consensus in the literature that resections not exceeding one lobe lead to very little permanent functional deficit, whereas pneumonectomies cause a permanent deficit which is bigger for pulmonary function than for exercise capacity.

#### **New expectations with lung volume reduction surgery?**

The treatment of end-stage pulmonary emphysema had been entirely medical until COOPER *et al.* [152] reported very promising results after bilateral surgical volume reduction in a series of patients with severe COPD. This procedure had originally been introduced by BRANTIGAN and MUELLER [153] in 1957, but was subsequently abandoned because of a high mortality rate. In the series of COOPER *et al.* [152], there was no mortality and the FEV<sub>1</sub> improved by 82%. The basic concept is to reduce hyperinflation through resection of poorly functioning lung parenchyma, which leads to a marked decrease in total lung capacity (TLC) and RV. These changes are associated with marked symptom relief, and improvement in exercise tolerance and quality of life. The field of lung volume reduction surgery (LVRS) is currently rapidly expanding but still needs validation over time [154].

The concept of removing lung parenchyma to improve pulmonary function is, of course, almost contrary to what has been traditional in the surgical treatment of high-risk lung resection candidates, where the minimal amount of tissue is removed to achieve curative resection. This should rarely be less than a lobectomy, as lesser resections are fraught with a clearly higher local tumour recurrence rate [155]. The thought of combin-

ing LVRS with tumour resection in functionally inoperable lung cancer patients is, therefore, understandably attractive. First reports on successful operations in highly selected patients have appeared in a letter from GONZALEZ MUNOZ *et al.* [156], who reported on an emphysematous patient with a carcinomatous nodule of the left upper lobe. The patient had severely impaired pulmonary function with an FEV<sub>1</sub> of 660 mL (21% pred) and a  $\dot{V}_{L,CO}$  of 37% pred. A wedge resection of the nodule combined with volume reduction of about 20% of the lower lobe was performed with an uneventful postoperative course, the FEV<sub>1</sub> being 696 mL (22% pred) at 2 weeks. Another three emphysematous patients, with FEV<sub>1</sub> values of 29, 30 and 33% pred, respectively, were reported by COOPER *et al.* [157]. These patients underwent median sternotomy, formal lobectomy and LVRS. Their postoperative FEV<sub>1</sub> was 44, 44 and 48% pred, respectively.

These early reports are promising indeed. Long-term follow-up, however, will determine whether the thresholds of functional operability can be further lowered in such highly selected patients. In a recent editorial, OLSEN [158] speculated that eventually almost no one might be considered inoperable for pulmonary reasons. One caveat remains: enthusiasm over the technical feasibility should not lead surgeons to perform minimal resections in high-risk lung cancer patients, jeopardizing their chance of a curative resection [155].

#### **Summary**

Over the last 40 yrs, many single and combined parameters of functional operability for pulmonary resection have been proposed and reviewed regularly [38, 40, 45, 159–163]. Despite tremendous advances in operative techniques and perioperative care, surgical morbidity and mortality after pulmonary resections remain relatively high. An overall mortality of  $\pm 5\%$  has to be termed good. So far, no ideal single parameter for the assessment of functional operability in lung resection candidates has been found. PFTs adequately assess the pulmonary risk, and baseline or stress ECG, echocardiography and nuclear cardiac studies assess the cardiac risk. The increasing use of exercise testing with simultaneous measurement of pulmonary and cardiovascular parameters is a clear step towards this "ideal" parameter.

The recent development in the functional evaluation before pulmonary resection emphasizes the importance of the predicted postoperative function. This is possible with pulmonary perfusion scans and has been shown to be quite accurate by many authors [34, 48, 115–117, 124, 125]. Surprisingly, the same simple formula can be used to predict not only the postoperative FEV<sub>1</sub>, but also the  $\dot{V}_{L,CO}$  [34, 47, 48] and, most recently, the  $\dot{V}'O_{2,max}$  [48, 124, 125]. The calculated ppo-values take the extent of resection into account, which permits good individual risk assessment.

Apart from the split-function studies, the trend of the last decade seems to favour exercise testing with the measurement of  $\dot{V}'O_{2,max}$ . The majority of reports found  $\dot{V}'O_{2,max}$  a good independent risk predictor. Maximal exercise tests are fairly easy to standardize, and, in our opinion,  $\dot{V}'O_{2,max}$  represents the single best parameter to

evaluate both the pulmonary as well as the cardiovascular reserves.

A further trend lies in the increasing use of percentage of predicted normal rather than absolute values mainly for the FEV<sub>1</sub> [34, 43, 45] and TLCO [34, 47] but, most recently, also for V'O<sub>2,max</sub> [59, 60]. This trend has the advantage of taking age, sex and height into consideration. This notion will probably gain importance, especially with the current massive increase in lung cancer in females. Many established criteria of operability have been proposed following studies conducted in United States veterans administration institutions, where the patients were almost exclusively male [28]. Furthermore, the majority of lung resection candidates in industrialized nations suffer from lung cancer, a disease with a mortality approaching 100% when not treated surgically. In these patients, postoperative complications can, therefore, almost always be accepted unless they are fatal.

In analysing the literature, it is therefore important to differentiate between morbidity and mortality. Only parameters which have consistently been shown to indicate the latter, e.g. a V'O<sub>2,max</sub> <10 mL·kg<sup>-1</sup>·min<sup>-1</sup>, are prohibitive for surgery. The recent emergence of minimally invasive procedures in the field of thoracic surgery may well help to decrease perioperative mortality [164] and allow surgical resection in patients who, so far, would have been deemed functionally inoperable. Finally, the combination of lung cancer surgery with lung volume reduction is an attractive concept in selected patients who would otherwise be deemed functionally inoperable by any existing test.

Patients with normal or only slightly impaired pulmonary function (forced expiratory volume in one second and transfer factor of the lung for carbon dioxide ≥80% pred) and no cardiovascular risk factors tolerate pulmonary resections up to a pneumonectomy without any problems. Resections involving not more than one lobe usually lead to an early functional deficit followed by later recovery. Their permanent functional loss in pulmonary function is small (≤10%) and their exercise capacity is only slightly reduced, or not at all. Pneumonectomy, on the other hand, leads to an early permanent loss of about 33% in pulmonary function and 20% in exercise capacity [148, 150]. Thus, pulmonary function tests alone overestimate the functional loss after lung resection. Knowledge of these changes depending on the extent of resection is useful for the preoperative counselling, including the estimation of a patient's postoperative working capacity.

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