Lung resection remains the treatment of choice in the curative approach to non-small cell lung cancer. Because most lung cancer patients are current or former smokers, they are at increased risk of chronic obstructive pulmonary disease and coronary artery disease, conditions associated with increased surgical morbidity and mortality. Careful preoperative assessment of the cardiopulmonary reserves is therefore of great importance. Various single and combined parameters for the functional assessment before surgery have been proposed. Currently, the emphasis is on the determination of forced expiratory volume in the first second, the diffusing capacity for carbon monoxide, and exercise testing with the measurement of maximal oxygen uptake. Adherence to established algorithms for this preoperative evaluation, advances in operative technique (video-assisted thoracoscopic surgery and combined operations of lung cancer surgery with lung volume reduction surgery), and perioperative care permit resections in patients who until recently would have been considered functionally inoperable.

Keywords
lungs resection, preoperative evaluation, pulmonary function tests, exercise testing

know the functional status of the patient before operating. This functional evaluation or the assessment of operability is the third part of the assessment of a lung cancer patient (Fig. 1), and is the main topic of this review.

**Parameters of functional operability**

All functional parameters must be measured when patients are at their best. For pulmonary function tests this often implies an intensive course of antiobstructive therapy, consisting of a systemic steroid trial of approximately 40 mg prednisone daily for 3 to 4 weeks, and inhalational therapy with bronchodilator drugs. Chest physiotherapy and, if possible, a short exercise program should be initiated during the same period. Smoking cessation should be encouraged. The effect of treatment must be analyzed by repeat pulmonary function tests. In lung cancer the natural course of the disease often limits the window for functional improvement to 1 or 2 months at the most. Table 1 illustrates important currently used parameters for the functional evaluation, which are discussed in the following paragraphs.

### Age

Increasing age, usually defined as more than 70 years, is associated with complications after pulmonary resections [6–8], but this increased risk is mainly the result of comorbidity in this age group. Patients older than 70 years with a good performance status (Karnofsky score ≥70 points) and intact cardiopulmonary reserves have a long-term survival comparable with younger surgical patients [9]. Therefore, elderly patients in a good state of health should not be excluded from surgery solely on the basis of their age.

### Cardiac risk

Postoperative complications after pulmonary resections are not only the result of pulmonary causes, but are clearly influenced by cardiac comorbidity as well. An abnormal electrocardiogram is associated with an increased risk for sustaining an intraoperative or postoperative cardiac event, defined as heart failure, arrhythmia, or myocardial infarction. A myocardial infarction within the previous 6 months [10], but especially within the previous 3 months [11] is associated with a very high operative risk. If necessary, coronary artery bypass surgery has to be performed before patients with coronary artery disease undergo any other planned surgery.

### Spirometry

Of all the different spirometric parameters and indices recommended in the past, only measurements of the forced expiratory volume in the first second (FEV₁) have stood the test of time. Early recommendations of FEV₁ values for safe resections were more than 2 L for pneumonectomy [12] and more than 1.5 L for lobectomy [13]. These values, however, have never been universally accepted, which is easily understandable because they do not take gender, height, weight, and age into consideration, nor do they consider the functional state of the tissue to be removed. Recent interest has therefore shifted to postoperative remaining function. This function, the so-called predicted postoperative (ppo) function, has to be estimated. The techniques used for this estimation are discussed later in the split function section because they are not only used to measure FEV₁-ppo but also the postoperative diffusing capacity of carbon monoxide (DL<sub>CO</sub>-ppo) and maximal oxygen consumption on exercise testing (VO₂max-ppo).

### Diffusing capacity

The DL<sub>CO</sub> measured with the single-breath technique has gained increasing importance, with values of less than 50% of predicted being regarded as risky [14], and values less than 60% regarded as insufficient for “major pulmonary resections” [15]. Pulmonary complications are more frequent in patients with a low DL<sub>CO</sub> [16,17].
In analogy to FEV\textsubscript{1}-ppo, DL\textsubscript{CO}-ppo has been suggested as a predictor of postoperative complications [18], a concept that is discussed later in the split function section.

**Blood gas measurements**

The predictive value of arterial blood gas measurements for functional operability is less than certain. There is no consensus regarding a value of the arterial oxygen tension that would indicate a clearly increased risk for pulmonary resections. For arterial carbon dioxide tension, on the other hand, considerable agreement exists that a raised value of more than 45 mmHg represents an increased risk for pulmonary resections [19,20], but an elevated arterial carbon dioxide tension value alone should not exclude patients from surgery.

**Extent of resection**

The estimation of the amount of lung tissue that can be removed safely is very important. There is a clear correlation between the extent of resection, and postoperative morbidity and mortality [21]. Segmental or wedge resections have the lowest risk, and pneumonectomies have the highest risk [22], with the mortality after pneumonectomy usually two times or more than that after lobectomy. By international standards, an overall 30-day mortality rate of ±5% can be considered good—and less than 2%, excellent—provided that poor-risk patients are not excluded from surgery. Most of these data have been obtained in patient series in which patients have been operated by standard open thoracotomy. Newer techniques such as muscle-sparing thoracotomies or video-assisted thoracoscopic surgery may lower mortality rates further [4].

**Split function studies**

The development of split function studies (or studies of regional lung function) has allowed surgeons to calculate the function of the tissue to be removed relative to the total function of both lungs, and thereby to predict postoperative function.

This is important in patients with impaired pulmonary function. The most frequently used postoperative predicted parameter is FEV\textsubscript{1}-ppo, which can be obtained in various ways. The most accurate predictions are obtained with a split perfusion scan using intravenous Tc-99m, or with quantitative CT [23,24•]. Simple anatomic calculations using the number of segments or subsegments to be removed are less accurate but are often acceptable, provided that a distinction between open and occluded segments is made [24•,25]. The formula used for all methods to calculate FEV\textsubscript{1}-ppo is:

\[
\text{FEV}_{1}\text{-ppo} = \text{preoperative FEV}_{1} \times (1 - \text{functional contribution of the parenchyma to be resected})
\]

For safe resection the FEV\textsubscript{1}-ppo value should be more than 40% of predicted. The use of absolute values should be discouraged because they do not take patient gender, age, and height into consideration. The same formula to predict FEV\textsubscript{1}-ppo has also been used successfully to predict DL\textsubscript{CO}-ppo [17], as well as VO\textsubscript{2}\text{max}-ppo [26]. Interestingly, as for FEV\textsubscript{1}-ppo, a value of less than 40% of predicted normal for both DL\textsubscript{CO}-ppo [18] and VO\textsubscript{2}\text{max}-ppo [26] has been found to indicate increased risk.

**Exercise testing**

All parameters discussed so far examine specific aspects of a patient’s functional reserves. Exercise testing seems to be an ideal overall parameter for the assessment of cardiopulmonary reserves because it looks at the fitness of a patient, which is an equivalent of 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, heart, and vasculature interact to deliver oxygen to the tissues. A thoracotomy with pulmonary resection imitates the stress of exercise to a certain extent.

Currently, maximal or symptom-limited exercise tests with a cycle or treadmill are recommended. They have the advantage of good reproducibility, assess ischemia with online electrocardiographic monitoring, and are short in duration (usually not longer than 15–20 minutes). The current emphasis is on the measurement of VO\textsubscript{2}\text{max}, but in the absence of equipment measuring VO\textsubscript{2}\text{max}, Watts can also be used and the VO\textsubscript{2}\text{max} values can be calculated. A VO\textsubscript{2}\text{max} value of more than 20 mL/kg per minute or more than 75% predicted [27] qualifies for resection up to pneumonectomy, whereas a value less than 10 mL/kg per minute (or less than 40% predicted) is generally prohibitive for any resection. Another frequently used cutoff for safe resection of at least one lobe is a VO\textsubscript{2}\text{max} value of ≥ 15 mL/kg per minute [17,19,28]. So far, there have been two studies that indicate that VO\textsubscript{2}\text{max}-ppo should be more than 10 mL/kg per minute [26,29•].

In the absence of sophisticated exercise equipment there is considerable evidence that tests of minimal achievements can also be used to estimate the postoperative risk [30]. The most frequently used test by far is stair climbing. The ability to climb three or more flights of stairs [31,32] and five or more flights of stairs [31] has been suggested as a safe indication to undergo resections of a lobectomy and pneumonectomy respectively. Other studies concluded that climbing 4.6 flights (83 steps, 15.35 m) corresponded to a VO\textsubscript{2}\text{max} value of 20 mL/kg per minute, which has been shown to qualify for a pneumonectomy [33]. Climbing more than 44 steps was acceptable for high-risk patients [34]. More recently, Brunelli et al. [29•] suggested that climbing more than
14 m qualified patients for major resections without any further pulmonary function tests. The current recommendation when using stair climbing is to adhere to a standard protocol during which the patient is encouraged, climbs at a constant speed, does not use railings, and must achieve a predetermined number of flights or height in meters to qualify for a certain extent of resection.

**Algorithms for the functional evaluation of lung resection candidates**

Despite 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 can be costly and may not be universally available. This stresses the need for an algorithm for preoperative functional evaluation [35]. Figure 2 illustrates such an algorithm: Patients undergo successive steps of functional testing based on the proposed cutoff values until they qualify for varying extents of resection or are deemed inoperable [36]. This algorithm, originally proposed by Bolliger and Perruchoud [37], has been validated [35] and widely accepted. Recently, a simpler algorithm, adapted in part from the one proposed by Bolliger and Perruchoud [37], has been proposed [38] but still needs prospective evaluation.

**Figure 2. Algorithm for the assessment of the cardiorespiratory reserves of lung resection candidates**

Patients undergo successive steps 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 corner. The dashed line leading from exercise testing back to the cardiac workup is for patients with a negative cardiac history and a normal electrocardiogram (ECG), who show symptoms or signs of ischemia during exercise testing. FEV1, forced expiratory volume in the first second; DLCO, diffusing capacity of carbon monoxide; VO2 max, maximal oxygen uptake during exercise; ppo, predicted postoperative. *Consider eligibility for combined tumor resection and lung volume reduction surgery in carefully selected patients. Reprinted with permission [36].
Recent developments
The state of the art of lung cancer surgery is still a thoracotomy with careful intraoperative assessment of hilar and mediastinal lymph nodes. There is, however, increasing evidence that video-assisted thoracoscopy is technically feasible [39●], reduces complications during the postoperative period [4], and that 5-year survival after lobectomy compares favorably with results from open surgery [40●●]. Minimally invasive techniques could therefore become the new gold standard, at least for certain pulmonary resections, which might lead to a further lowering of the cardiopulmonary reserves necessary to qualify for lung resection.

The latest development in the field of thoracic surgery is lung volume reduction surgery (LVRS) to improve pulmonary function in patients with severe emphysema [41]. Such patients (deemed inoperable according to the most recent classic pulmonary function tests and exercise parameters, including the algorithm of Figure 2) may become eligible again through a combination of LVRS and simultaneous cancer surgery (see asterisks in Fig. 2). Early reports have shown the feasibility of this approach by removing functionally poor “target zones” of the lung with LVRS and, concomitantly, pulmonary nodules that were either within or outside these target zones [42,43]. Some of these nodules were stage I lung cancer, and were removed primarily by wedge resection. Recently, Edwards et al. [44] showed that a formal lobectomy could be performed safely in patients with an FEV1-pool value less than 40% but evidence of hyperinflation and emphysema in that lobe. DeMeester et al. [45●] reported a small series of five high-risk patients who successfully underwent lobectomy of the tumor-bearing lobe in combination with LVRS of one or more additional lobes. Both minimally invasive techniques and LVRS may push the frontiers of functional operability even further than they already are today.

In summary, I recommend performing the functional evaluation before lung resection for cancer according to a validated algorithm such as the one depicted in Figure 2. Select patients who are then excluded because of insufficient pulmonary reserves should be evaluated for a combined approach of cancer surgery and LVRS.

References and recommended reading
Papers of particular interest, published within the annual period of review, have been highlighted as:
• Of special interest
** Of outstanding interest


326 Neoplasms of the lung


In this Italian study comprising 160 patients, stair climbing of at least 14 m was a good predictor of a safe outcome after major lung resection.


In this Japanese study video-assisted thoracoscopic nodal dissection was compared with open thoracotomy nodal staging in 29 patients with stage I lung cancer. Video-assisted thoracoscopic staging was found to be comparable with the open procedure.


In this retrospective, multicenter US study comprising 298 patients who underwent a standard video-assisted thoracoscopic lobectomy for lung cancer stages I, II, and IIIa, the 5-year survival was identical to the one obtained by lobectomy done by thoracotomy.


In a series of five patients with marginal lung function, a lobectomy of the tumor-bearing lobe could be performed safely with lung volume reduction in one or more additional lobes.