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Pre-operative pulmonary evaluation of lung cancer patients: a review of the literature

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ABSTRACT: Complete anatomical resection of the primary tumour is still the standard of care in patients with early stage lung cancer. Because these patients are usually smokers who also suffer from chronic obstructive pulmonary disease, regional differences in pulmonary function due to lung tissue destruction exist.

The purpose of the present article is to evaluate the currently available guidelines and to discuss novel methods for the pre-operative functional and anatomical pulmonary evaluation in lung cancer patients.

Despite the fact that knowledge on the pre-operative evaluation of the pulmonary function has substantially increased during the past decade, the majority of the studies are small, underpowered and, with exception of a proposed algorithm, not prospectively validated in independent cohorts.

The future harmonisation of guidelines is required and novel imaging techniques should be incorporated in the pre-operative evaluation in chronic obstructive pulmonary disease patients with borderline pulmonary function.

KEYWORDS: Diffusing capacity, exercise tests, imaging techniques, lung cancer, operability, spirometry

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Complete anatomical resection of the primary tumour by (bi)lobectomy or pneumonectomy with removal of the involved intrapulmonary, hilar and mediastinal lymph nodes remains the treatment of choice for patients with early stage lung cancer [1, 2]. This approach is based on a prospectively randomised study, in which patients with early stage I or II nonsmall cell lung cancer (NSCLC) were randomised between a limited, nonanatomical resection (segmentectomy, wedge or extended wedge resection) or an anatomical resection [3]. Nonanatomical resections were associated with an increased risk of loco-regional recurrence and a nonsignificant trend towards impaired overall survival. Although sublobar resections only lead to an insignificant loss of pulmonary function, anatomical resections are still the treatment of choice for early stage NSCLC until data from randomised studies become available [3, 4]. Nonanatomical resections can be performed in patients with impaired cardiopulmonary function [5]. The present article will focus on recent new advances in the possibilities to predict the post-operative respiratory function, taking regional functional differences into account [6]. Because lung cancer patients often also suffer from chronic obstructive pulmonary disease (COPD) [7–12], regional differences in pulmonary function due to lung tissue destruction exist. These important regional differences have to be taken into account in the pre-operative evaluation of a lung resection in patients with COPD. After lobectomy, COPD patients may only have a nonsignificant loss of forced expiratory volume in one second (FEV_1) [6] or even an improvement in lung function [13]. In addition, the long-term results from lung volume reduction surgery (LVRS) in COPD patients are promising [14–18]. The American College of Chest Physician (ACCP)

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guidelines [19] have already adopted the possibility of resecting hyperinflated lung areas when evaluating COPD patients for lung cancer surgery. Data from LVRS also suggest that the predicted post-operative FEV_1 is often underestimated after lobectomy [20].

EPIDEMIOLOGY

Lung cancer is the most important cause of cancer-related death in both males and females in Europe and other countries [21, 22]. Epidemiological data indicate that lung cancer accounts for 25% of all cancer deaths in females and >30% in males [2]. In general, lung cancer 5-yr-survival rates are <15%, because the disease is often diagnosed in an advanced stage [21]. Lung cancer, like many other solid tumours, is a typical disease of the elderly patient. More than 50% of all patients with NSCLC are aged >65 yrs and about one-third of all patients are aged >70 yrs when the disease is diagnosed [23]. COPD and lung cancer are both related to smoking [19] and the incidence rate of lung cancer in smokers with COPD is two- to five-fold higher compared to smokers without COPD [7, 8]. Of all lung cancer patients, 90% are smokers [24] and up to 75% have COPD [8, 24] according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria [25].

PRE-OPERATIVE CONSIDERATIONS FOR PULMONARY RESECTION

Acceptable mortality following resection varies in the different guidelines between 4–7% for lobectomy and 8–14% for pneumonectomy, which partly explains the rather wide variability in the available guidelines that will be discussed below [19, 26, 27]. Individual patient characteristics define the surgical risks of resection in lung cancer. Guidelines extrapolate this risk from known data, and compare it to the risk for patients with adequate cardiopulmonary reserve as a basis for estimating relative risk. Whether a patient accepts these thresholds for resection, as given above, has to be discussed individually taking into account both risks and benefits for standard surgical resection of lung cancer. Also less conventional treatment options, such as minimal invasive techniques with smaller muscle sparing incisions and less rib damage [14, 15, 28], sublobar resections and nonsurgical options, such as radiotherapy and radiofrequency ablation, should be discussed [19]. Patients can develop both cardiac and pulmonary complications after pulmonary resections including arrhythmias, myocardial infarctions, cerebrovascular accidents, pulmonary embolisms, pneumonias, empyemas, airway dehiscence and bronchopleural fistulas [29]. None of these complications can be predicted by pre-operative pulmonary function tests alone [30]. Perioperative cardiovascular risk factors should be assessed by proper pre-operative cardiological evaluation whenever a patient presents with one of these risk factors [31]. BIRIM *et al.* [32] were the first to develop a comprehensive risk model by which individual long-term survival after surgery for lung cancer could be estimated based on pre- and post-operative risk factors, including sex, age, impaired pulmonary function, congestive heart failure, renal disease, prior malignancies, clinical and pathological disease stage, body weight, the extent and sidedness of surgery and the type of resection [33]. Post-operative complications are also increased in low volume hospitals and in situations with less experienced surgeons [30, 34–36]. Some investigators reported an increased post-operative mortality ranging up to 11.8% for lobectomies [37] and 16–20% for pneumonectomies in elderly patients aged >70 yrs, which can be explained by the high incidence of pulmonary and cardiovascular risk factors in this population [29, 38]. Right-sided pneumonectomies have been associated with even higher mortality rates in this population [30, 39]. Other studies found more acceptable mortality rates, *i.e.* <3% for lobectomies and even 0% for pneumonectomies [34, 40, 41]. Because of this conflicting evidence, most guidelines recommend that surgery in elderly patients with lung cancer should not *a priori* be withheld [19, 26, 27, 42].

As a result of improved post-operative care, the morbidity and mortality of standard open lung resection procedures has improved over the past decades [28, 34]. In addition, lung resection surgery has become increasingly minimal invasive with smaller muscle sparing incisions and less rib damage [14, 15, 28]. The increased use of minimal invasive techniques and video-assisted thoracoscopy, have further decreased mortality and morbidity as well as the duration of hospital stay [4, 5, 19, 26]. Identifying patients at risk of developing post-operative complications and managing these patients is still a challenge. Few risk-reduction strategies are effective in preventing complications as described previously. Pre-operative smoking cessation and inspiratory muscle training are effective, whereas proper anaesthetic and analgesic agents may contribute by preventing airway closure generating atelectasis or by minimally affecting respiratory muscle tone. Lung expansion manoeuvres are helpful since the adverse effects of surgery on lung and chest wall mechanics predispose patients to atelectasis and retained secretions in the post-operative period [43].

SPIROMETRY AND DIFFUSING CAPACITY

In particular, FEV_1 and the transfer factor for carbon monoxide ($T_{L,CO}$) are the most commonly used tests to evaluate the suitability of patients with lung cancer to undergo a pulmonary resection [19, 26, 27, 42]. It is remarkable that the various guidelines dictate different criteria by which to accept a patient for a pneumonectomy (table 1) or lobectomy (table 2). The vast majority of the data is based on absolute values from predominantly young male patients [44], but all guidelines offer the possibility to use percentages of predicted, although there are less data to support this. Therefore, future harmonisation between the different guidelines is needed. For a pneumonectomy the British Thoracic Society (BTS) recommends an absolute pre-operative FEV_1 value of >2.0 L or a post-operative % pred FEV_1 and a post-operative % pred $T_{L,CO}$ of >40% [26]. For a lobectomy the BTS recommends an absolute pre-operative FEV_1 value of >1.5 L [26]. The ACCP guidelines use the same FEV_1 criteria but, in addition, the pre-operative FEV_1 has to be >80% pred and there should not be any signs of interstitial lung disease or exercise induced airflow obstruction before accepting a patient for resection without further evaluation [19]. The Dutch National guidelines consider a patient operable without additional investigations if pre-operative FEV_1 and $T_{L,CO}$ are >80% pred, provided that there is no exercise induced airflow obstruction [27]. These recommendations are based on the algorithm hypothesised by BOLLIGER and PERRUCHOUD [42] and WYSER *et al.* [45] in which a pre-operative FEV1 and $T_{L,CO}$ >80% pred are regarded as a safe threshold for a pneumonectomy if no cardiovascular disease is present. Several investigators have recommended using percentage predicted values for FEV1 and $T_{L,CO}$ instead of the absolute values [44–47]. A simple approach to estimate the post-operative % pred FEV1 value is the segment method, which is based on the proportion of open and functional lung segments that will be removed [48].

$$\text{Post-operative \% pred FEV1} = \text{pre-operative FEV1} \times (1-(\text{number of segments resected}/19)) \quad (1)$$

This formula can also be used to calculate the post-operative % pred $T_{L,CO}$, although it does not take into account the functional contribution of the different segments [49]. Despite this shortcoming, both post-operative % pred FEV1 and $T_{L,CO}$ appeared to be good predictors for the direct post-operative morbidity and mortality [50, 51]. In addition, the post-operative % pred FEV1 correlated well with the post-operative FEV1 6 months after surgery in patients who underwent a lobectomy. However, for post-pneumonectomy patients the post-operative FEV1 value 6 months after surgery was under-estimated up to an average of 500 mL [52]. VARELA *et al.* [50] found a poor correlation between the direct post-operative absolute FEV1 and the post-operative % pred FEV1 value following a lobectomy, with an overestimation of the post-operative % pred FEV1. In the same study, COPD patients had a better post-operative pulmonary function than predicted due to the removal of hyperinflated nonfunctional pulmonary parenchyma [50]. In addition, measuring $T_{L,CO}$ may differ in COPD patients due to uneven ventilation, implying that other more reliable test methods should be used [53].

There is general consensus that FEV1 % pred and $T_{L,CO}$ % pred can be used to identify patients with a normal pulmonary function (>80%) in whom no additional tests are needed. Another similarity between the different guidelines is that patients with a borderline pulmonary function and a post-operative % pred FEV1 and $T_{L,CO}$ <40% based on quantitative perfusion scanning are recommended to undergo exercise testing [19, 26, 27, 42] (fig. 1). However, one should realise that although post-operative % pred FEV1 and $T_{L,CO}$ values based on the segment method or quantitative perfusion scintigraphy are more reliable than absolute estimates of spirometric parameters they are still not accurate enough to predict the post-operative pulmonary function, especially not in COPD patients [51, 54].

EXERCISE TESTING

Cardiopulmonary exercise tests (CPET) are used to predict oxygen uptake as well as cardiopulmonary reserve. The exercise test is a better predictor of post-operative complications than resting cardiac and pulmonary function [6, 55]. CPET is a complex physiological test procedure that allows estimation of the maximal oxygen uptake (V'_{O_2max}) during exercise. By increasing the external load a patient will reach

TABLE 1 Overview of the different guidelines for undergoing a lobectomy

Risk	BOLLIGER [42]	British Thoracic Society [26]	COLICE [19]	VAN MEERBEECK [27]
Low	Post-op % pred FEV1 ⩾40% and post-op % pred $T_{L,CO}$ ⩾40%	FEV1>1.5 L Post-op % pred FEV1⩾40% and post-op % pred $T_{L,CO}$ ⩾40% and S_{a,O_2} >90% SWT >25 shuttles# and desaturation <4% and V'_{O_2peak} >15 mL·kg^{-1}·min^{-1}	FEV1>1.5 L Post-op % pred FEV1⩾40% and post-op % pred $T_{L,CO}$ ⩾40%	FEV1 >80% and $T_{L,CO}$ >80% Post-op % pred FEV1⩾40% and post-op % pred $T_{L,CO}$ ⩾40% Post-op % pred FEV1<40% and post-op % pred $T_{L,CO}$ <40% and V'_{O_2max} >15 mL·kg^{-1}·min^{-1}
Intermediate	Not reported	Not reported	Not reported	Post-op % pred FEV1<40% and post-op % pred $T_{L,CO}$ <40% Post-op % pred FEV1<40% or post-op % pred $T_{L,CO}$ <40% and post-op % pred V'_{O_2max} >10 mL·kg^{-1}·min^{-1}
High	Post-op % pred V'_{O_2max} <40% or V'_{O_2max} <10 mL·kg^{-1}·min^{-1} Post-op % pred FEV1<40% and post-op % pred $T_{L,CO}$ <40% Post-op % pred V'_{O_2max} <35% or post-op % pred V'_{O_2max} <10 mL·kg^{-1}·min^{-1}	FEV1⩽1.5 L Post-op % pred FEV1<40% and post-op % pred $T_{L,CO}$ <40% Post-op % pred FEV1 <40% or post-op % pred $T_{L,CO}$ <40% or S_{a,O_2} ⩽90% and SWT <25 shuttles# or desaturation>4% SWT >25 shuttles# and desaturation<4% and V'_{O_2peak} <15 mL·kg^{-1}·min^{-1}	Post-op % pred FEV1<30% whenever the product of post-op % pred FEV1 × post-op % pred $T_{L,CO}$ <1650 Post-op % pred FEV1 <40% or post-op % pred $T_{L,CO}$ <40% and V'_{O_2max} <10 mL^{-1}kg^{-1}min^{-1} Post-op % pred FEV1<40% and post-op % pred $T_{L,CO}$ <40% and V'_{O_2max} <15 mL^{-1}kg^{-1}min^{-1} SWT <25 shuttles#	Post-op % pred V'_{O_2max} <10 mL·kg^{-1}·min^{-1}

All data assume there is no unsuspected dyspnoea or evidence of interstitial lung disease. Post-op: post-operative; % pred: % predicted; FEV1: forced expiratory volume in one second; $T_{L,CO}$: transfer factor for carbon monoxide; V'_{O_2max}: maximal oxygen uptake; S_{a,O_2}: arterial oxygen saturation; SWT: shuttle walk test; desaturation: peripheral desaturation during the SWT; V'_{O_2peak}: peak oxygen uptake. #: 25 shuttles equals 250 m.

TABLE 2 Overview of the different guidelines for undergoing a pneumonectomy

Risk	Bolliger [42]	British Thoracic Society [26]	Colice [19]	van Meerbeeck [27]
Average	$FEV_1 \geqslant 80\%$ and $T_{L,CO} \geqslant 80\%$ $FEV_1 < 80\%$ or $T_{L,CO} < 80\%$ and $V'_{O_2max} > 75\%$ or > 20 mL·kg^{-1}·min^{-1}	$FEV_1 > 2.0$ L Post-op % pred $FEV_1 \geqslant 40\%$ and post-op % pred $T_{L,CO} \geqslant 40\%$ and $S_{a,O_2} > 90\%$ SWT > 25 shuttles# and desaturation $< 4\%$ and $V'_{O_2peak} > 15$ mL·kg^{-1}·min^{-1}	$FEV_1 > 2.0$ L or $FEV_1 > 80\%$ Post-op % pred $FEV_1 \geqslant 40\%$ and post-op % pred $T_{L,CO} \geqslant 40\%$	$FEV_1 > 80\%$ and $T_{L,CO} > 80\%$ Post-op % pred $FEV_1 \geqslant 40\%$ and post-op % pred $T_{L,CO} \geqslant 40\%$ Post-op % pred $FEV_1 < 40\%$ and post-op % pred $T_{L,CO} < 40\%$ and $V'_{O_2max} > 20$ mL·kg^{-1}·min^{-1}
Inter-mediate	Not reported	Not reported	Not reported	Post-op % pred $FEV_1 < 40\%$ and post-op % pred $T_{L,CO} < 40\%$ Post-op % pred $FEV_1 < 40\%$ or post-op % pred $T_{L,CO} < 40\%$ and post-op % pred $V'_{O_2max} > 10$ mL·kg^{-1}·min^{-1}
High	$V'_{O_2max} < 40\%$ pred or $V'_{O_2max} < 10$ mL·kg^{-1}·min^{-1} Post-op % pred $FEV_1 < 40\%$ and post-op % pred $T_{L,CO} < 40\%$ Post-op % pred $V'_{O_2max} < 35\%$ pred or post-op % pred $V'_{O_2max} < 10$ mL·kg^{-1}·min^{-1}	$FEV_1 \leqslant 2.0$ L Post-op % pred $FEV_1 < 40\%$ and post-op % pred $T_{L,CO} < 40\%$ Post-op % pred FEV_1 or post-op % pred $T_{L,CO} < 40\%$ or $S_{a,O_2} \leqslant 90\%$ and SWT < 25 shuttles# or desaturation $> 4\%$ SWT > 25 shuttles# and desaturation $< 4\%$ and $V'_{O_2peak} < 15$ mL·kg^{-1}·min^{-1}	Post-operative % pred $FEV_1 < 30\%$ whenever the product of post-op % pred $FEV_1 \times$ post-op % pred $T_{L,CO} < 1650$ Post-op % pred $FEV_1 < 40\%$ or post-op % pred $T_{L,CO} < 40\%$ and $V'_{O_2max} < 10$ mL·kg^{-1}·min^{-1} Post-op % pred $FEV_1 < 40\%$ and post-op % pred $T_{L,CO} < 40\%$ and $V'_{O_2max} < 15$ mL·kg^{-1}·min^{-1} SWT < 25 shuttles#	Post-op % pred $V'_{O_2max} < 10$ mL·kg^{-1}·min^{-1}

All data assume there is no unsuspected dyspnoea or evidence of interstitial lung disease. FEV_1: forced expiratory volume in one second; $T_{L,CO}$: transfer factor for carbon monoxide; V'_{O_2max}: maximal oxygen uptake; % pred: % predicted; S_{a,O_2}: arterial oxygen saturation; SWT: shuttle walk test; desaturation: peripheral desaturation during the SWT; V'_{O_2peak}: peak oxygen uptake. #: 25 shuttles equals 250 m.

their limitations and V'_{O_2max}. This V'_{O_2max} is supposed to be to best indicator of aerobic capacity and cardiorespiratory fitness. By calculating V'_{O_2max}, CPET provides an objective evaluation of the functional capacity of both the lungs and heart and is known as a safe test procedure [56–58]. All guidelines recommend that in case of borderline spirometry values with post-operative % pred FEV_1 and $T_{L,CO}$ values $<40\%$, an exercise test should be performed to measure the V'_{O_2max} [19, 26, 27, 42]. The inability to perform a pre-operative exercise test is an indication of limited aerobic capacity. The V'_{O_2max} usually decreases after lobectomy by 0–20% and by 20–28% after pneumonectomy [6, 51, 59]. The wide range of these findings can be explained by the variation in the time interval between the operation and the performance of the test. It is generally accepted that if V'_{O_2max} is >20 mL·kg^{-1}·min^{-1} post-operative morbidity will be $<10\%$ and mortality close to zero [60]. When the pre-operative V'_{O_2max} is <10 mL·kg^{-1}·min^{-1} there is a high risk of post-operative complications [26, 60]. Despite this commonly accepted gold standard, one study questions whether post-operative complication rates can be stratified by the V'_{O_2max} [61], but the overwhelming majority of studies clearly confirm the value of V'_{O_2max}.

A shortcoming of the CPET is that there are no normal values for V'_{O_2max} available for a wide age range and body weight range. Consequently, the use of absolute CPET values may lead to the exclusion of patients who are actually fit enough to undergo curative surgery [56]. The predicted value of V'_{O_2max} according to Hansen and Wasserman [62] has important limitations. For males and females the equation is weight dependent. When these prediction equations are applied to patients with the same age and sex, the person with the lowest body weight has the lowest predicted V'_{O_2max} and, therefore, V'_{O_2max} % pred is best. Paradoxically this could mean that a person with the largest weight loss due to constitutional symptoms is accepted for curative surgery, although their prognosis is poorer. Hansen *et al.* [62] propose the use of only height and age in the calculation of V'_{O_2max} % pred under conditions of overweight. Other studies found that V'_{O_2max} correlated better with a measure of lean body mass than total body weight. Therefore, the use of lean body mass is recommended [62–64]. There is mounting evidence that predicted V'_{O_2max} values correlate better with post-operative morbidity and mortality than the absolute values [42, 56, 65]. Win *et al.* [56] recently proposed a threshold for the V'_{O_2max} between 50–60% pred, above which they observed no excess in surgical mortality, but this value has not yet been confirmed in larger studies. In another study, this threshold was set at 75% of the predicted V'_{O_2max}, leading to uneventful operations in nine out of 10 patients [65]. Patients with a value $<50\%$ pred

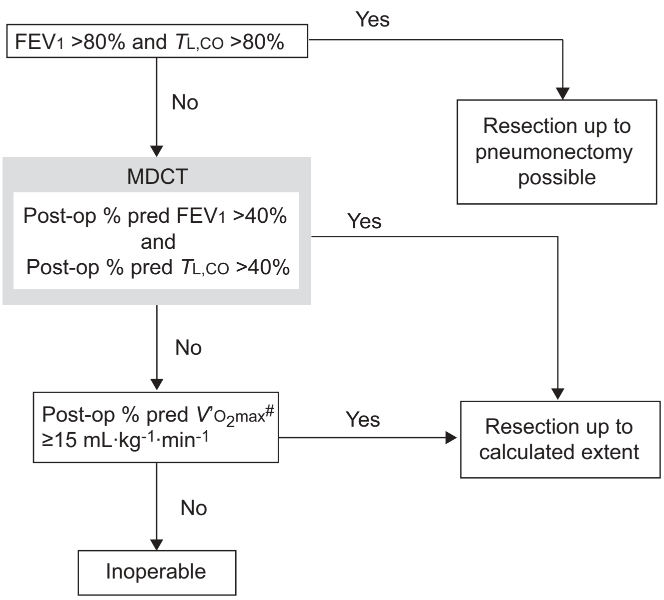

FIGURE 1. Proposed flowchart for pre-operative evaluation. FEV_1: forced expiratory volume in one second; $T_{L,CO}$: transfer factor for carbon monoxide; MDCT: multi-detector computer tomography; % pred: % predicted; V'_{O_2max}: maximal oxygen uptake. #: V'_{O_2max} or peak oxygen uptake is used interchangeably.

are regarded as being at high risk for post-operative pulmonary complications, while most patients have a good outcome when this value is >65% [56, 66].

WALKING TESTS

6-min walk distance test

The 6-min walk distance (6MWD) test, evolved from studies in the late 1960s [67], was first introduced by GUYATT *et al.* [68] as a modification of the 12-min walk test of MCGAVIN *et al.* [69]. It shows good reliability and validity as a measure of functional capacity [69–71]. The 6MWD test represents a peak oxygen uptake (V'_{O_2}) of ~15 mL·kg^{-1}·min^{-1} when a distance of 500 m is covered without stopping [72]. Despite the increasing number of studies investigating the value of the 6MWD, so far the results are inconsistent [73, 74]. A major limitation of the test is that the distance walked in minutes is not standardised [75, 76]. The 6- and 12-min field walk tests are self-paced and reflect a combination of peak performance and endurance capacity [77]. Previous studies have shown that knowledge of the imposed time limit of a test influences pacing and the distance covered [68]. Despite these limitations of the 6MWD, there are also benefits. Due to its self-paced protocol and the possibility to rest it might be better tolerated in patients with COPD and in that sense superior to CPET in detecting exercise-induced hypoxaemia [72].

Stair climbing test

Stair climbing is another method used to predict V'_{O_2} and cardiopulmonary reserve [77, 78]. In a retrospective review of patients undergoing pneumonectomy, VAN NOSTRAND *et al.* [79] noted an unacceptably high mortality rate of 50% in those who were unable to climb two flights of stairs. In contrast, in a prospective study, BRUNELLI *et al.* [80] demonstrated that the inability to perform a stair climb test appeared to be an independent predictor of mortality but not of the post-operative morbidity. Several studies have used a lower limit of two flights of stairs as a criterion to undergo a pulmonary resection. In these studies, only a 0–2% post-operative mortality was found [77, 81, 82]. However, it has been reported that patients who climb three flights of stairs are expected to have an FEV_1 >1.7 L, a value that on its own asks for further testing [83]. V'_{O_2max} can also be estimated during symptom-limited stair climbing [78] because the number of flights climbed can serve as an indicator of cardiopulmonary reserve and of a patient's ability to tolerate pre- and post-operative cardiopulmonary stress. Climbing two flights of stairs corresponds to a V'_{O_2max} of ~12 mL·kg^{-1}·min^{-1}, whereas the V'_{O_2max} exceeds 20 mL·kg^{-1}·min^{-1} in those who are able to climb five flights of stairs [78]. Therefore, limiting the minimum number of flights that should be climbed might be most useful for large-scale screening of patients of all ages undergoing high-risk surgery [80, 84–86].

A limitation of the stair climbing test is, as for the walking tests, that the different variables (height of each step, number of steps per flight, duration of the test and reasons for stopping) have not been standardised. In a recent study, KOEGELENBERG *et al.* [86] proposed a new concept of standardising stair climbing by looking at the speed of ascent and not just height achieved. PATE *et al.* [87] expressed the number of steps climbed as height climbed in meters to provide standardisation. When this standardised value was applied in elderly patients undergoing a lobectomy it proved to be an important predictor of post-operative cardiopulmonary complications [84]. Another limitation of the stair climbing test is that it cannot estimate aerobic metabolic capacity adequately because stair climbing generally takes no more than 1 min. In addition, during the first minute of exercise oxygen-independent pathways play a role and oxidative phosphorylation only occurs after >1 min of exercise [85]. These limitations of the stair climbing test favour longer lasting exercise tests, such as the CPET or the shuttle walk test.

Shuttle walk test

Both the BTS and ACCP guidelines recommend the use of the incremental shuttle walk test (ISWT) because it is reproducible, correlates well with V'_{O_2max} and can serve as a good alternative if CPET is unavailable [19, 26]. The ISWT has been standardised and partly covers a CPET [88]. Both the ISTW and CPET are externally paced, incremental and stop at maximal exercise. In ISWT, patients walk a distance of 10 m between two shuttles. A fully calibrated audio cassette signals each augmentation and an operator assists the patient throughout the test. When the patient is too breathless to proceed or cannot keep up with the pace the test is ended. Apart from the total distance covered, the pulse and saturation at 30-s intervals, Borg score, recovery time and reason for ending the test are documented. Patients who cannot complete 25 shuttles on two occasions will have a V'_{O_2max} <10 mL·kg^{-1}·min^{-1} [89], and are regarded at high risk for surgery. The minimum value of V'_{O_2max} for pulmonary surgery is >15 mL·kg^{-1}·min^{-1}, which corresponds to a distance of 450 m [90]. Recently, a close correlation between ISWT and V'_{O_2max} by treadmill walking test was demonstrated in a prospective study in patients with a normal lung function and COPD [74]. It should be stressed that ISWT is the preferred test for COPD patients unable to undergo a CPET [74, 88]. The present authors' recommendation would be to use the ISWT only when the CPET is unavailable or in COPD patients unable to undergo a CPET. If the ISWT is used, the complete distance of 450 m should be covered to avoid incorrect exclusion of patients from pulmonary surgery [74]. The current authors disagree with the BTS guidelines that a desaturation of >4% during shuttle walk tests should be incorporated in the decision. The main reason for this objection is the number of shuttles that are covered, since this is correlated to V'_{O_2} [74].

NUCLEAR IMAGING

Pulmonary perfusion scintigraphy with planar acquisition provides two-dimensional images of the lung, which can be used to estimate the post-operative FEV1. A quantitative radionuclide perfusion scan is performed to measure the relative function of each lung and its segments [91]. In general, the areas of the lung affected by lung cancer tend to have a decreased perfusion, but in some cases an increased perfusion has been reported with underestimation of the post-operative % pred spirometric parameters [92, 93]. A limitation of this method is that it does not take the spatial overlapping of pulmonary areas with different functions into account. In order to further improve the pre-operative assessment of the regional pulmonary function, single-photon emission computed tomography (SPECT) is being used. For example, SPECT can assess the amount of pulmonary emphysema in specific regions of the lung without loss of accuracy by the superposition of lung tissues [94]. Otherwise inoperable patients tolerated a pulmonary resection of a nonfunctional part of the lung without increased risk of respiratory failure during the post-operative period when evaluated by SPECT [95]. However, in some studies SPECT appears to be equally accurate in the prediction of the post-operative lung function compared with planar acquisitions [49, 96].

NOVEL IMAGING TECHNIQUES

The multi-detector computer tomography technique (MDCT) allows objective and reproducible identification of emphysematous areas [95]. Using the lung density as expressed in Hounsfield units, emphysema can even be identified on a segmental level and quantified electronically by three-dimensional reconstructions. Using this method an accurate reflection of pulmonary function and exercise capacity can be provided [95]. Quantitative MDCT upgrades risk prediction, even in patients with borderline pulmonary function undergoing a lobectomy [95, 97]. With the increased use of MDCT as a screening tool for lung cancer [98–101], it will become possible to estimate the regional pulmonary function at the same time. At present, pulmonary function is also investigated by magnetic resonance imaging (MRI) [102, 103] up to the level of diffusion measurements and acinar airway geometrical characteristics. Uptake of ^{133}Xe detected by SPECT can be combined with dynamic MRI images. In this way, areas of hyperinflation can be detected because air trapping may regionally impair diaphragm and chest wall motion [95]. These methods have already been used in pre-operative evaluation of LVRS patients [94]. By combining the anatomic imprecise SPECT images with the precise MRI or MDCT data an optimal post-operative estimate of the pulmonary function can probably be provided [95, 104]. Recent publications of the data on the calculation of post-operative values have shown that quantitative computed tomography scanning is as good as perfusion scanning. [96, 97, 103]. Therefore, the present authors suggest the replacement of perfusion scan by computed tomography calculated predictions, as MDCT is performed as part of the lung cancer staging process (fig. 1). A very promising technique is the *in vivo* lung morphometry based on diffusion MRI with hyperpolarised ^{3}He gas, which provides important regional information on lung microstructure and emphysema. It is safer and might be more sensitive for the diagnosis of emphysema than computed tomography [102]. These novel imaging technologies could be incorporated in the estimation of the post-operative % pred FEV1 and $T_{L,CO}$ in patients with COPD in whom the post-operative V'_{O_2max} is <15 mL·kg^{-1}·min^{-1} and pulmonary surgery would otherwise have been denied (fig. 1).

SUMMARY

Despite the fact that current knowledge on the pre-operative evaluation of pulmonary function has substantially increased during the past decade, cardiopulmonary exercise tests remains the method of choice for the assessment of pulmonary operability. However, the majority of the current studies are small, underpowered and, with the exception of the algorithm proposed by Bolliger and Perruchoud [42], not prospectively validated in independent cohorts. Harmonisation of guidelines is needed and novel imaging techniques could be incorporated in future pulmonary evaluation algorithms in patients with borderline pulmonary function.

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