



Lung function assessment before anatomical lung resections—is everything so clear?—a narrative review

Dragan Subotic

General Hospital Acibadem Bel Medic, Belgrade, Serbia

Correspondence to: Prof. Dragan Subotic. General Hospital Acibadem/Belmedic, Koste Jovanovica 87, 11000 Belgrade, Serbia.

Email: profsubotic@gmail.com.

Background and Objective: Several aspects of the influence of the lung resection to the lung function still remain unclear. As the reliable prediction of postoperative complications, especially in patients at risk, may be challenging, a non-systematic review of the literature on the topic of the influence of the lung resections to the postoperative lung function was done.

Methods: Inclusion and exclusion criteria: The analysis included adult patients who underwent anatomical lung resections with curative intent (segmental resection, lobectomy, bilobectomy and pneumonectomy), independently of the operative approach—video-assisted thoracic surgery (VATS)/thoracotomy. Studies on combined benign and malignant pathology were included provided the majority of the included patients had lung cancer. Both retrospective and prospective studies were included, review articles, case reports and case series with less than 10 patients were excluded. Within the search strategy, the following terms were combined: lung resection, lobectomy, pneumonectomy, lung function, forced expiratory volume in the first second (FEV₁), small airways, diffusion, oxygen consumption, lung function prediction, postoperative, complications, mortality, diaphragm motion and outcome.

Key Content and Findings: The prediction of the postoperative lung function after the lung resection is currently the standard in most of the centers. Both the postoperative lung function loss and recovery are well documented and both should be taken into account during the lung function prediction. In patients with chronic obstructive pulmonary disease (COPD) patients the predicted postoperative lung function parameters may be initially underestimated *vs.* non-COPD patients, but COPD patients have the limited capacity of later lung function improvement. The prediction of the postoperative lung function after lobectomy is reliable in many aspects, but the influence of the upper *vs.* lower lobectomy either independently, or depending of the side of the operation, requires further analysis. Issues related to pneumonectomy are sufficiently evidence-based and combining of lung function analysis and cardiorespiratory risk assessment is now an accepted standard.

Conclusions: The existing guidelines should be adhered in the everyday practice. However, some evidence gaps and specific situations given in the review should be taken into consideration as well.

Keywords: Lobectomy; segmentectomy; lung function; prediction; postoperative

Received: 12 July 2022; Accepted: 22 September 2022; Published: 25 September 2022.

doi: 10.21037/amj-22-19

View this article at: <https://dx.doi.org/10.21037/amj-22-19>

Introduction

Several aspects of the influence of the lung resection to the lung function still remain unclear. After the lung resection, the lung function recovers till some point, but it may take 1–2 weeks to more than 2 months to reach the desired/predicted value (1,2). The main problem, despite all available hi-tech methods of the lung function assessment and prediction, still remains the impossibility to reliably predict the probability of complications during that period, especially in patients at risk (3). A non-systematic review of the literature on the topic of the influence of the lung resections to the postoperative lung function is performed with the following aims: first, to avoid unjustified upfront rejection from surgery of some patients that at first sight may seem as unfit for surgery; second, to avoid offering surgery to patients, who are under the functional limit for safe surgery according to the existing evidence. I present the following article in accordance with the Narrative Review reporting checklist (available at <https://amj.amegroups.com/article/view/10.21037/amj-22-19/rc>).

Methods

This is a non-systematic review of the literature on the topic of the influence of the lung resections to the postoperative lung function.

Inclusion criteria

The analysis included adult patients who underwent anatomical lung resections with curative intent (segmental resection, lobectomy, bilobectomy and pneumonectomy), independently of the operative approach—video-assisted thoracic surgery (VATS)/thoracotomy. Studies on combined benign and malignant pathology were included provided the majority of the included patients had lung cancer. Both retrospective and prospective studies were included, review articles, case reports and case series with less than 10 patients were excluded.

Search strategy

The searching included only journals (without language restrictions) cited in the following databases: Medline, Current contents (CC), Science Citation Index (SCI) and Science Citation Index expanded (SCIE) after 1995. References published before 1995. were included

exceptionally and only as key-references for the understanding of the particular sub-topic. Within the search strategy, the following terms were combined: lung resection and lung function and prediction; lung function and lobectomy and segmentectomy; operative morbidity and lobectomy and pneumonectomy and segmentectomy; forced expiratory volume in the first second (FEV₁), and prediction; diffusion and lobectomy and pneumonectomy; oxygen consumption and pneumonectomy and complications; lobectomy and pneumonectomy and mortality, diaphragm motion lung function.

Titles and abstracts of potentially eligible studies were initially screened and the eligibility of the full texts was assessed depending on whether the particular study covered at least one of the following study endpoints: differences between the measured and predicted values of FEV₁, vital capacity (VC), diffusion capacity (DLco), oxygen consumption in effort (VO₂); differences in preoperative *vs.* postoperative lung function parameters depending on site and type of lobectomy (upper *vs.* lower); differences in the lung function parameters depending on operative approach (VATS *vs.* open surgery); differences between preoperative and postoperative FEV₁ and VC in patients with chronic obstructive pulmonary disease (COPD) *vs.* non-COPD patients. Studies addressing at least one of the listed endpoints were included, provided the bias was low, as assessed on the basis of the size of the reported series, consistency and precision of the reported data, study limitations as presented by the authors and on the basis of the 30 years of specialist experience of the author of the present review.

The search strategy is summarized on *Table 1*. The main characteristics of the analysed studies are presented on *Table S1* (3-23).

The evidence synthesis followed a stepwise process: subdividing each article into different research topics; grouping the evidence about the same research topic together; identifying similar or opposite findings; based on personal experience in the field, identifying research gaps whose clarifying could be of practical benefit.

Results

Based on the performed literature survey, the following areas of interest were identified: (I) the pattern of the early and late postoperative lung function recovery; (II) the differences in postoperative lung function between VATS and open surgery; (III) some specificities in COPD *vs.* non-COPD patients and (IV) the influence

Table 1 Search strategy summary

Items	Specification
Date of search	07/05/2022
Databases and other sources searched	PubMed and Google search
Search terms used (including MeSH and free text search terms and filters) (Table S1)	Lobectomy, pneumonectomy (MeSH), Segmentectomy, Spirometry (MeSH), postoperative complications (MeSH), prediction
Timeframe	1995–2022
Inclusion and exclusion criteria	Inclusion: anatomical lung resection with curative intent; exclusion: combined benign-malignant pathology in case that the majority of patients did not have lung cancer; review articles, case reports and case series with less than 10 patients
Selection process	The entire selection process was performed by the corresponding author

of the type of lobectomy; (V) accuracy of the lung function prediction methods; (VI) functional aspects of segmentectomy. These topics represent the primary study end-point. Secondly, the aim of this review is to underline strengths and limits of different methods of the postoperative lung function prediction, to identify some gaps in the existing evidence and to suggest the areas for future research.

Early postoperative lung function recovery

Different lung function parameters do not recover after the lung resections in the same way. In patients with lobectomy and without postoperative complications, it was demonstrated that forced vital capacity (FVC) and %VC recovered rapidly between two weeks and one month after surgery, whilst the recovery of FEV₁ was greater 1 to 3 months after surgery, with Tiffeneau index (FEV₁/FVC ×100) remaining unchanged after surgery (4). Similar findings were reported in other studies, suggesting that the postoperative recovery within 30 postoperative days might be due to the repair of surgical injury to the chest wall and the resulting pain alleviation (24).

It was also demonstrated that the trend of the postoperative lung function recovery persists in patients with postoperative complications as well. In a group of 60 patients at increased risk, in patients with respiratory complications, the improvement between days three and 7 was greater than in patients of other types of complications and without complications, independently of patient- and tumor-related factors and extent of resection (17). Concerning oxygenation in the arterial blood, partial pressure of oxygen (pO₂) was decreasing

during the first three postoperative days in a similar way in patients with respiratory, surgical complications and in patients without complications. In patients with cardiac complications, a steep drop occurred at the moment of the complication onset. A slight hypercapnia registered on the first postoperative day was gradually abolished in all groups except in patients with cardiac complications (17). These results incline to some extent to support the decision to offer surgery to some patients with borderline cardiorespiratory reserve.

Late postoperative lung function recovery

After both lobectomy and pneumonectomy, a certain definitive lung function defect persists. Although values vary across studies, after pneumonectomy, the FVC may decrease by 30% from preoperative values, FEV₁ by 28%, whilst the reported decreases for DLco and peak oxygen consumption are 39% and 28%, respectively; after lobectomy, the definitive FVC loss was reported to be 13%, whilst FEV₁ drops of only 8% of the preoperative value were reported; the permanent DLco and peak oxygen consumption drops are around 20% and 12%, respectively (25).

Similar data were obtained in other studies, with 23% FEV₁ decrease after pneumonectomy and 8% after lobectomy and decreases in exercise capacity by 16% after pneumonectomy and 13% after lobectomy (26).

Some studies demonstrated even smaller lung function losses after lobectomy—for FVC by 7%—and for maximal oxygen consumption only by 1% of preoperative values (22). In line with these reports, the study measuring the lung function preoperatively and more than 6 months

postoperatively, showed that in patients with lobectomy, 6 months after surgery, VC and FEV₁ loss was around 10%, whilst the maximal oxygen consumption per square meter recovered to 86.7% (2).

The relatively low reported loss in FEV₁ after lobectomy may lead to the underestimation of the value of the postoperative lung function prediction (see later) and misleading decisions in preoperative patient selection in a way that “almost every patient should tolerate a lobectomy”. Rare studies specifically addressing differences in postoperative lung function changes between COPD and non-COPD patients help to avoid this pitfall. The average loss of FEV₁ was about 8.6–19.0% after lobectomy for non-COPD patients, whilst the postoperative change of FEV₁ in patients with COPD was between –18.3% and 5%. COPD (27). Such an interval of values can be explained by the quality of the resected lung tissue. Indeed, patients with a low preoperative FEV₁ and COPD index >1.2 may have restrictive diseases and can be expected to sustain a 5% to 20% loss of function (FEV₁) after lobectomy. Unlike them, patients with a COPD index <1.0, in whom the nonfunctioning lobe has remained, seem to lose higher percentage of their FEV₁ with resection of a functioning lobe (26). It was also demonstrated that the reduction in FEV₁ was lower in COPD *vs.* non-COPD patients (6% *vs.* 13%, P=0.0002), but residual postoperative FEV₁ values were lower in COPD patients as well (62% *vs.* 74%, P<0.0001), despite much lower FEV₁ loss compared with preoperative values (28). The presented data clearly confirm the need to take all these elements into account during the preoperative patient selection.

Concerning differences in the postoperative lung function recovery between COPD and non-COPD patients, a study on 76 patients with the lung function assessment preoperatively and up to one year postoperatively, showed that postoperative FEV₁ values significantly increased only in non-COPD patients (29). The postoperatively measured DLco up to one year after surgery was again significantly higher in non-COPD than in COPD patients. This improvement was not observed after thoracotomy.

VATS *vs.* thoracotomy

The most of the studies on sufficient number of patients showed the functional advantage of VATS *vs.* thoracotomy. In a study on 51 patients with VATS and with 52 with postero-lateral thoracotomy, the FVC and the shoulder

function recovered significantly better in the VATS group after 7 days, one and three months, whilst the FEV₁ recovery was also better in the VATS group, but without the statistical significance (7).

Similar results were obtained by some other studies, like the one by Nakata *et al.* that found that peak flow rates, FEV₁, and FVC were higher at one and two weeks after VATS lobectomy than after thoracotomy (30). Another study demonstrated that the recovery rates were dependent on the postoperative pain, being significantly lower in the VATS group on the day of operation and on the first, 7th and 14th postoperative days (31).

Unlike these reports, a study on two well matched VATS and thoracotomy groups with 60 patients each, found no significant differences in the recovery of FEV₁, FVC, or of the peak flow rate between VATS and thoracotomy group during the 1 year follow up (5). Similarly, several small series have suggested that the outcomes after VATS lobectomies in COPD patients could be similar to those in non-COPD patients (32,33).

It should be mentioned that the above reports refer to full thoracotomy, so that firm conclusions concerning the influence of the operative approach should not be extended to other types of thoracotomy, like mini-thoracotomy (up to 10 cm incision with small rib spreader), limited antero-lateral or axillar incision with sparing of the muscles, whose impact on the postoperative lung function could be different.

COPD patients

Several authors have reported that the loss in FEV₁ in COPD patients was smaller or was even improved postoperatively compared with FEV₁ changes in non-COPD patients (20-22), especially during 3 first postoperative months, probably due to some kind of the lung volume reduction (LVR) effect (1).

A trend of the measured postoperative FEV₁ to exceed the predicted value was reported in COPD-patients 1 month after surgery (P=0.06), but without a subsequent increase (17). Unlike that, the postoperative FEV₁ in the non-COPD patients corresponded to the predicted value 1 month after surgery, but it significantly increased till 6 months, and remained approximately the same after 1 year (85.1% of the preoperative value) (17).

Bobbio and colleagues reported that the maximal oxygen consumption decreased by 20% three months after

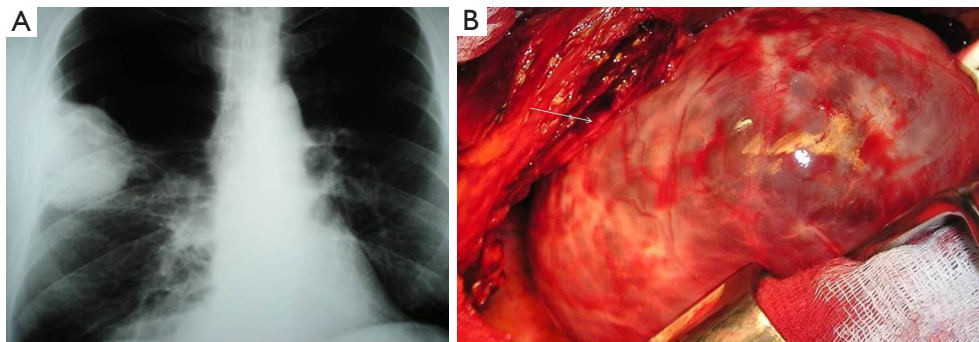


Figure 1 Primary lung cancer and a big bulla in the same lobe. (A) Preoperative PA radiography: right upper lobe with a big bulla and carcinoma invading the chest wall; (B) operative view: a big bulla protruding through the thoracotomy incision; arrow: area of the initial extrapleural dissection, subsequently extended to partial rib resection because of the direct rib invasion. PA, postero-anterior.

lobectomy in COPD-patients (34).

The problem within these considerations is that there is not sufficient data to distinguish between the true LVR effect of lobectomy in patients with clear bullous emphysema and accordingly expected LVR effect postoperatively (*Figure 1*) and patients with chronic obstructive bronchitis.

In patients with a pneumonectomy, a definitive remodeling of the chest exists, with mediastinal shift and sometimes a major lung hernia towards the operated side. Overdistension of the remaining lung occurs as an adaptive response. It was demonstrated that patients with a low body mass index (BMI) ($<20 \text{ kg/m}^2$) showed a significantly greater degree of lung herniation towards the operative side than those with a high BMI ($\geq 20 \text{ kg/m}^2$) (9). Although COPD itself has no effect on lung herniation, in COPD patients this can cause an LVR effect, whilst in non-COPD patients a vicariate emphysema occurs. Of practical importance is the report that COPD patients with a pneumonectomy may have the smaller postoperative FEV₁ drop and greater decrease in hyperinflation than non-COPD patients (8). These findings may be helpful in preoperative patient selection.

Site of lobectomy and postoperative lung function

Despite certain amount of evidence (20,35,36), some aspects of the influence of the site of lobectomy are not absolutely clear. Although more lung volume is removed by lower lobectomy, the lung function after this operation was not inferior to that after upper lobectomy (37). In a study on 72 patients (33.3% COPD), the percent of FVC loss after

the lower lobectomy was significantly higher compared with the upper lobectomy 6 months postoperatively, but this difference disappeared 12 months after surgery (6). Another study analyzed the duration of the postoperative air leak and demonstrated that the time necessary for the air leak to stop was shorter after lower and middle compared to upper lobectomy, thus in some way suggesting that the early functional consequences of the lower lobectomy must not always be inferior than those after upper lobectomy (19).

The understanding of this aspect is additionally complicated by some reports suggesting the influence of COPD. In fact, the postoperative FEV₁ was underestimated in COPD patients 1 and 6 months after upper lobectomy compared with non-COPD patients (38). It means that COPD might influence FEV₁% at both the early and late stages after upper lobectomy, making firm conclusions about the influence of the site of lobectomy even more difficult.

Prediction of the postoperative lung function

Several methods of the postoperative lung function prediction have been confirmed as reliable in terms of the FEV₁ prediction 3–6 months after surgery. However, it was demonstrated that the FEV₁ can be overestimated during the first postoperative days, when, in fact, the most of the severe complications may occur. Many years ago it was clearly demonstrated that in patients with lobectomy, the FEV₁ measured on the first postoperative day, may be 30% lower than predicted (3).

The choice of the postoperative lung function prediction depends not only of institutional protocols preferences,

Table 2 Accuracy of the postoperative lung function prediction-meta analysis of 17 studies

Author, year	No. of cases	Operation	Method of the lung function prediction	Measured outcome
Taube (39), 1980	27	Pneumonectomy	Perfusion scintigraphy	FEV ₁
Egeblad (40), 1986	30	Lobectomy + pneumonectomy	Segment counting	FEV ₁
Wu (41), 1994	38	Lobectomy + pneumonectomy	CT volume and density	FEV ₁
Bolliger (42), 1995	22	Wedge, segmentectomy, lobectomy, pneumonectomy	Perfusion scintigraphy	FEV ₁ , DLco
Larsen (43), 1997	23	Lobectomy + pneumonectomy	Perfusion scintigraphy	FEV ₁
Beccaria (44), 2001	62	Lobectomy + pneumonectomy	Segment counting	FEV ₁
Wu (45), 2002	34	Lobectomy + pneumonectomy	Perfusion scintigraphy, CT volume and density	FEV ₁
Wang (25), 2006	28	Segmentectomy, Lobectomy + pneumonectomy	Segment counting	DLco%
Sudoh (46), 2006	22	Lobectomy + segmentectomy	subsegment counting; SPECT-CT	FEV ₁
Ohno (47), 2007	60	Lobectomy + pneumonectomy	Perfusion Scintigraphy; ventilation Scintigraphy; SPECT	FEV ₁
Yoshimoto (48), 2009	37	Lobectomy	Segment counting; CT volume and density; SPECT	FEV ₁
Yamashita (49), 2010	14	Lobectomy + pneumonectomy	Perfusion scintigraphy; CT perfusion	FEV ₁
Yanagita (50), 2013	30	Lobectomy + pneumonectomy	SPECT; CT ventilation	FEV ₁
Chae (51), 2013	51	Lobectomy + pneumonectomy	Perf. scintigraphy; CT perfusion	FEV ₁
Ohno (52), 2015	60	Segmentectomy; Lobectomy; pneumonectomy	Segment counting; Perf. scintigraphy; CT volume and density	FEV ₁
Yabuuchi (53), 2016	49	Lobectomy	Subsegment counting; CT volumetry; CT volume and density	Only FEV ₁ change
Fourdrain (54), 2017	23	Lobectomy + pneumonectomy	Segment counting; subsegment counting; perfusion + ventilation scintigraphy	FEV ₁

CT, computed tomography; SPECT, single-photon emission computed tomography; FEV₁, forced expiratory volume in the first second; DLco, diffusion capacity for carbon monoxide.

but of availability of modern technical equipment and of organizational issues as well.

A recent meta-analysis of 17 studies (*Table 2*) analyzed the accuracy of the postoperative FEV₁ prediction of different techniques: segment counting, subsegment counting, perfusion scintigraphy, ventilation scintigraphy, single photon-emission computer tomography (SPECT), computer tomography volume and density and computer tomography volume and partial density.

The prediction of FEV₁ after the lung resection was the most accurate when CT volume and density measures were combined, the minimum clinically important difference in FEV₁ being set up at 100 mL (10). This minimal cut off value means that, if the difference between the measured

and predicted value is less than 100 mL, it should not be clinically noticeable (55). The evidence about the prediction of the postoperative DLco was weak, but the segment counting seems to be more accurate than perfusion scintigraphy.

Another study analysed the lung function preoperatively and 3–4 months postoperatively and demonstrated that volumetric CT was more accurate than segment counting or scintigraphy in terms of prediction of FEV₁, VC, DLco and peak oxygen uptake (11). However, both segment counting methods (Juhl-Frost and Nakahara), together with FEV₁ prediction by means of perfusion lung scintigraphy are still in the widespread use (56,57). The advantage of the Nakahara *vs.* Juhl-Frost method is taking into account the

number of obstructed segments:

$$\text{ppoFFE}V_1 = \text{preopFE}V_1 \times [1 - (S - N) / (19 - N)] \quad [1]$$

(S= number of segments to be resected; N= number of obstructed or consolidated segments; 19= total number of segments in both lungs; ppo = predicted postoperative; preop = preoperative).

The method based on the perfusion lung scintigraphy is also suitable for clinical practice:

For lobectomy,

$$\text{ppoLoss in FE}V_1 = \text{preopFE}V_1 \times \% \text{ perfusion of the affected lung} \times n/n1 \quad [2]$$

$$\text{ppoFE}V_1 = \text{preopFE}V_1 - \text{ppoLoss in FE}V_1 \quad [3]$$

(n= number of segments to be removed; n1= number of segments in the operated lung).

For pneumonectomy,

$$\text{ppoFE}V_1 = \text{preopFE}V_1 \times \% \text{ perfusion of the healthy lung} \quad [4]$$

The main concern with this method is that it uses only the percents of perfusion distribution between the right and left lung, not giving the insight into the quality of the perfusion itself. That is why the preoperative diffusion assessment is of the key importance and that is why the aforementioned volumetric (quantitative) CT by determining the extent of the lung zones with density ranging between -900 and -500 HU enables to determine the volume of the functioning lung tissue. The lung zones with the aforementioned density can be extracted by the appropriate software as proposed by Wu *et al.* (45). The removal of the lung zones outside the density range -910 to -500 HU is not expected to cause a major lung function loss.

In recent years, several methods of the postoperative lung function prediction have been reported, like SPECT, 4-dimensional CT ventilation, positron emission tomography/CT or dynamic contrast-enhanced perfusion magnetic resonance imaging. However, the correlation coefficients between measured and predicted postoperative FEV₁, ranging from 0.81 to 0.99, do not favor them over volumetric CT (58-61). In addition, they are less-accessible and, in some cases, involve additional radiation for the patient.

Independently on the used postoperative lung function prediction technique, the common goal is to assess whether the calculated ppoFEV₁ value exceeds or not 30–35%

for the particular extent of resection. This cut of value represents the limit under which surgery should not be offered to the patient.

However, even if ppoFEV₁ slightly exceeds this cut-off value, it does not mean that the patient will not be exposed to the increased risk of postoperative complications. This should always be kept in mind in surgical candidates with limited lung function. The prediction of postoperative oxygen consumption (VO₂) better reflects this type of risk. It can be determined by combining the preoperative measured VO₂ and percent of perfusion of particular lung lobe: max.ppoVO₂ = max.preop.VO₂ × (1 - *fr*), where *fr* means fraction of the function of the part of the lung to be removed. With the maximal ppoVO₂ being <10 mL/kg/min. the risk of operative mortality is unacceptably high (42).

Many years ago it was demonstrated that that the pattern of the DLco increase in effort is the most reliable in terms of complications prediction. With <10% DLco increase in effort (from rest to 70% of maximal workload) the complication rate is 100%, *vs.* 10% complication rate in case of >10% DLco increase (62). By using the same equations as for FEV₁ prediction by means of perfusion lung scintigraphy (see above), the postoperative DLco can be predicted as well.

The ERS/ESTS guidelines for fitness for surgery address the above issues in a practice-oriented way with calculation methods that are suitable for practical use (63).

Functional aspects of anatomical segmentectomy

Before presenting the evidence about functional effects of anatomical segmentectomy, it should be mentioned that, since the publication of the Lung Cancer Study Group Trial, dealing primarily with oncological aspects of segmentectomy *vs.* lobectomy, it has been suggested that segmentectomy brings nonsignificant, if any, functional advantage over lobectomy (64). In fact, in that trial there were no significant differences only in postoperative FVC between patients with lobectomies *vs.* limited resections, whilst a significant benefit of limited resection in preserving FEV₁ was demonstrated. Despite this, the authors' conclusion that there was no functional advantage of limited resection compared with lobectomy, continued to be widely accepted. A similar conclusion appeared after the study of Takizawa and coworkers who compared patients with segmentectomy and lobectomy and found that the choice of the procedure had no effect on postoperative FVC at 12 months, although a significant impact on postoperative

FEV₁ was demonstrated (65). Both of these studies have suggested that lobectomy should remain the procedure of choice despite the slight functional advantage in favor of limited resection.

During the past 20 years anatomical segmentectomy is in the widespread use for stage one lung cancer smaller than 2 cm in diameter and is considered as advantageous *vs.* lobectomy because it preserves the lung function, and allows patients to benefit from eventual future resection in case of metachronous lung cancer as well (66). The pool of evidence about functional effects of segmentectomy increases and in general supports such a statement, although some conflicting and opposite results were also reported.

In the study of Tane and co-workers with well-matched groups (74 VATS segmentectomies and 74 VATS lobectomies), the postoperative lung function was significantly better preserved in the segmentectomy than in the lobectomy group (61). The same study demonstrated that after both segmentectomy and lobectomy, the regional FEV₁ of the ipsilateral non-affected lobe was increased in comparison with the preoperative value, whereas that of the residual lobe rescued by segmentectomy was decreased. Interestingly, the preservation rate of the residual lobe inversely correlated with the extent of the resected segment, possibly because of inflation of the unaffected ipsilateral lobe causing limited expansion of the residual lobe. Conversely, the preservation rate of the unaffected lobe directly correlated with the extent of the resected segment. In other words, the larger the extent of resection of the segment, the greater the increase in the lung function of the ipsilateral nonaffected lobe.

The similar functional advantage of segmentectomy was demonstrated in the study on 147 patients with lobectomy and 54 patients with segmentectomy for stage I non-small cell lung cancer, where the preoperative lung function was significantly worse in the segmentectomy group (FEV₁ 75.1% versus 55.3%; $P < 0.001$) (42). After 1 year, in the lobectomy group, significant drops in forced VC (85.5% to 81.1%), FEV₁ (75.1% to 66.7%), maximum voluntary ventilation (72.8% to 65.2%), and DLco (79.3% to 69.6%) existed, whilst in the segmentectomy group, the only significant change was a decline in DLco.

Some other reports are in line with the aforementioned results. In one study, the suitability of segmentectomy for <2 cm peripheral T1N0M0 lung cancers was suggested based on the small postoperative decline in lung function—only 11.3% in FVC and 13.4% in FEV₁ (67). Another

study on 103 patients with segmentectomy and the same number with lobectomy showed that the lung function was significantly better preserved after segmentectomy, because the operated lobe retained 48%±21% of the preoperative function. Furthermore, the function of the ipsilateral non-operated lobe increased only after segmentectomy (14).

Some reports, although not denying the functional effects of segmentectomy, express some concerns. Firstly, according to the available evidence, the mean decrease in FEV₁ seems to range from -9% to -24% of the preoperative value after two months and -3 to -12% 12 months after segmentectomy (68). Despite the significantly lower lung function reduction than after lobectomy, segmentectomy saves only a few percents of the preoperative FEV₁ value, so that the question arises about the real benefit of this procedure. Moreover, the published data do not clearly confirm the functional benefit of segmentectomy in patients with poor lung function (68). Secondly, it was also demonstrated that, although the lung function was better after segmental resection than after lobectomy after 6 months, the actual lung function did not reach the predicted-postoperative value at 1 month after surgery (15). It means that after segmentectomy, the early postoperative pulmonary function may be significantly less than the expected value.

In some studies no functional advantage for segmentectomy could be demonstrated, like in the study on 37 patients with segmentectomy and 33 patients with lobectomy for T1aN0M0 non-small cell lung cancer. In this study, no statistically significant difference was demonstrated neither for recovery ratios of the FVC nor of the FEV₁ (16). Similarly, the recovery ratios for radiologic lung volume and weight followed the similar pattern in both groups ($P = 0.46$ and $P = 0.22$).

Unlike lobectomy, anatomical segmentectomy has some technical points that may cause differences between predicted and actual lung function of the residual lobe and these points are addressed in the literature as well (12). Developing the intersegmental plane by using electrocautery and stapler may cause the restricted reexpansion of the preserved segments. Similarly, in order to achieve tumor-free margins, dissection of the parenchyma is directed towards the residual segment, thus additionally restricting its function. Finally, because of the segmental anatomy, resection of the 6th segment, as technically less complicated (well defined, only one intersegmental surface), is more likely to cause better preservation of the residual lobe's

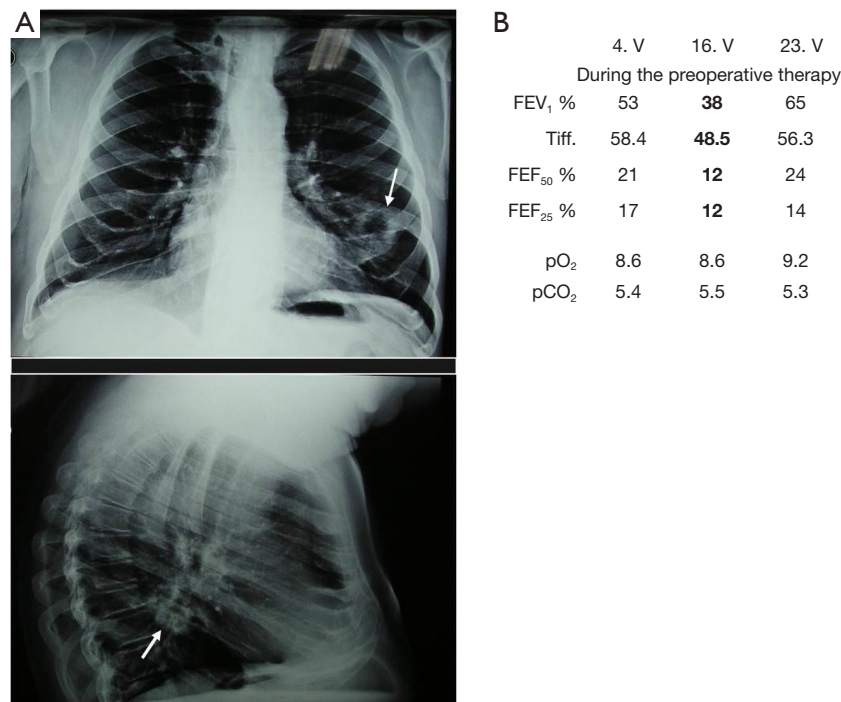


Figure 2 Transitory lung function worsening during the preoperative bronchodilation treatment. (A) Postero-anterior (above) and lateral view (below): excavating tumour centrally in the left lower lobe (arrows). (B) From left to right: transitory worsening and recovery of the ventilatory parameters during the preoperative therapy; no synchronous worsening of the preexisting slight hypoxaemia, clear improvement at the end of the therapy. FEV₁, forced expiratory volume in the first second; Tiff, Tiffeneau index (100FEV₁/vital capacity); FEF₅₀, FEF₂₅, forced respiratory flows at 50% and 25% of vital capacity; pO₂, partial pressure of oxygen in the arterial blood in kPa; pCO₂, partial pressure of carbon monoxide in the arterial blood in kPa.

function, compared with posterior-basal segmentectomy, requiring dissection at multiple surfaces at an acute angle and with deeply located point of divergence of the bronchus and vessels.

Finally, by considering these functional effects of segmentectomy, it should be remembered that preservation of lung function makes sense only if these patients will not be exposed to an increased risk of local or regional recurrence. In only one report both aspects were synchronously analyzed (13). Segmentectomy was also reported as associated with longer mean operative time (270±70 *vs.* 202±67 min) and more frequent postoperative complications (19.6% *vs.* 6.5%, P=0.03) compared with lobectomy (69) and it should be kept in mind in preoperative patient selection.

Some specific considerations

As the above considerations relate to patients with

borderline respiratory reserve (mostly COPD), it is useful to remind that sometimes, transitory worsening of the lung function may occur in form of unexpected FEV₁ drops during the combined bronchodilation treatment (*Figure 2*). This is a phenomenon known as paradoxical response to bronchodilation (70). Although it is attributed to transitory decrease of the small airways' wall tonus and subsequent collapse during the forced expiration under this type of therapy, the exact mechanisms are not clear. They include incorrect inhaler use, bronchospasm from the propellant or the benzalkonium chloride, chlorofluorocarbons, and oleic acid contained in inhalers were suggested as possible causes (71-73). Airway thickness is significantly increased in the paradoxical bronchodilator response group, and may reduce the response to bronchodilators (74). Paradoxical bronchoconstriction after short-acting beta-agonists was suggested as a possible mechanism as well (75). These patients should be carefully monitored, rather than being upfront rejected from surgery.



	Before OP	p.op. d. 1	p.op. d. 5
pO ₂	8.2 kPa	9.7	13.2
pCO ₂	5.7 kPa	7.1	6.9
pH	7.44	7.36	7.39

	Before bronchodilatation	After bronchodilatation
FEV ₁	1.72 (69%)	2.19 (87%)
FVC	3.28 (111%)	3.72 (126%)
FEF ₅₀	0.51 (13%)	1.11 (29%)
FEF ₂₅	0.13 (9%)	0.36 (24%)

Figure 3 Unexpected oxygenation worsening despite reversible bronchoobstruction, good responding to preoperative bronchodilation therapy. Upper row left: postero-anterior radiography showing a tumour in the right upper lobe; upper row right: oxygenation before and after lobectomy—refractory preoperative hypoxaemia disappeared after surgery; lower row: lung function parameters before (left) and after bronchodilation therapy (right). p.op. d. 1, postoperative day one; p.op. d. 5, postoperative day 5; FEV₁, forced expiratory volume in the first second; FVC, forced vital capacity; FEF₅₀, FEF₂₅, forced respiratory flows at 50% and 25% of vital capacity; pO₂, partial pressure of oxygen in the arterial blood; pCO₂, partial pressure of carbon monoxide in the arterial blood; pH, potential of hydrogen, quantitative measure of acidity or alkalinity.

Similarly, despite a good therapeutic response to preoperative bronchodilation treatment in patients with mild to moderate COPD, a refractory and unexpected hypoxemia may occur during the treatment, putting into question the planned surgery. Here again, the reversibility of the bronchoconstriction is an important argument to offer surgery to these patients provided the diffusion problems and embolism are excluded. Such a scenario can be partly explained by the impaired function of the small airways—forced expiratory flow at 50% and 25% of the VC (FEF₅₀ and FEF₂₅), as can be seen on *Figure 3*. The function of the small airways is usually not so much in focus during the postoperative lung function prediction. A single center series of 35 COPD and 47 non-COPD patients confirmed the importance of synchronous improvement of the small airways' function after preoperative bronchodilation treatment (76).

In candidates for pneumonectomy, a so called “functional effect of pneumonectomy” may exist preoperatively. In this case, the measured spirometry values may be very low, corresponding to severe mixed or purely restrictive disorders and as such at first sight not allowing a pneumonectomy. In

these patients either the main bronchus may be completely occluded by the tumor, both lobar bronchi may be occluded by the extraluminal compression, or only one lobar bronchus may be occluded from outside in presence of a big tumor in another lobe (*Figure 4*). The correct interpretation of the endoscopic aspect will qualify these patients for pneumonectomy, because their preoperative lung function in fact corresponds to that after the operation.

Furthermore, the preservation *vs.* scarifying of the phrenic nerve during surgery has for a long time been considered as non-relevant for the postoperative lung function. However, the study from Ugalde *et al.* (in 2008) nicely demonstrated that the postoperative FEV₁ in patients with preserved phrenic nerve was significantly higher *vs.* patients with both immobile diaphragm and patients with paradoxical diaphragm movements (18).

Finally, diaphragm motion should be always taken into consideration before the planned lung resection. In a prospective pilot-study on 27 patients, we demonstrated that diaphragm movements may influence the accuracy of the postoperative lung function prediction (23). It can be easily checked either by ultra-sound or under fluoroscopy.

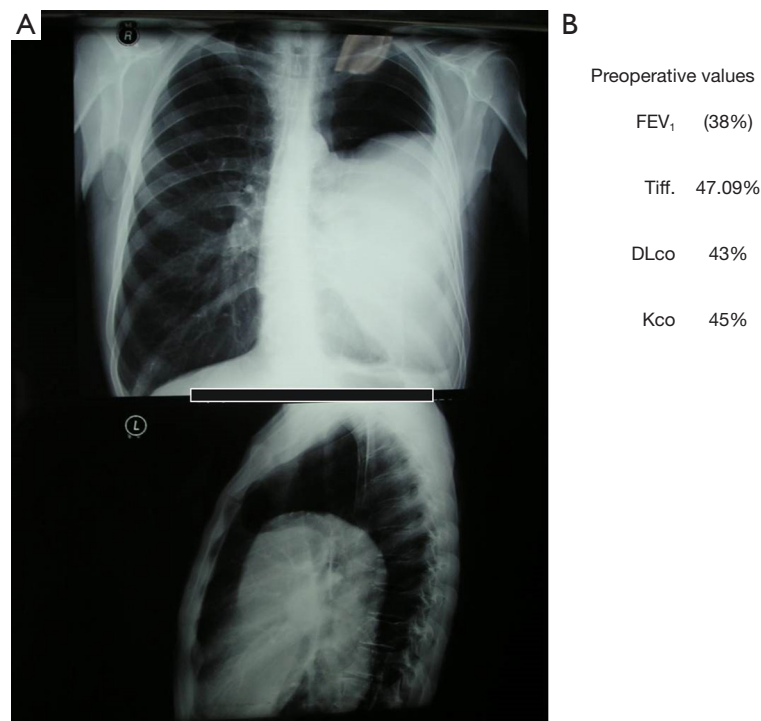


Figure 4 Functional effect of pneumonectomy before surgery. (A) Postero-anterior (above) and lateral view (below)—big tumour of the left lung with occlusion of both lobar bronchi. (B) Preoperative ventilatory parameters and diffusion values. FEV₁, forced expiratory volume in the first second; Tiff, Tiffeneau index (100FEV₁/vital capacity); DLco, diffusion capacity for carbon monoxide; Kco, diffusion coefficient (DLco/effective alveolar surface).

Study limitations

There are three main limitations of this study. The first one is a non-systematic type of the review, making the evidence quality assessment unreliable. The second limitation is the aim of the study, that was focused not only to the existing evidence, but to the evidence gaps as well. The problem is to define what are “evidence gaps”—are those only topics with insufficient data or those with sufficient, but conflicting data as well? Furthermore, our awareness of gaps depends also on the preference of particular teams, in a way that some of them are more inclined to get the update information about a particular surgical technique, relying upon the functional assessment by pulmonologists. Finally, as in recent years the percentage of studies dealing with modern noninvasive techniques steadily increases, functional aspects were not frequently specifically addressed, but rather (if at all) as a part of the presented data, usually including one or two analyzed parameters. That is why the structure of the papers included in this study does not adequately mirrors the real percentage of evidence covering a particular topic, like, for

example for diaphragm-related issues with only a couple of studies that could be benefit for the everyday practice.

Conclusions

The prediction of the postoperative lung function after the lung resection is currently the standard in most of the centers. Both the postoperative lung function loss and recovery are well documented and both should be taken into account during the lung function prediction. In COPD patients the predicted postoperative lung function parameters may be initially underestimated *vs.* non-COPD patients, but COPD patients have the limited capacity of later lung function improvement. The prediction of the postoperative lung function after lobectomy is reliable in many aspects, but the influence of the upper *vs.* lower lobectomy either independently, or depending of the side of the operation, requires further analysis. Issues related to pneumonectomy are sufficiently evidence-based and combining of lung function analysis and cardiorespiratory risk assessment is now an accepted standard. The cut-

off values for safe surgery given in the existing guidelines should be adhered, taking into account the above-mentioned evidence gaps and issues given under “specific considerations” of this text. In brief, the preoperative lung function assessment is a dynamic process and the published data should be used cautiously, with the awareness of the presented evidence gaps, uncertainties and controversial data as well.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The author has completed the Narrative Review reporting checklist. Available at <https://amj.amegroups.com/article/view/10.21037/amj-22-19/rc>

Peer Review File: Available at <https://amj.amegroups.com/article/view/10.21037/amj-22-19/prf>

Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at <https://amj.amegroups.com/article/view/10.21037/amj-22-19/coif>). DS serves as an unpaid Associate Editor-in-Chief of *AME Medical Journal* from March 2020 to April 2024. The author has no other conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/amj-22-19

Cite this article as: Subotic D. Lung function assessment before anatomical lung resections—is everything so clear?—a narrative review. *AME Med J* 2022;7:27.

Table S1 Characteristics of the analysed studies

Study ID	Type of research	Patients characteristics	Surgery type	Findings summary
Nagamatsu Y, 2007 (4)	Retrospective analysis of prospectively collected data	18 patients	Lobectomy	The recovery of exercise capacity was 95% 1 year after surgery
Park TY, 2016 (5)	Retrospective study	120 patients with primary lung cancer	60 VATS lobectomy, 60 open lobectomy	There were no significant differences in pulmonary function recovery during the late postoperative period in NSCLC patients receiving VATS versus thoracotomy
Seok Y, 2014 (6)	Prospective	72 patients with primary lung cancer	VATS lobectomy	The postoperative lung function depended on the lobe resected and presence of COPD
Pu Q, 2013 (7)	Prospective	103 patients with primary lung cancer	51 VATS and 52 open lobectomy	FEV ₁ recovery was better in VATS group, but not significantly; VATS lobectomy generates less pain and preserves better the lung function in the early postoperative phase
Luzzi L, 2008 (8)	Retrospective	27 patients with lung cancer	Pneumonectomy	COPD patients with a pneumonectomy may have the smaller postoperative FEV ₁ drop and greater decrease in hyperinflation than non-COPD patients
Fujimoto T, 2002 (9)	Retrospective cohort study	27 patients with lung cancer	Pneumonectomy	Patients with a low body mass index (BMI) (<20 kg/m ²), however, showed a significantly greater degree of lung herniation than those with a high BMI (≥20 kg/m ²)
Oswald NK, 2019 (10)	Meta-analysis of 17 studies	610 patients with lung cancer	Lobectomy, pneumonectomy, segmentectomy	FEV ₁ prediction was the most accurate when CT volume and density measures were combined
Varella G, 2006 (3)	Prospective	161 patients with lung cancer	Lobectomy	in patients with lobectomy, the FEV ₁ measured on the first postoperative day, may be 30% lower than predicted
Fernández-Rodríguez L, 2018 (11)	Retrospective	114 patients with lung cancer	Anatomical lung resections	volumetric CT was more accurate than segment counting or scintigraphy in terms of prediction of FEV ₁ , vital capacity, diffusion capacity and peak oxygen uptake
Tane S, 2019 (12)	Retrospective	148 patients with lung cancer	74 segmentectomies, 74 lobectomies	Segmentectomy preserved the lung function better than lobectomy
Keenan R, 2004 (13)	Retrospective	201 patients with lung cancer	54 segmentectomies, 147 lobectomies	segmental resection offers preservation of pulmonary function compared with lobectomy and does not compromise survival
Nomori H, 2018 (14)	Retrospective cohort study	392 patients with lung cancer	184 segmentectomies, 208 lobectomies	Segmentectomy preserves the lung function better than lobectomy; it also improves the function of non-operated lobe
Saito H, 2014 (15)	Retrospective	178 patients with lung cancer	52 segmentectomies, 162 lobectomies	Pulmonary function at 6 months after surgery is better after segmental resection than after lobectomy
Suzuki H, 2017 (16)	Retrospective	70 patients with lung cancer	37 segmentectomies, 33 lobectomies	No functional advantage for segmentectomy was observed during long-term follow-up
Ercegovic M, 2014 (17)	Prospective cohort study	60 patients with lung cancer	5 sublobar resections, 41 lobectomies, 14 pneumonectomies	Extent of the lung resection and postoperative complications do not significantly influence the trend of the lung function recovery after lung resection for lung cancer
Ugalde P, 2008 (18)	Retrospective	88 patients with lung cancer	Pneumonectomy	Phrenic nerve preservation during pneumonectomy is of significant functional benefit postoperatively
Kushibe K, 2009 (19)	Retrospective	186 patients with lung cancer	Lobectomy	The time necessary for the air leak to stop was shorter after lower and middle- compared to upper lobectomy
Sekine Y, 2003 (20)	Retrospective	521 patients with lung cancer	Lobectomy	In patients with COPD who had lower or middle-lobe lobectomies was better preserved than predicted
Baldi S, 2005 (21)	Retrospective	137 patients with lung cancer	Lobectomy	Patients with mild to severe chronic obstructive pulmonary disease could have a better late preservation of pulmonary function after lobectomy than healthy patients
Edwards JG, 2001 (22)	Retrospective	29 patients with lung cancer	Lobectomy	Effect of lobar volume reduction allows for an extension of the selection criteria
Subotic D, 2013 (23)	Prospective plot-study	27 patients with lung cancer	Lobectomy and pneumonectomy	The preoperative diaphragm motion influences the postoperative lung function prediction

NSCLC, non-small-cell lung cancer; VATS, video-assisted thoracic surgery; COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in the first second.