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# Improvement of pulmonary function after lobectomy for non-small cell lung cancer in emphysematous patients[1]

Angelo Carretta[a,*], Piero Zannini[a], Armando Puglisi[a], Giuseppe Chiesa[a], Angelo Vanzulli[b], Achille Bianchi[c], Alessia Fumagalli[c], Sebastiano Bianco[c]

[a]*Department of Thoracic Surgery, Scientific Institute H San Raffaele, University of Milan, Milan, Italy*
[b]*Department of Radiology, Scientific Institute H San Raffaele, University of Milan, Milan, Italy*
[c]*Department of Respiratory Medicine, Scientific Institute H San Raffaele, University of Milan, Milan, Italy*

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**Abstract**

**Objective**: Pulmonary emphysema is frequently associated with lung cancer and, because of the impaired pulmonary function involved, it may contraindicate surgical treatment. However, improvement of pulmonary function has been observed after surgical resection in patients with advanced emphysema. The aim of this study was to evaluate whether pulmonary emphysema, as assessed by pulmonary function tests and radiological evaluation, can influence postoperative respiratory function after lobectomy for non-small cell lung cancer (NSCLC). **Methods**: Respiratory function was evaluated before and after lobectomy for NSCLC. Radiological evaluation of emphysema was performed on chest X-ray and CT scan. Patients that had undergone chemo- or radiotherapy or had segmental or lobar atelectasis were excluded from the study. **Results**: Thirty-five patients entered the study. A decrease in static lung volumes was observed after surgery. Total lung capacity (TLC) decreased from 6.58 ± 0.92 to 5.46 ± 0.77 l; functional residual capacity (FRC) from 3.70 ± 0.88 to 2.96 ± 0.73 l and residual volume (RV) from 2.93 ± 0.78 to 2.2 ± 0.53 l. However, in a subgroup of 10 patients (Group 1), dynamic volumes after surgery were unchanged or slightly increased (forced vital capacity (FVC) from 3.23 ± 0.65 to 3.3 ± 0.68 l; forced expiratory volume in 1 s (FEV1) from 2.14 ± 0.51 to 2.25 ± 0.54 l), and airway resistances (sRaw) decreased from 15.58 ± 5.18 to 11.42 ± 5.25 cm $H_20$/s. Preoperative data showed that these patients had a greater obstruction, with FEV1 changing from 69 ± 12.42 to 72.70 ± 13.72% of predicted, as compared with a change from 87 ± 12.7 to 72.08 ± 13.10% in the other group of 25 patients (Group 2). Correlation analysis reached statistical significance between FEV1% variation (ΔFEV1%) and preoperative FEV1 and FVC% ($r = –0.49$, $P = 0.002$ and $r = –0.5$, $P = 0.001$, respectively) and between Δ (FEV1)% and radiological scores for 3-level CT ($r = 0.39$, $P = 0.04$) and the sum of chest X-ray, single and 3-level CT scores ($r = 0.49$, $P = 0.01$). **Conclusions**: Pulmonary function may remain unchanged or even increase after lobectomy in patients with a pronounced emphysematous component of airway obstruction. The identification of preoperative parameters that identify this group of patients could extend the indications for the treatment of lung cancer in patients with pulmonary emphysema. 

*Keywords:* Emphysema; Lung cancer; Surgery; Radiology; Pulmonary function

## 1. Introduction

Due to common risk factors such as smoke, pulmonary emphysema may frequently coexist with lung cancer. Although surgery still remains the main treatment for early-stage non-small cell lung cancer (NSCLC) [1], the impairment of respiratory function in patients with chronic obstructive pulmonary disease (COPD) may contraindicate surgical resection. Prediction of postoperative respiratory function is therefore of paramount importance when assessing indication to surgery in such patients. Parameters such as predicted postoperative forced expiratory volume in 1 s (ppoFEV1), carbon monoxide diffusing capacity (DLCO) and oxygen consumption are usually used to assess operability [2].

* Corresponding author. Tel.: +39-2-2643-7138; fax: +39-2-2643-7147.
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A reduction of about 15% of pulmonary function, as evaluated by FEV1, is usually observed after lobectomy [3]. The experience obtained in recent years with lung volume reduction surgery (LVRS) has, nevertheless, demonstrated that some improvement in pulmonary function may be observed after resection of pulmonary parenchyma in patients with advanced emphysema, in some cases by performing anatomical resections such as lobectomy [4]. A recent report by DeMeester et al. [5] has also demonstrated that the improvement obtained with LVRS may extend the indications for the resection of lung cancer to patients with advanced emphysema. Whether a similar concept could also be applied to lung cancer patients with a lesser degree of emphysema is still unknown. Furthermore, postoperative reduction of pulmonary function has actually been found to be lower in patients with severe functional impairment [3]. Other authors have even reported functional improvement in selected cases after resection of pulmonary parenchyma for the treatment of lung cancer [6,7]. The aim of this study was to evaluate whether pulmonary emphysema, as assessed by pulmonary function tests and radiological evaluation, can influence postoperative respiratory function after lobectomy for lung cancer.

## 2. Methods

From June 1997 to March 1998, 78 patients underwent a lobectomy for early-stage NSCLC at the Department of Thoracic Surgery of the Scientific Institute H San Raffaele, University of Milan, Italy. Thirty-five patients entered the study. The remaining patients were excluded from the study because of preoperative atelectasis of a pulmonary segment or a lobe, adjuvant chemo- or radiotherapy, poor performance status and bullae larger than 3 cm. Preoperative oncological assessment included total-body CT scan, bone scan and bronchoscopy. Pulmonary function tests and pletismography were performed in all 35 patients preoperatively and after a mean period of 4.7 (2–7) months after surgery with V6200 Autobox equipment (Sensormedics, Yorba Linda, CA). The measurements were recorded according to the American Thoracic Society (ATS) criteria [8]. The following parameters were assessed: flow/volume loop (FEV1, forced vital capacity (FVC), FEV1/FVC, FEF 25–75%), static lung volumes (total lung capacity, TLC; functional residual capacity, FRC; residual volume, RV). Preoperative radiological documentation was available for retrospective evaluation in 26 out of the 35 patients. Radiological grading of emphysema was thus retrospectively assessed in these patients by a radiologist (A.V.) who was blinded to the results of the pulmonary function tests. The radiological evaluation was performed on a lateral chest X-ray and on CT scan obtained at full inspiration using the grading system described by Slone and Gierada [9]. The chest CT examination was included in the oncological evaluation and was obtained with a spiral CT scanner (Toshiba X-press, Toshiba Medical Systems, Tokyo, Japan). The thoracic region was scanned with 7 mm thick slices, a table movement of 10 mm/s (Pitch 1.3) and contiguous reconstructions (7 mm). Hyperinflation and flattening of the diaphragm on the lateral chest X-ray was graded as: 0-normal, 1-mild, 2-moderate, 3-marked, 4-severe. The grading of emphysema was evaluated on CT scan at the mid-portion of the lobe to be resected and at three levels: the first at the top of the aortic arch, the second 2 cm below the carina and the third 2 cm above the diaphragm. The score was rated as follows: grade 0, normal lung; grade 1 (mild), more lung than airspace (<25%); grade 2 (moderate), even distribution of airspace and lung (25–50%); grade 3 (marked), more airspace than normal lung (>50%); grade 4 (severe), no normal lung. The scores of the radiological evaluation were used to make up the following indexes: A – chest X-ray; B – (single-level CT) CT in the lobe to be resected; C – (3 level CT score) sum of the CT scores evaluated at three levels; D – (comprehensive radiology score) sum of A, B and C.

## 3. Statistical analysis

Data are expressed as mean values ± standard deviation. Correlation between variables was assessed using Spearman rank correlation coefficients. Comparison of radiological scores between groups of patients were made using the non-parametric Wilcoxon rank sum test. A *P*-value lower than 0.05 was used as a threshold for statistical significance.

## 4. Results

Two patients were female and 33 male. The mean age was 64 years (49–79). Twenty-five patients underwent an upper lobectomy, seven a lower lobectomy and three a middle lobectomy. All the operations were performed through a standard muscle-sparing lateral thoracotomy. Mean tumor size was 3.3 cm (1–6). Postoperative pathological staging was T1N0 in 12 patients, T2N0 in 12, T1N1 in three, T2N1 in three, T3N0 in one, T2N2 in three and T3N1 in one. A decrease in static lung volumes was observed after surgery: TLC decreased from 6.58 ± 0.92 to 5.46 ± 0.77 l; FRC from 3.70 ± 0.88 to 2.96 ± 0.73 l and RV from 2.93 ± 0.78 to 2.20 ± 0.53 l. However, in a subgroup of 10 patients (Group 1), dynamic volumes after surgery were unchanged or slightly increased. In these patients, who had a higher degree of airway obstruction, FVC increased from 3.23 ± 0.65 to 3.30 ± 0.68 l (80.33 ± 8.29 to 83.20 ± 13.11% of predicted) while FEV1 increased from 2.14 ± 0.51 to 2.25 ± 0.54 l (69 ± 12.42 to 72.70 ± 13.72% of predicted); airway resistances (sRaw) decreased from 15.58 ± 5.18 to 11.42 ± 5.25 cm $H_2O$/s. In the remaining 25 patients (Group 2), FVC and FEV1 decreased respectively from 3.52 ± 0.61 to 2.94 ± 0.55 l (99 ± 13.45 to 82.76 ± 14.61% of pre-

dicted) and from 2.47 ± 0.48 to 2.03 ± 0.43 l (87 ± 12.7 to 72.08 ± 13.10% of predicted); sRaw varied from 14.39 ± 8.85 to 13.38 ± 6.50 cm $H_2O$/s. RV was higher in Group 1, and changed from 3.27 ± 0.87 to 2.23 ± 0.69 l, as compared with a decrease from 2.78 ± 0.70 to 2.19 ± 0.47 l after surgery in Group 2 (Table 1). Correlation analysis between changes in Δ(FEV1)% and preoperative FEV1 and FVC% values reached statistical significance ($r = -0.49$, $P = 0.002$ and $r = -0.5$, $P = 0.001$, respectively). Radiological scores assessed by chest X-ray and CT scan were higher in Group 1 than in Group 2 (Table 2), although these data did not reach statistical significance. In all the patients with radiological evidence of emphysema, a heterogeneous distribution was observed. Correlation analysis also reached statistical significance between changes in Δ(FEV1)% and radiological scores for 3-level CT ($r = 0.39$, $P = 0.04$) and the sum of chest X-ray, single and 3-level CT scores ($r = 0.49$, $P = 0.01$) (Fig. 1). The last score also significantly correlated with preoperative FEV1% ($r = -0.39$, $P = 0.04$). This was consistent with a higher degree of emphysema at chest X-ray and CT scan in patients with higher airway obstruction.

## 5. Discussion

Despite the recent advances in radio- and chemotherapy regimens, surgery remains the treatment of choice in early-stage NSCLC. Since most lung cancer patients are smokers, COPD frequently coexists and causes a limitation of pulmonary function that may contraindicate surgery or require the use of limited and therefore less radical resections [10]. A pulmonary resection usually involves a significant reduction of pulmonary function. In the early postoperative period, this is due to the surgical trauma to the lung and to the chest wall, to the increase of bronchial secretions and to postoperative pain, which may significantly impair postoperative respiratory function. Despite advances in anesthesia, surgical techniques and postoperative treatment with the intensive use of chest physiotherapy, minitracheostomy and epidural analgesia, further reduction in pulmonary function exposes patients with an already limited respiratory function to an increased risk of postoperative morbidity and mortality [11,12]. Three to six months after surgery, there is a partial recovery of respiratory function although a reduction in FEV1 of 9–17% and 31–36% of the preoperative values is still observed after lobectomy and pneumonectomy, respectively [13–15]. This may impair the quality of life or even increase morbidity in patients who had a limited pulmonary function preoperatively [16]. The prediction of long-term postoperative function is therefore of great importance when assessing operability.

Several functional factors have been studied as predictors of outcome after pulmonary resection. Preoperative evaluation usually includes tests such as spirometry, blood gas analysis, DLCO and prediction of postoperative pulmonary function, by means of split lung function perfusion scanning and by calculating the contribution of the resected segments to total lung function [17,18]. Specific tests are also used to assess exercise capacity and to identify parameters that seem to be associated with postoperative outcome, such as maximum oxygen consumption and blood oxygen desaturation [18–20].

Several functional criteria have been associated to operative risk. Gaensler [21] in 1955 identified a correlation between spirometric values and outcome, and observed that a maximal voluntary ventilation (MVV) lower than 50% of predicted was associated with an unfavorable outcome. Olsen suggested that a ppoFEV1 under 800 ml was to be considered a contraindication to surgical resection since it could theoretically be associated with carbon dioxide retention [22]. Ferguson [23] observed that predicted postoperative DLCO% was an important predictor of postoperative morbidity. Markos et al [18] noted that predicted postoperative FEV1 (ppoFEV1), DLCO, predicted postoperative DLCO (ppoDLCO), and oxygen desaturation during exercise were predictive of postoperative pulmonary complications. They recommended operability if ppoFEV1 was equal or higher than 40% of predicted and inoperability if ppoFEV1 was lower than 30% [18]. Bechard and Wet-

Table 1

Summary of preoperative and postoperative pulmonary function tests (PFTs) data

| | Group | Preoperation | Postoperation | Δ% |
|---|---|---|---|---|
| FVC (l) | 1 | 3.23 ± 0.65 | 3.30 ± 0.68 | 2.16 |
| | 2 | 3.52 ± 0.61 | 2.94 ± 0.55 | –16.4 |
| FEV1 (l) | 1 | 2.14 ± 0.51 | 2.25 ± 0.54 | 5.14 |
| | 2 | 2.47 ± 0.48 | 2.03 ± 0.43 | –17.8 |
| TLC (l) | 1 | 6.75 ± 0.85 | 5.56 ± 1.16 | –17.6 |
| | 2 | 6.50 ± 0.95 | 5.41 ± 0.7 | –16.8 |
| RV (l) | 1 | 3.27 ± 0.87 | 2.23 ± 0.69 | –31.8 |
| | 2 | 2.78 ± 0.70 | 2.19 ± 0.47 | –21.2 |
| FRC (l) | 1 | 4.04 ± 1.24 | 3.05 ± 0.84 | –24.5 |
| | 2 | 3.54 ± 0.63 | 2.92 ± 0.69 | –17.5 |
| Raw ($cmH_2O$/s) | 1 | 15.58 ± 5.18 | 11.42 ± 5.25 | –28.9 |
| | 2 | 14.39 ± 8.85 | 13.38 ± 6.50 | –7.1 |

FVC, forced vital capacity; FEV1, forced expiratory volume in 1 s; TLC, total lung capacity; RV, residual volume; FRC, functional residual capacity; sRaw, specific airway resistance; Δ%, % change preoperative to post-

Table 2

Radiological visual assessment of emphysema

| Score | Group 1 | Group 2 (*P*-value in parenthesis) |
|---|---|---|
| A | 1.63 ± 1.41 | 0.78 ± 1.07 (0.13) |
| B | 1.13 ± 1.13 | 0.61 ± 0.78 (0.26) |
| C | 3.00 ± 2.45 | 1.67 ± 1.94 (0.18) |
| D | 5.75 ± 4.27 | 3.06 ± 3.32 (0.08) |

Group 1, patients with stationary or improved postoperative function; Group 2, patients with postoperative functional decrease. A, chest X-ray; B, CT (resected lobe); C, 3 level CT; D, sum of A, B and C.

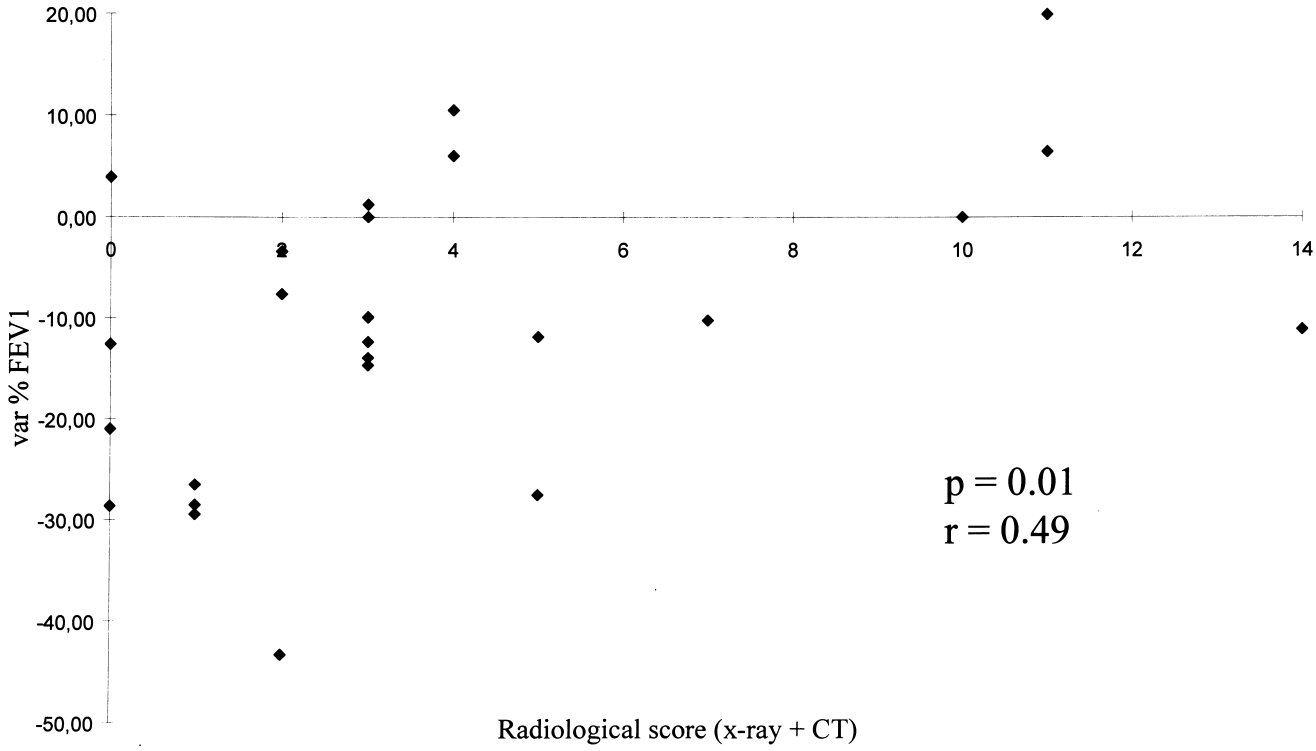


Fig. 1. Correlation between radiological emphysema score (X-ray + CT) and % change in FEV1.

stein [19] observed that patients with a maximal oxygen consumption (MV02) lower than 10ml/kg per min had a prohibitive surgical risk, while patients with an MV02 greater than 20 ml/kg per min had a low risk of postoperative complications after pulmonary resection. Pierce et al. [3] developed a predictive index of postoperative morbidity by combining ppoFEV1% and ppoDLCO%. Melendez and Barrera [24] modified this index by including (ppo DLCO%)$^2$ and A-a P02 and identifying a relationship between these data and pulmonary complications, mortality and hospital stay.

However, despite the sophisticated preoperative evaluation techniques currently available, Olsen [25] has recently stressed the difficulty of establishing standard criteria for the operability of lung cancer patients. This may be particularly true for patients with emphysema. The development of lung volume reduction surgery (LVRS) has in fact raised new interest in the functional evaluation of emphysema patients undergoing thoracic surgery. The possibility of improving lung function in patients with advanced diffuse emphysema has been demonstrated after LVRS [4]. The mechanisms of improvement seem to be related to a restoration of the elastic recoil of pulmonary parenchyma, which leads to a reduction in airway resistance along with an improvement of diaphragmatic and respiratory mechanics [26]. The functional improvement that is obtained with the resection of emphysematous parenchyma may also allow the resection of viable parenchyma, as reported by DeMeester et al. [5] in the treatment of associated diseases.

Patients with a lesser degree of emphysema represent the great majority of patients that undergo surgery for NSCLC. The influence of the resection of lung parenchyma in this group of patients still has to be thoroughly evaluated. In particular, the correlation between emphysema and reduction of postoperative respiratory function could be important in the selection of surgical candidates. Pierce et al. [3] have in fact observed a relationship between the change in FEV1 after surgery and the baseline predicted FEV1%, therefore indicating that the functional loss is proportionally less severe in patients with lower pulmonary function. Accordingly, Larsen et al. [6] observed that patients with a lower preoperative FVC had the smallest postoperative deterioration in pulmonary function. In their series, patients with a preoperative FEV1 of less than 74% (median) had a lower postoperative reduction in FVC as compared with patients with a FEV1 higher than 74%. Four patients with a preoperative FEV1 of less than 50% actually improved their postoperative FVC after the operation [6]. Recently, Korst et al. [7] observed functional improvement after lobectomy for NSCLC, in patients with a FEV1 of less than 60% of predicted and a FEV1/FVC ratio of less than 0.6. They also developed a scoring system combining these two parameters to identify preoperatively patients that could have a limited reduction or even improvement of pulmonary function [7].

The severity of emphysema can be evaluated not only by means of pulmonary function tests, but also radiologically, and a significant correlation has been demonstrated between these two tests [27]. The radiological evaluation of emphy-

sema may therefore also be an important factor in the preoperative evaluation of candidates for surgical resection. A significant correlation between functional improvement and radiologic assessment has been demonstrated by Slone and Gierada [9] in patients submitted to LVRS, and has been confirmed by other authors [28,29].

In this study the degree of emphysema was assessed by both pulmonary function tests and radiological evaluation. A significant correlation was observed between the modification of FEV1 measured preoperatively and after surgery, preoperative respiratory function and preoperative radiological grading of emphysema. Patients with a lower preoperative FEV1% had a smaller reduction in postoperative function, and some cases actually improved their respiratory function. The radiological index that best correlated with the improvement in postoperative function combined the evaluation of hyperinflation and diaphragmatic flattening, as evaluated by lateral chest X-ray, and CT evaluation both at the level of the resected lobe and at three levels. This index had a higher correlation with the modification in FEV1% than the severity of emphysema of the resected lobe, therefore suggesting that the global degree of emphysema together with the severity of emphysema of the resected parenchyma may influence postoperative results. Patients in Group 1, who had an unchanged or improved function also had higher RV and TLC and had a significant reduction in airway resistance as compared with patients in Group 2, who had a worsened function after surgery. However, we were not able to identify a scoring system that could combine radiological evaluation and preoperative pulmonary function tests to identify preoperatively individual patients who would improve their pulmonary function after surgery. Further studies on a larger series of patients are needed to achieve this aim.

In conclusion, patients with a more pronounced emphysematous component of airway obstruction, as assessed by pulmonary function tests and radiological evaluation, may have unchanged or even increased pulmonary function after lobectomy. The identification of preoperative parameters capable of identifying this group of patients would enable the indications for the treatment of lung cancer to be extended in patients with pulmonary emphysema.

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## Appendix A. Conference discussion

***Dr J. Hasse*** (*Freiburg, Germany*): What is the influence on the perioperative treatment, and the eventual stopping of smoking? Both could interfere with your assumption that the resection itself was beneficial.

***Dr Carretta***: We didn't evaluate the preoperative period in this study, but, what we may say is that we have learned with lung volume reduction surgery that it is possible to operate on patients with limited respiratory function with acceptable morbidity. Also, that we could possibly apply what we have learned with lung volume reduction surgery to other patients, to other patients with a lesser degree of emphysema.

***Dr W. Klepetko*** (*Vienna, Austria*): I think you very nicely pointed out that there is a huge potential with emphysema surgery, even for patients with bronchial carcinoma. However, I cannot follow your conclusions, because I think that what you suggest is very dangerous.

Basically, if I correctly understood, you suggested that, the more sick patients are, the more advanced emphysema they have, the better will be the functional outcome after the lobectomy. I think emphysema is a very different entity. You have homogenous forms and very heterogeneous forms, and you should divide your patients in those groups. In addition, patients, who have the tumor within the most destroyed area of lung will benefit of course. But the other ones, who have not the tumor in the area of destroyed parenchyma, they can experience a lot of harm by that operation. So I wonder whether you have made any attempts on doing an anatomical landmarking of the situation of the tumors, where they were situated, and what was the grouping of the patients in terms of homogeneity and heterogeneity?

***Dr Carretta***: I certainly agree with you in saying that, of course, these are preliminary results that only evaluate the pulmonary function after recovery from the perioperative period, about 4 months after surgery. We didn't assess the exact perioperative complications in this group of patients.

What is interesting to note, even if this is a limited group of patients, is that we had a good correlation between improvement of respiratory function and radiological assessment with CT scan performed at the upper, middle and lower pulmonary fields. The global degree of emphysema, apart from the emphysema in the lobe to be resected, could also influence these patients' functional improvement.

***Dr Klepetko***: Could you precisely tell me how many of your patients had the lesions within areas of resection, how many of them were in other areas where you normally would not resect for an ordinary emphysema surgery?

***Dr Hasse***: I think we should discuss that later. We have one very quick question.

***Dr S. Ambazidis*** (*New South Wales, Australia*): Have you considered doing perfusion ventilation scans just as a way of defining the area you're going to resect?

***Dr Carretta***: No, we didn't perform perfusion-ventilation scans in these patients. We have started a new study to better assess the emphysema of the area to be resected by combining ventilation perfusion scan, anatomical evaluation of emphysema and a stress test. However, we didn't perform this systematically in this group of patients, only in selected ones.