485. Staging of lung cancer

E5437
Relevance of clinical TNM-staging in small cell lung cancer (SCLC) for survival – A retrospective case study in 633 patients

Background: SCLC staging is based on a dichotomous system first issued by the VASLG differentiating between limited and extensive disease. The application of the TNM-staging system proposed by UICC is feasible in SCLC, but its value in clinical staging is under discussion.

Aim and objectives: This retrospective case study assessed the benefit of the TNM-staging system (UICC, 6th edition) for clinical staging SCLC patients with regard to survival time.

Methods: Using our monocentric tumour database, all patients diagnosed with SCLC between 1.1.2002 and 31.12.2008 were identified. Kaplan-Meier-analyses were performed on all cases with a complete TNM staging (UICC, 6th edition) as well as documented dates of death or last follow up.

Results: A total of 633 SCLC cases were identified: 397 men (62.7%) and 236 women (37.3%). Mean age was 65.1 yrs. (range 32.0-89.4 yrs., median 65.3 yrs.). Survival times displayed a minimum of 0 and maximum of 2568 days (mean 483.6 d; median 349 d).

Conclusions: In our cohort TNM-staging in SCLC seemed feasible only in ad-/limited stage. From stage IV onward TNM staging resulted in poor prognosis, whereas survival for stage IVa was comparable to that of stage III patients. Our results confirm that TNM staging in SCLC patients may be useful for clinical staging but not for survival analysis.

Figure 1. Staging values of reMS according to the intensity of the first MS.

E5438
The relation between clinical tumor stage and metastasis according to sixth TNM staging and new revised TNM staging in non-small lung cancer patients
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The TNM staging system was used for lung cancer is the sixth staging system that was arranged in 1997. The new proposed TNM revision model (seventh staging system) is prepared according to survival of patients that lead to changes in tumor, node, metastasis descriptors. In our study we aimed to investigate the relation between clinical T stage (CT) and metastasis (M) in 6th and new revised 7th staging system 136 non-small cell lung cancer patients hospitalized between January 2007- June 2009 were included in the study. Age, sex, smoking history, radiological diagnostic procedures, bronchoscopic findings, diagnostic and metastasis screening methods were recorded. Patients were clinically classified according to 6th and 7th staging system. Forty one of the patients was found squamous cell lung cancer, 29 of them was adenocarcinoma and in 66 of them histopathological subtype couldn’t be diagnosed. Among 136 patients 23 them moved to another stage and 113 of them remained in the same stage. The most remarkable changes were observed between stage 3A and 3B and no change was observed in stage 1. Down staging was observed in 16 patients and in 1 of the treatment protocol was revised. In 6th staging system the relation between CT stage and M was poorly positive (r: 0.170; p=0.048). In the new revised 7th staging system the relation between CT stage and M was found moderately positive (r: 0.190; p=0.027). Both staging systems were compared and consistency was found 96.9%. As a conclusion this revised staging model will give way to considerable changes especially in treatment protocol of stage 3 patients.

E5439
A thorough mediastinoscopy does not preclude an accurate re mediastinoscopy
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Background: Some authors believe that an extensive initial mediastinoscopy (MS) will result in more adhesions and fibrosis, causing mediastinoscopy (reMS) to be more difficult and inaccurate. The objective of this study is to evaluate the technical feasibility and the accuracy of reMS in restaging non-small cell lung cancer (NSCLC) after induction therapy according to the intensity of the first MS.

Methods: From July 1992 to February 2009, 80 patients (75 men; mean age: 58.2 years), underwent 84 reMS (4 patients required a repeat reMS) for restaging after induction therapy. Patients with positive reMS underwent definitive chemo or chemoradiotherapy. Patients in whom reMS was negative underwent thoracotomy for lung resection and systematic nodal dissection, which was the gold standard to compare the negative results of reMS. Pathologic findings were reviewed and staging values were calculated using the standard formulas.

Results: The staging values according to the intensity of the first MS are described in figure 1. There were no statistically significant differences between both groups.

Conclusions: reMS is a useful procedure to select patients for lung resection with high accuracy independently of the intensity of the first MS.

E5440
Mediastinal staging in lung cancer: A rational approach
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Introduction: Nowadays, several techniques are available and may be adopted to approach mediastinal staging. Some of these, i.e. PET and ultrasound-guided needle aspiration, provide very sensitive and specific results. TBNA alone, on the other hand, although highly specific, has not proved to be sufficiently sensitive and may provide false negative results.

Aims and objectives: The aim of this analysis is to suggest a reasoned model, based on evidence, for N factor mediastinal staging in non small cell lung cancer.

Methods: Bayesian analysis of the probability of nodal metastasis after a certain examination, taking into account, “pre-test” probabilities of each examination are taken into account, “post-test probabilities” after every diagnostic step are then calculated and surgery
is arbitrarily considered a possible choice whenever probability of mediastinal metastasis falls below 10%.

Conclusions: Application of the proposed “algorithmic staging” may provide a rational opportunity to tackle the complexity of mediastinal staging of lung cancer. The proposed protocol, on the basis of data provided by literature and of plain statistical concepts, may lead to a better use of available resources in terms of cost/benefit.

**ES441 Utility of PET/CT in staging of lung cancer: Results from 245 patients**

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Background: Recently published international guidelines recommend integrated positron emission tomography and diagnostic CT (PET/CT) for staging of lung cancer in patients considered for curative treatments. We wanted to assess the role of PET/CT in NSCLC-staging prospectively and report our experience with the first 245 patients.

Patients and methods: Between 2007 and 2010 245 patients (132 men) aged 30-85 (mean 65) years were consecutively included. 185 (75%) of the patients were operated. No patient was excluded from surgery on the basis of PET/CT alone. All patients with PET positive and/or enlarged lymph nodes underwent EUS/EBUS-FNAC and if negative, thoracotomy. All pathologic extrathoracic FDG-uptake was confirmed as malignant or benign. Clinical and postoperative lymph node stations (v international TNM-classification) were compared.

Results: Distant metastases were detected in 25 of 245 patients (10%). 9 had stage I or II disease before PET/CT. N2 or N3 disease was suspected by PET/CT in 74 patients (30%), 31 proved to be false positive. 43 patients with positive PET-scan underwent further investigation (EUS/EBUS/thoracotomy) which verified the N-stage. In 13 patients further investigation/thoracotomy showed that N PET was false negative. This provides for N2/3-disease as detected by PET/CT sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of 77%, 84%, 58%, 92% and 82%, respectively.

Conclusions: In lung cancer PET/CT shows high specificity but lower sensitivity in mediastinal nodal staging. The high negative predictive value of PET/CT allows avoidance of invasive staging. This method is of value in the detection of occult distant metastases.

**ES442 Clinical and pathologic staging – PET/CT impact**

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Introduction: Integrated PET/CT has become a promising image technique used in lung cancer staging. The aim of this study was to evaluate the impact of including PET/CT in the clinical assessment of patients with non-small cell lung cancer (NSCLC) submitted to surgical treatments.

Objectives: To evaluate the impact of including PET/CT in the clinical assessment of patients with non-small cell lung cancer (NSCLC) submitted to surgical treatments.

Material and methods: Retrospective study of patients with NSCLC, who underwent potentially curative thoracic surgery, from January 1999 to July 2009. Results: We evaluated 150 patients, 78% male, with a median age of 65 years old. PET/CT was performed in 41%. Pulmonary resection included lobectomy in 82% of the patients, pneumonectomy in 13% and bilobectomy in 5%, together with mediastinal lymphadenectomy. In 51% of the cases, clinical staging matched to the pathological, in 40% occurred upstaging and in 9% down staging. The main changes were T2N0c to T2N1p (20%) and T1N0c to T2N0p (18%). A global agreement of 51% (κappao.36) was obtained. There was a statistical significant difference between clinical and pathological staging in the group of patients who underwent PET/CT (p=0.003), when compared to the group who did not do it. Inclusion of PET/CT was associated to a decrease in 37% of the upstaging, an increase of 12% in down staging and an increase in 25% of the cases in which the clinical and pathological staging were coincident. Globally, these results reflected an improvement of the agreement between clinical and pathological staging in the group of patients who underwent the PET/CT (67%, κappao.574 versus 40%, κappao.229).

Conclusion: Inclusion of PET/CT in the pre-surgical assessment of NSCLC improved clinical staging, allowing a higher accuracy and achieving a good agreement with pathological staging.
Conclusion: As a result, the success of TTNB is associated with SUVmax. Definite diagnosis is possible by TTNB even if there was no pathologic FDG uptake in lesion on thorax CT.

ES445 Synchronous primary malignancies identified during staging 18F-FDG PET scan in lung cancer patients
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Introduction and aims: 18F-FDG PET scan is used to screen patients with lung malignancy to identify potential metastasis that might have been missed by the conventional staging CT protocol. Incidental synchronous other primary malignancies are often found in patients undergoing this procedure. Our aim was to indentify the proportion of patients with other primary malignancies incidentally found during 18F-FDG PET scanning in our cohort of lung cancer patients.

Results: 86 patients have undergone scanning 18F-FDG PET as a part of lung cancer staging during the period of 2007-2009. Mean age of 69. 64% males and 35% females. There were additional findings in 28 occasions with further investigations needed in 22 patients. 7 patients (8%) had synchronous other primary malignancies (Table 1). Non-malignant uptakes were also noted mainly in the bowel and were related to inflammatory processes such as colitis, diverticulitis and colonic polyps.

Table 1. Synchronous malignancies detected
<table>
<thead>
<tr>
<th>Cancer types</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel Cancer</td>
<td>4</td>
</tr>
<tr>
<td>Bladder cancer</td>
<td>1</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>1</td>
</tr>
<tr>
<td>Carcinoma of vulva</td>
<td>1</td>
</tr>
</tbody>
</table>

Conclusions: FDG PET may detect other primary malignancies during lung cancer staging. In our cohort of population the rate of incidental secondary primary tumor is higher than previously published detection rates. Histological confirmation may help to differentiate secondaries form synchronous primary tumors that may often mimic metastasis, as this will undoubtedly alter treatment strategies.


ES446 The importance of positron emission tomography/computed tomography (PET-CT) to identify distant metastasis in non-small cell lung cancer (NSCLC)

Aim: Investigation of the value of PET-CT to detect distant metastasis in NSCLC.

Methods: The files of patients whose thoracic CT Tupper abdominal CT, whole body bone scintigraphy (WBBS), cranial MR and PET-CT were taken, have been reviewed to stage the cases.

Results: It was determined by using PET-CT that 45 of 128 cases (35.2%) revealed the presence of distant metastasis where 38 cases (64.8%) didn’t (When PET-CT and WBBS were compared, it was found that in 104 cases (81.2%) both methods were negative, in 19 cases (14.8%) both methods were positive and in 5 cases (3.9%) PET-CT was negative while WBBS was positive. In the evaluation of bone metastasis, the sensitivity, specificity, positive predictive value and negative predictive value were found respectively 100%, 97.2%, 97.5%, 100% for WBBS and 90.3%, 100%, 98.2% for PET-CT. When 12 cases, that were diagnosed with surrealn metastasis by using PET-CT, were reviewed with MR, it was accepted that in 4 of these cases (33.3%) there was no surrealn metastasis. Biopsy was done to the 5 cases, in which metastasis to other organs was detected by using PET-CT, and all resulted negative.

Conclusion: No significant difference was found in evaluating the bone metastasis of NSCLC between using PET-CT or using WBBS, although the number of cases was low. It was recommended that the cases in which only surrealn metastasis takes place should be verified via MR and/or biopsy, and for the other organ metastasis, PET-CT is not reliable and evaluation should be done absolutely by biopsy.

ES447 FDG-PET is superior to conventional CT in predicting histologic responses after induction therapy for locally advanced NSCLC

Background: A lot of studies have demonstrated that positron emission tomography with the glucose analog fluoro-deoxyglucose (FDG-PET) is useful for evaluating lung cancer staging. However the efficacy of PET for re-staging after induction treatment for locally advanced non-small cell carcinoma (NSCLC) is still controversial.

Objectives: The aim of this study was to compare the efficacy of PET to conventional CT in predicting histologic responses after induction treatment.

Methods: Six patients who underwent induction treatment followed by resection for locally advanced NSCLC were retrospectively studied. Changes in values of SUV in the primary lesions on PET and the reduction rates of tumor size on CT were evaluated, and the correlation with the histologic responses was studied. Histologic responses were classified according to Japanese criteria in Pathological Record of Lung Cancer: Ef1a; more than 2/3 of residual cells are viable, Ef1b; viable cells are 1/3 or more, but not exceeding 2/3 of residual cells, Ef2; less than 1/3 of cell are viable, and Ef3; no viable cells.

Results: After induction treatments, four patients showed partial response and two patients had stable disease based on RECIST criteria. Histologic responses were Ef1a in 3 patients, Ib in 1, 2 in 1, and 3 in 1. Although three cases showed more than 40% reduction in size on CT scan, histologic responses of these were 1a, 1b, and 2, respectively. On the other hand, three cases with more than 76% decrease in SUV represented relatively good histologic responses (1b, 2, and 3).

Conclusion: The changes of SUV is a more useful predictor of histologic responses compared with the size evaluation on CT scan.

ES448 Radiological features of primary lung lung cancer subtypes at Tygerberg Academic Hospital, Cape Town, South Africa; a one year retrospective review
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Background: There are no published studies on the radiological features of lung cancer in Africa.

Objective: To describe the radiological features of the histological subtypes of lung cancer in an African population at the time of diagnosis.

Methods: Study Site: Tygerberg Academic Hospital, Cape Town, South Africa Single center, retrospective data review study. All available CT scans of primary lung cancer patients with clearly defined histological subtypes presenting between 01 January, 2010 and 31 December, 2010 were reviewed. Fourteen radiological parameters were assessed.

Results: Total patients and CT scans reviewed-204. Histological subtypes: adenocarcinoma (AC) (53.9%), squamous cell (SqC)-25.9%, small cell (SCC)-14.2%, large cell (LC)-2.4%, broncoalveolar lung cancer (BAC)-1.5%, others-2%. Medium size of tumour (mm): AC-53.4, SqC-80.2, SCC-80.8, LC-74.2 and BAC-50.0. Overall tumour location: central-43.6%, periphery-46.6%, indeterminate-9.8%, medistral-11.3%, right lung-53.4%, left lung-15.3%. 16% of the patients had tuberculous-related fibrosis, but only 11 patients (5.4%) had coexisting tumour and fibrosis at the same site. There was no difference in the proportion of coexisting fibrosis between AC (n=8) and SqC. Only one patient with SCC had co-existing fibrosis at the tumour site. Only 6.4% had potentially operable cancer (Stages IA to IB).

Conclusion: In this African population, patients with lung cancer present late, have radiologically larger tumours with a proportion coexisting with tuberculosis-related fibrosis, and only a much smaller proportion are potentially operable, compared to patients in Europe and North America.

ES449 Tumour metabolic-flow difference as a potential predictor of survival in non-small cell lung cancer (NSCLC)
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Aim: The metabolic-flow difference is a potential marker of tumour aggression. This study assesses the relationship between the metabolic-flow difference and survival in patients with NSCLC.

Methods: Over 42 months 41-patients (mean age 68.2±7.8 years 21-male and 11-female) undergoing 18F-FDG-PET for potentially operable NSCLC were recruited for dynamic contrast-enhanced CT using an integrated 64-slice PET/CT. Analysis of the temporal changes in tumour attenuation following injection of intravenous contrast material yielded tumour permeability and the Standardized Perfusion Value (SPV). The uptake of 18F-FDG was quantified using the Standard Uptake Value (SUV) to assess tumour metabolism. The metabolic flow difference was expressed as SUV-SPV associations between 9-month survival with metabolic and vascular parameters were investigated using unpaired t-tests.

Findings: 20/41 patients died within 9-months. The mean tumour SUVmax was 14.7±4.0 in patients with a 9-month mortality and those who survived 9 months was 10.5±4.4 (p=0.0127). The mean tumour permeability was 22.9±13.9 in patients with a 9-month mortality and those who survived 9 months was 26.5±20.4 (p=0.591). The mean SUV was 5.8±3.2 in patients with 9-month mortality and 9958

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E5450
Quantitative tumor perfusion assessment with 64-slice multisegment-detector-row CT (MDCT): Evaluation before and after antiangiogenic chemotherapy
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Purpose: To evaluate whole lung tumor perfusion before and after antiangiogenic chemotherapy.

Methods and materials: Nine consecutive patients were prospectively enrolled in this study aimed at evaluating the therapeutic response to antiangiogenic chemotherapy, including patients with lung adenocarcinoma (n=8) and malignant mesothelioma (n=1). Quantitative tumor perfusion was sequentially evaluated with 64-slice multisegment-detector-row CT (MDCT) before (T0: n=9) and after chemotherapy (T1: n=9; T2: n=7; T3: n=5; T4: n=2) with an interval of 3 weeks between the therapeutic sessions. The CT parameters evaluated included: (a) the tumor height and diameter; (b) the tumor blood volume (BV) and capillary permeability (CP), calculated using the Fickian analysis.

Results: Whole tumor coverage (maximum mean height: 6.06 cm) was possible in all patients with generation of colored parametric maps of CP and relative BV as well as quantitative data. Comparing T0 and T1: (a) the mean (±SD) tumor diameters were significantly smaller at T1 (T1: 4.4±2.1 cm vs T0: 5.6±2.8 cm; p<0.0001); (b) the tumor BV showed a trend towards reduction (BV at T1: 6.6 vs T0: 9.19 mL/100 mL; p=0.3808) while the CP was significantly reduced (CP at T1: 7.32 vs T0: 10.57 mL/100 mL/mm; p=0.0038). No statistically significant differences in the CT functional parameters were found between T1 and T4.

Conclusion: Whole tumor perfusion analysis at T0 shows restoration of tumor vessel permeability and reduction of tumor blood volume under antiangiogenic drugs, pieces of information previously not accessible in the invivo monitoring of lung tumors.

E5451
EGFR mutations analysis in CT-guided transthoracic fine-needle aspiration samples
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Evaluation of localized pulmonary parenchymal abnormalities by CT-guided transthoracic fine-needle aspiration (FNA) is accurate, rapid and cost-effective. In lung neoplasms, additionally to histological diagnosis it is important the EGFR mutations status. We report the first systematic EGFR mutations analysis in primary pulmonary tumors samples obtained by transthoracic FNA and respective results.

Methodology: Patients with peripheral parenchymal lung lesion suspected of malignancy were subjected to CT-guided transthoracic FNA. The resulting sample was prepared on slides, hematoxylin-eosin stained and subjected to extemporaneous analysis. After confirmation of lung cancer, cellular debris contained in the needle was recovered by washing with saline solution and stored in buffer at -20°C till transportation to molecular biology laboratory. Here, DNA was extracted and exons 18 to 21 of EGFR gene subjected to PCR and sequencing analysis.

Results: Of 18 patients undergoing FNA since 01/01/2010 to 28/02/2010, 15 were diagnosed with lung cancer: 9 adenocarcinoma, 4 squamous cell carcinoma, 2 poorly-differentiated NSCLC. In all 15 patients, the material obtained through needle washing was enough to perform PCR amplification and sequencing of the EGFR gene. We found EGFR mutation in one case (exon 19, E746-A750del). Mutation rate was 6.6% and mean time between FNA and sequencing was 5 days.

Conclusions: Analysis of EGFR mutations in FNA material is achievable, quick and cost-effective, enabling a better characterization of tumor, which may be translated into a different therapeutic approach. The low rate of mutation can be justified by the small sample size.

E5452
EGFR and KRAS mutational profiling in NSCLC cells obtained through fine needle aspiration cytology (FNAC)
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Correlation between mutations in cancer alleles and drug response is a crucial point to identify drugs that match the genetic profile of individual tumors. In NSCLC genetic lesions affecting EGFR pathway act as predictive markers of response to EGFR inhibitors. Inappropriate EGFR phosphorylation is mainly consequent to somatic mutations in receptor tyrosine kinase (TK) domain. Incidence of EGFR mutations is 71% in erlotinib/gefitinib responders while it is 7% in unsensitive cases; mutations are more frequent in adenocarcinomas (ADK) aroused in not smokers and females. Downstream KRAS mutations are highly specific negative predictors of response to single agent EGFR inhibitors. We evaluated in a cohort of NSCLC patients the EGFR and KRAS mutations prevalence by analyzing tumor cells directly obtained through CT-guided trangasthoracic biopsy, which represents a proper diagnostic tool for peripheral lesions, such as ADKs – actually accounting for 40% of all NSCLC diagnosis. This procedure allows acquisition of samples enriched by cancer cells which selectively display CT contrast enhancement. In an ongoing study we have till now evaluated 84 cases, 56 males and 28 females. 65% of them are smokers. We found EGFR somatic mutations in 6 (7.14%) patients (F:M=4:2) affected by ADK. KRAS mutations occurred in 5 (5.95%) patients (F:M=3:2), affected by ADK and 2 by squamous cell cancer. All EGFR mutated patients were not smokers. EGFR and KRAS mutations are mutually exclusive. Results have been validated by performing analysis on corresponding paraffin-embedded samples and obtaining the same mutational results. Response of patients treated with erlotinib will be also presented.

E5453
Analysis of prognostic factors in patients with stage IIB, IV non-small cell lung cancer
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Objective: The aim of present study is to determine the prognostic factors of advanced stage NSCLC patients.

Material and methods: A total of 400 patients who were diagnosed as stage IIB,IV non-small cell lung (NSCLC) cancer between January 1995 and July 2008 were analysed retrospectively. Effects of demographic, clinical and laboratory data before treatment on survival was investigated.

Results: Of the patients, 308 (77%) were male and 92 (23%) were female with mean age of 58.0±9.3 years. Mean life span was found to be 13.8±12.6 months with Kaplan Meier analysis. Although the facts that performance score to be zero at all (ECOG), being younger than 65 years, not having weight loss, good response to the treatment were found to be important factors related to life span (p=0.0011, 0.0017, 0.031, 0.0001), there was no relation between survival and anemia, leukocytosis, smoking, gender, histological subgroup, presence of comorbid conditions, pleural fluid. Older patients with pleural fluid were found to have a shorter life span compared to young patients (p=0.004).

In conclusion, pleural effusion is an important factor related to short life span in the elderly with advanced stage lung cancer.

E5454
The accuracy of the predicted postoperative pulmonary function in patients undergoing lung resection
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Introduction: To predict postoperative pulmonary function in patients undergoing lung resection a calculation based on the number of resected segments can be used. Aim: Our aim was to determine the accuracy of this simple calculation in predicting postoperative pulmonary function in a prospective way. In the past this has mainly been studied in retrospective studies or small populations.

Methods: We performed forced expiratory volume in one second (FEV1), transfer factor (TLCO) and if necessary a maximal cardiac pulmonary exercise test (CPET), before and 6 months after surgery. The predicted postoperative pulmonary function was calculated using the following formula: predicted postoperative value = preoperative value x (1 – S x 1/18); where S = number of resected segments. Pre- and actual postoperative results were compared by using the linear regression analysis and the Bland & Altman method.

996s
Results: Of the 124 operated patients included, 73 were eligible for the study and 27 performed a CPET. The FEV1 (r=0.83) and FEV1%predicted (r=0.75) showed good correlations between the predicted and the actual postoperative function. Also significant correlations were found for the predicted and actual TLCO (r=0.67) and VO2 max (r=0.60). However, the actual postoperative absolute FEV1 showed a significant underestimation of the calculated FEV1 of 0.35 litre, and the limits of agreement were large (±0.37 and ±0.88 litre).

Conclusions: The predicted postoperative pulmonary function shows a good correlation with the 6 months actual postoperative lung function for FEV1, TLCO and VO2 max. However, there is a considerable underestimation and weak agreement.