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A model to predict the immediate postoperative FEV1 following major lung resections

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Abstract

Objective: FEV1 measured on the first postoperative day has shown to be a better predictor of complications than traditional ppoFEV1. Therefore, its estimation before operation may enhance risk stratification. The objective of this study was to develop and validate a model to predict FEV1 on the first postoperative day after major lung resection. **Methods:** FEV1 was prospectively measured on the first postoperative day in 272 patients submitted for lobectomy or pneumonectomy at two centers. A random sample of 136 patients was used to develop a model estimating the first day FEV1 by using multiple regression analysis including several preoperative and operative factors. The model was then validated by bootstrap analysis and tested on the other sample of 136 patients. **Results:** Factors reliably associated with postoperative first day FEV1 were age ($p = 0.002$), preoperative FEV1 ($p < 0.0001$), the presence of epidural analgesia ($p < 0.0001$), and the percentage of non-obstructed segments removed during operation ($p = 0.001$). The following model estimating the first day postoperative FEV1 was derived: $-2.648 + 0.295 \times \text{age} + 0.371 \times \text{FEV1} + 8.216 \times \text{epidural analgesia} - 0.338 \times \text{percentage of non-obstructed segments removed during operation}$. In the validation set, the mean predicted first day postoperative FEV1 value did not differ from the observed one (42.6 vs 42.0, respectively; $p = 0.3$) and the plot of the observed versus the predicted first day FEV1 showed a satisfactory calibration. **Conclusions:** We developed a model predicting the first day postoperative FEV1. If future analyses will prove its role in stratifying the early postoperative risk, it may be integrated in preoperative evaluation algorithms to refine risk stratification.

Keywords: Lung surgery; Lobectomy; Pneumonectomy; Pulmonary function test; Postoperative management; Risk stratification

1. Introduction

Predicted postoperative FEV1 (ppoFEV1) is one of the most used parameters for selecting patients for pulmonary resection [1,2]. However, even though ppoFEV1 is fairly accurate in predicting the residual FEV1 3—6 months after operation [3—13], it may overestimate the actual FEV1 during the first postoperative days when most of the complications occur [13,14]. Therefore, for risk stratification purposes, the value of ppoFEV1 as it is traditionally estimated appears questionable. Indeed, we recently demonstrated that the FEV1 measured the first day after major lung resection is a better predictor of complications compared to ppoFEV1 [15]. Therefore, estimating before the operation the value of FEV1 that a patient will have in the immediate postoperative period may be useful for refining risk stratification.

The objective of the present study was to develop and validate an equation to predict the first day postoperative FEV1 after major lung resection, which could possibly be used in future risk stratification activities.

2. Methods

This was a prospective multi-institutional study performed on 272 patients submitted for lobectomy (242) or pneumonectomy (30) from November 2004 through December 2006 at two dedicated European thoracic surgery units (165 patients in unit A, 107 in unit B). Patients submitted for chest wall or diaphragm resections were excluded from the study. All patients gave their informed consent to participate in the study, which was approved by the local IRBs of each center. Criteria of operability were the same in all participating centers and included a sufficient pulmonary

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reserve (ppoFEV1 and ppoDLCO above 30% of predicted) and sufficient exercise tolerance (VO_2 peak above 10 ml/kg/min or height at stair climbing test above 12 m). Operations were performed for malignant (262) or benign [10] diseases by qualified general thoracic surgeons through an anterolateral muscle sparing (225) or video-assisted small axillary thoracotomy (47). After a few hours in the recovery room, all patients were transferred to the cardiothoracic wards where chest physiotherapy was started. Postoperative analgesia was achieved by epidural bupivacaine and opiates plus oral dexketoprofen (unit B), or continuous infusion of a combination of tramadol and ketorolac (unit A) for the first 3 days after operation, and was titrated to achieve a visual pain score below 30–40 in a scale from 0 to 100 mm (pain score was assessed twice daily during the morning and afternoon rounds). Chest tubes remained in place until no air leak and a daily effusion under 300 ml were evident.

FEV1 was measured in every patient at hospital admission and on the afternoon of postoperative day 1, under maximal bronchodilator therapy according to the American Thoracic Society criteria. Visual pain score was assessed before the postoperative PFT. The FEV1 recordings were performed by a trained physician three times by means of a calibrated portable spirometer (SpiroPro E. Jaeger GmbH), with the patient seated or standing up, and the best value selected. All patients were able to perform FEV1 measurements in the immediate postoperative period after proper instruction and pain control.

FEV1 was expressed as percentage of predicted normal values for age, gender, and height, according to the European Community for Steel and Coal prediction equations [16].

Predicted postoperative FEV1 was estimated for each patient based on the number of non-obstructed pulmonary segments to be resected, as assessed by bronchoscopy [6]. The percentage of functioning parenchyma to be resected (Func. loss %) was calculated by the following formula: Func. loss % = (number of non-obstructed segments to be resected/total number of preoperative non-obstructed segments) $\times$ 100 (i.e., in case of a right upper lobectomy with one obstructed segment: $(2/18) \times 100 = 11.1\%$). In case of pneumonectomy candidates, a quantitative lung perfusion scan was used to estimate the percentage of functioning parenchyma removed during operation [1].

3. Statistical analysis

Two random samples of 136 patients each were generated. The first sample was used for model building. Multivariate regression analysis was used to develop the model. The dependent variable was the FEV1 measured on the first postoperative day. The following variables were used as independent variables: age, gender, body mass index, type of operation, type of approach (muscle sparing vs VATS), type of analgesia (epidural vs systemic, epidural was coded as 1 for present or 0 for absent), preoperative FEV1, percentage of functioning/non-obstructed segments to be resected at operation (Func. loss %), COPD status (according to GOLD criteria, FEV1 $< 80\%$ and FEV1/FVC ratio < 0.7). The stability of the model was assessed by bootstrap analysis. In the bootstrap procedure, 1000 samples of 136 patients were sampled with replacement. Multivariate regression analysis was applied to every bootstrap sample. The stability of the final model was assessed by comparing the frequency of occurrence of the variables of the final model in the bootstrap samples. If the predictors occurred in more than 50% of the bootstrap models they were judged to be reliable and were retained in the final model [17–19].

The final predictive model was assessed in the second random sample of 136 patients. Predicted and observed FEV1 values were compared by means of the Wilcoxon matched-pairs signed rank test. Furthermore, to assess the precision of the predictive ability of the model, we plotted the cumulative predicted first day FEV1 against the observed first day FEV1 ordered by groups of increasing values of predicted first day FEV1.

Data were prospectively entered in each center and then sent to a centralized dataset where they were checked for accuracy and consistency by a data manager. All variables entered in this study were complete.

All statistical tests were performed on Stata 8.2 (Stata Corp., College Station, TX).

4. Results

The characteristics of the development and validation groups are shown in Table 1.

The first random group of 136 patients was used to derive the model by multivariate regression analysis, whose results are shown in Table 2. Factors reliably associated with postoperative first day FEV1 were age ($p = 0.002$), preoperative FEV1 ($p < 0.0001$), the presence of an epidural analgesia ($p < 0.0001$), and the percentage of functioning/non-obstructed segments resected during operation, Func. loss % ($p = 0.001$). The following model estimating the early postoperative FEV1 was derived: $-2.648 + 0.295 \times \text{age} + 0.371 \times \text{FEV1} + 8.216 \times \text{epidural analgesia} - 0.338 \times \text{Func. loss \%}$ ($R^2 = 0.40$). This model was then used to predict the first day postoperative FEV1 in the second random sample of 136 patients. The mean predicted first day postoperative FEV1 value did not differ from the observed one (42.6 ± 8.5 vs 42.0 ± 12.7, respectively; $p = 0.3$).

Table 1
Characteristics of the patients in the derivation and validation groups

Variables	Derivation set	Validation set	*p*-Value
Age	65.7 (10.5)	65.1 (11)	0.7[a]
Gender, male (*n*, %)	104 (76)	112 (82)	0.2[b]
BMI (kg/m^2)	26.1 (3.7)	26.1 (4.2)	0.8[a]
FEV1 %	85.7 (20.2)	82.2 (19.4)	0.2[c]
PpoFEV1 %	67.3 (17.8)	63.4 (16)	0.06[c]
COPD (*n*, %)	40 (29)	46 (34)	0.4[b]
Pneumonectomy (*n*, %)	16 (12)	14 (10)	0.7[b]
VATS (*n*, %)	19 (14)	28 (21)	0.15[b]
Epidural analgesia (*n*, %)	56 (41)	52 (38)	0.6[b]
VAS score first postoperative day	30.1 (23.6)	28.5 (24.2)	0.6[a]

Results are presented as means $\pm$ standard deviations unless otherwise specified. BMI, body mass index.
[a] Mann–Whitney test.
[b] Chi-square test.
[c] Unpaired Student's *t*-test.

Table 2
Results of the multivariate regression analysis (dependent variable: first day postoperative FEV1)

Variables	Coefficients	SE	*p*-Value	Bootstrap %
Intercept	−2.648	7.5		
Age	0.295	0.09	0.002	90
FEV1	0.371	0.05	<0.0001	100
Epidural	8.216	2.1	<0.0001	98
Func. loss %	−0.338	0.09	0.001	97

Parsimonious model. Epidural analgesia was coded as 1 for presence and 0 for absence. Func. loss %, percentage of functioning parenchyma removed during operation. Bootstrap %, frequency of significancy ($p < 0.05$) in 1000 bootstrap samples.

Fig. 1 plots the cumulative predicted against the observed first day postoperative FEV1 with the patients ordered by increasing values of predicted first day postoperative FEV1. The two curves are almost superimposed showing a good precision of the model in a set of patients other than the one from which it was derived.

5. Discussion

PpoFEV1 is the most widely used parameter for patient selection before lung resection. Most of the published algorithms consider this index pivotal for deciding further tests (such as DLCO measurement or exercise tests) or even for excluding patients from operation [1,2]. However, although ppoFEV1 is fairly correlated with the residual FEV1 at 3–6 months after operation [3–13], it may overestimate the actual FEV1 measured on the first postoperative day by as much as 30% [13,14]. If the objective is to stratify the patients according to their risk of early postoperative morbidity and mortality, the usefulness of a parameter which is more correlated to the long-term outcome, such as ppoFEV1, appears at least questionable. In fact, we recently showed that the FEV1 measured on the first postoperative day after major lung resection was a better predictor of cardiopulmonary complications compared to ppoFEV1 [15]. Under this premise, we thought that predicting the first day postoperative FEV1 is a logical approach to improve risk stratification. Therefore, the objective of this study was to develop a regression equation for estimating the early postoperative FEV1. The model was developed from a random population of 136 patients operated on at the participating centers and its reliability was confirmed by bootstrap analysis. The model was then validated on an external sample constituted of a second random group of 136 patients. In this validation sample the predictive equation showed an excellent precision.

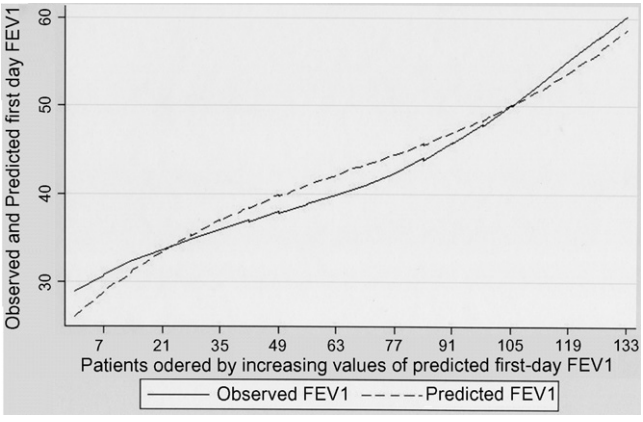

Fig. 1. Plot of the cumulative predicted vs observed first day FEV1 with the patients ordered by increasing values of predicted first day FEV1.

We found that age was directly associated with the value of postoperative FEV1. A lower loss in FEV1 after major lung resections was previously found in elderly patients by Brunelli et al. at discharge [20]. Younger patients have usually a better-preserved lung parenchyma compared to older ones. Therefore, the removal of a similar amount of lung tissue may determine a proportionally greater functional respiratory loss in these patients.

One of the most important factors associated with a higher first day postoperative FEV1 was the presence of an epidural analgesia. Although this was not a randomized study on postoperative analgesia, it confirmed previous evidence on the role of this procedure in improving postoperative respiratory function by better pain control [21]. In fact, it has been previously demonstrated that continuous epidural infusion of small doses of local anesthetics with opiates provides better control of dynamic pain without undue sedation and attenuates the neuroendocrine stress response by blocking the nociceptive inputs and sympathetic outflow [22,23].

It was surprising that the VATS approach was not significantly associated with a higher first day postoperative FEV1. However, it must be noted that all the VATS procedures were performed in only one of the centers and that all the open procedures were performed through a limited anterolateral muscle sparing thoracotomy, which caused only a slightly higher first day pain score compared to VATS (29 vs 22; $p = 0.1$). This difference may have been too small to influence the FEV1.

This study has potential limitations. First, postoperative FEV1 measurements were performed by multiple investigators at different centers by using different spirometers, which may introduce a procedural bias. However, PFTs were all performed by trained physicians, with all patients breathing room air and sitting in an upright position, after bronchodilator administration, according to standardized criteria (ATS). The portable spirometers used at the different centers were of the same company and model, and were recalibrated before each measurement.

Patients submitted for extended lung resections involving the chest wall or diaphragm were excluded from the analysis for the sake of homogeneity. Therefore, the model may not be accurate in predicting first day postoperative FEV1 in candidates for these types of resection. Larger numbers are required to assess the first day predicted postoperative FEV1 in this subset of patients.

In conclusion, we developed a model estimating the FEV1 that a patient will have on the first day after major lung resection. The model is intended for future risk stratification purposes only but not yet for patient selection. Future prospective analyses are needed to prove its role in predicting the early outcome.

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