

# Influence of age and predicted forced expiratory volume in 1 s on prognosis following complete resection for non-small cell lung carcinoma

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Received 20 September 1999; received in revised form 20 March 2000; accepted 12 April 2000

## Abstract

**Objective:** To evaluate age of the patient at the time of surgery and estimated postoperative forced expiratory volume in 1 s (FEV1%) as predictors of long-term survival following complete resection of non-small cell lung carcinoma (NSCLC). **Methods:** Retrospective, observational study. Records of patients operated on for NSCLC between January 1994 and December 1997 were reviewed. One hundred and ninety three patients who underwent complete pathological resection and survived surgery were included for study. Patients were divided in groups depending on age at the time of surgery and predicted postoperative FEV1% calculated according to the number of resected segments. Values of the 75th percentile of age (70.29 years) and 50th percentile of predicted FEV1% (52.9) were the cut-points selected for group division. To increase the power of the analysis pathological staging was also converted in a binary variable and resumed to localized (stage I) or extended (stage II–IIIB). Univariate analysis of the effect of each variable on survival was assessed by Kaplan–Meier method and log-rank test. Relationship between variables was investigated using  $2 \times 2$  tables and Fisher's exact test. Unrelated variables (extension, age and low estimated postoperative FEV1%) entered in a Cox-regression model to predict long-term survival following resection. **Results:** Pathological stage ( $P < 0.0001$ ), age ( $P = 0.01$ ) and low estimated postoperative FEV1% ( $P = 0.0007$ ) showed independent value to predict the outcome. **Conclusion:** Advanced age and low predicted postoperative FEV1% play an adverse effect on survival of completely resected NSCLC. © 2000 Elsevier Science B.V. All rights reserved.

**Keywords:** Non-small cell lung carcinoma; Surgical therapy; Chronic pulmonary disease; Advanced age; Long-term results

## 1. Introduction

Surgical treatment represents the best therapeutic choice for resectable non-small cell lung carcinoma (NSCLC). Anatomic extension of the neoplasm is the major determinant for long-term survival after complete resection [1]. Our surgical practice is influenced by progressively older population to deal with. In our region more than 21% of the population is 65 years old or more and chronic pulmonary disease is the third cause of death. Advanced age [2,3] and chronic obstructive pulmonary disease (COPD) [3] have been shown to have an adverse effect on operative mortality, but the influence of these clinical variables on the long-term outcome remains controversial.

This study was undertaken to evaluate if advanced age of the patient at the time of surgery and low predicted FEV1% after operation plays a role on prognosis after complete resection of NSCLC.

## 2. Materials and methods

We have reviewed the records of 193 patients who underwent complete resection of NSCLC (lobectomy or pneumonectomy and mediastinal lymphadenectomy) in our unit between January 1994 and December 1997. In-hospital mortality at any time after operation was excluded of the study. Records were reviewed for date of birth, preoperative FEV1%, tumour histology, pathological stage and long-term survival (from the date of surgery up to December 1998 or date of death by any cause). Postoperative FEV1% was calculated according to the number of resected segments during the operation as described by Juhl and Frost [4]. In most cases, follow-up was done by pneumologists or family physicians. Information on clinical state of the patients not followed-up at our centre was obtained by direct phone contact with the patient or their relatives.

Descriptive analysis of the data consisted in frequencies, means, standard deviations and percentiles. According to the value of the 75th percentile of the variable age the series was divided in two groups (younger or older). The value of the 50th percentile of the variable estimated postoperative

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FEV1% was also used to divide the series in two groups. Mean calculated postoperative FEV1% in younger and older groups were compared by unpaired *t*-test. To increase the power of the analysis pathological stage was also converted into a binary variable: localized (pI) or extended disease (pII–pIIIB). Tumour extension was classified according to the 1986 international classification [5].

Dependence of variables was assessed with contingency tables and Fisher's exact test. Univariate analysis of survival probability of each group was calculated by the Kaplan–Meier method and survival curves were compared with the log-rank test. Univariately significant variables were included in a stepwise Cox-regression model to find independent risk factors for mortality. For statistical analysis SPSS 8.0 software was employed.

### 3. Results

Three out of 193 patients were lost to follow-up and are not considered for survival analysis. Mean age of the series was 63.29 years (range: 34–79, SD 9.16, 75th percentile 70.29). Forty-seven patients were 70.29 years old or more at the time of surgery (elderly group). Data on preoperative pulmonary spirometry were not available in three cases (all patients had a previous laryngectomy). Mean calculated postoperative FEV1% (190 cases) was: 55.5 (range: 25.3–108.6; SD 17.6; 25th percentile 52.9). Mean predicted FEV1% was 55.2 (SD 17.4) in the younger group and 56.6 (SD 18.5) in the elderly ( $P = 0.66$ ). Pathological classification was: stage I 115 cases, stage II 19 cases; stage IIIA 52 cases; stage IIIB 7 cases; then 115 patients had localized and 78 extended disease. Most resected tumours (123 cases, 63.7%) were squamous carcinoma. A pneumonectomy was performed in 62 cases (32.1%) with a similar rate in both age groups (32.4% in younger and 31.2% in elderly cases).

On contingency tables advanced age at the time of surgery was neither related to pathological extension ( $P = 0.40$ ), calculated postoperative FEV1% ( $P = 0.86$ ) or tumour histology ( $P = 1.0$ ) (Table 1). A correlation was found between low FEV1% calculated after surgery and extended disease ( $P = 0.002$ ) (Table 2).

Three-year probability of survival of the series was 0.62. For patients with localized disease, 3-year probability of

Table 1  
Comparison of the rates of localized tumours, squamous carcinoma and low predicted postoperative FEV1% cases in younger and elderly groups<sup>a</sup>

	Younger patients ( <i>N</i> = 145)	Elderly patients ( <i>N</i> = 48)	<i>P</i>
Localized disease	89 (61.3)	26 (54.1)	0.40
Squamous carcinoma	92 (63.4)	31 (64.6)	1
Predicted FEV1% 52.9 or lower <sup>b</sup>	71 (50) <sup>b</sup>	23 (47.9)	0.87

<sup>a</sup> Values in parentheses are percentages.

<sup>b</sup> Three cases with a previous laryngectomy were excluded in this group.

Table 2  
Relation between tumour extension and predicted postoperative FEV1%<sup>a</sup>

Predicted FEV1%	Localized disease ( <i>N</i> = 113)	Extended disease ( <i>N</i> = 77)
Over 52.9	68	28
52.9 or under	45	49

<sup>a</sup> Data on 190 cases. Fisher's exact-test  $P = 0.002$ .

survival was 0.80 and 0.37 in the group of extended disease (log-rank test,  $P < 0.0001$ ). In the group of patients with higher calculated postoperative FEV1% 3-year probability of survival was 0.75; while it was only 0.48 for patients with low calculated FEV1% (log-rank test  $P = 0.0002$ ). Younger patients had higher 3-year probability of survival (0.65) than elderly cases (0.53; log-rank test  $P = 0.02$ ). Tumour histology did not have influence on survival (3-year survival for squamous carcinomas was 0.61 and for non-squamous 0.66; log-rank test  $P = 0.66$ ).

On multivariate study by stepwise Cox regression analysis, staging was the main prognostic factor ( $P < 0.0001$ ). Both low estimated postoperative FEV1% and advanced age also independently affected survival ( $P = 0.0007$  and 0.01, respectively). Data on univariate and multivariate analysis are shown on Table 3. Fig. 1 depicts the influence of each analyzed variable on survival.

### 4. Discussion

Advanced age [2,3] and poor pulmonary function [3] have been reported as predictors of high operative risk in patients with NSCLC. It is not the aim of this report to evaluate early morbi-mortality but long-term survival related to age and pulmonary function in completely resected cases of NSCLC.

In the last years some authors had stated that pulmonary resection for NSCLC is justified in patients over 70 years with good pulmonary function. According to Ishida et al. [6] 5-year survival rate in this subset of patients is 48% and it is

Table 3  
Univariate and multivariate analysis of survival

Variable	3-year probability of survival	Log-rank <i>P</i>	Cox-regression model <i>P</i>
<i>Extension</i>			
Localized	0.80		
Extended	0.37	< 0.0001	< 0.0001
<i>Age</i>			
Younger	0.65		
Older	0.53	0.02	0.01
<i>Predicted FEV1%</i>			
Over 52.9	0.75		
52.9 or under	0.48	0.0002	0.0007

not different to survival in the younger population (41%). Mizushima et al. [7] – in a series of patients undergoing pneumonectomy – found 11.5% overall 5-year probability of survival in patients over 70 and 30.5% in younger patients but they conclude that age is not a prognostic factor of long-term survival in patients after lung resection. In Europe, Thomas et al. [8] and Massard et al. [9] also report similar overall 5-year survival in elderly and younger patients operated for NSCLC. These three articles recommend careful preoperative assessment in elderly patients because of increased risk of operative mortality. It could be suspected that older population are carefully selected for surgery and that high-risk operations are avoided. Nevertheless, these reports show similar preoperative function and rates of cases with extended disease in both age groups.

Even when the age of 80 is selected as the cut-point to evaluate the results of lung cancer resection in the elderly, some investigators have published good long-term results, 5-year survival ranging from 16 to 43% [10–13]. Among these authors only Regnard and colleagues [10] report a rate of pneumonectomies similar to the expected in the general practice. The fact that some articles [11] found similar long-term survival after lung resection in octogenarians and in the younger population seems surprising and probably depends on very high restrictive selection criteria to indicate surgery in the elderly excluding from surgery patients with any other co-morbidity. Otherwise, as Ribet pointed out [14] should be concluded that having pulmonary resection for cancer makes you younger when you are over 70.

According to the cited reports, if operative mortality is

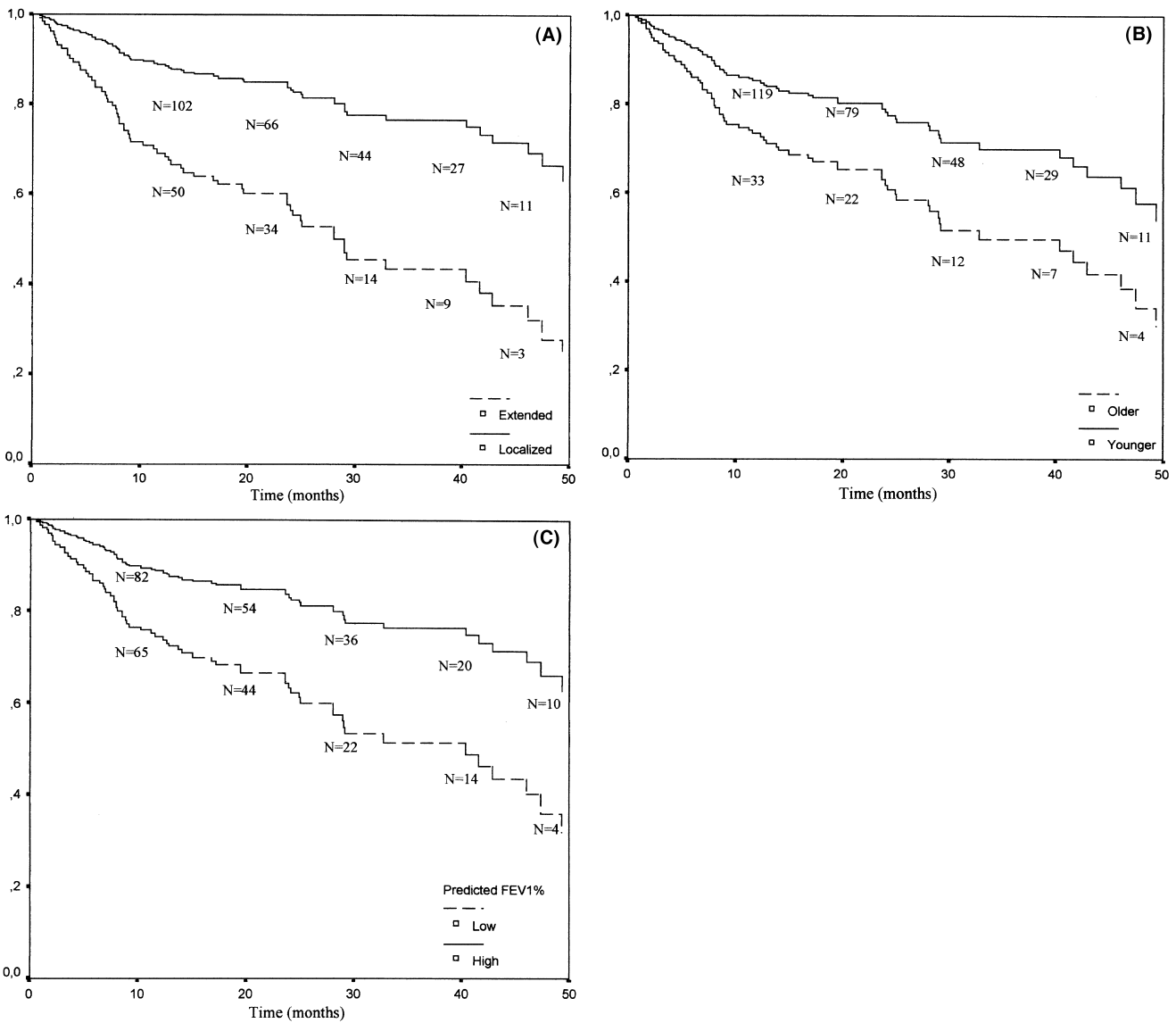


Fig. 1. Effect of each analyzed variable on cumulated survival. Cox-regression model. (A): Tumour extension. (B): Advanced age. (C): Predicted postoperative FEV1%.

excluded, age over 70 at the time of surgery should not be considered in the process of clinical decision-making when indicating surgery in NSCLC.

Our data contradicts this assertion and agrees with published reports on large unselected series in North America [15].

In COPD patients the value of FEV1% is one the more cited prognostic factors [16,17]. Kuller et al. [18] published that the lower the FEV1, the higher the risk of dying of lung cancer. So, we hypothesized that FEV1 should have independent influence on survival also in resected cases of NSCLC. In our series we have studied the effect of calculated postoperative FEV1% trying to evaluate both the effect of preoperative FEV1% and the extension of lung resection on survival. As we have shown in Table 2, a low predicted FEV1% after resection is related with the extension of neoplastic disease. Because of this relationship, it could have been suspected that postoperative FEV1% was not an independent predictor of survival. Data presented in Table 3 demonstrates the opposite.

The value of postoperative FEV1% estimation according to the number of resected segments, has been confirmed by some investigators [19]. An alternative formula excluding obstructed lung segments has been employed in clinical practice [20] to predict early postoperative morbidity.

Using predicted postoperative FEV1%, Cerfolio et al. [21] have found that an estimated value under 43% correlated with the need for home oxygen. In the series of Bousamra II et al. [22] median survival in patients with low predicted pulmonary capacity for carbon monoxide diffusion who underwent pulmonary resection was similar to those with normal postoperative DLCO, but the need for hospitalizations and home oxygen was superior in the first group. Wang and colleagues [23] in a similar study concluded that low DLCO predicts operative mortality but no lung-term survival after lung resection. In 1996, Koizumi et al [24] founded a significantly shorter survival in resected pI NSCLC patients having ventilatory disturbances – mainly restrictive respiratory diseases – combined with advanced age. In their series, the probability of survival in older patients with low calculated postoperative FEV1% was only 17%.

As we have described, most of our patients have not been followed-up at our hospital. Therefore the cause of death and the quality of life (QOL) after surgery have not been established. Thomas et al. [25] have studied a large number of elderly operated NSCLC cases in Canada. In their series, the causes of death in 96 out of 422 completely resected patients who survived the operation were not related to lung cancer. The assessment of QOL after lung resection have been reported in few published papers [26,27] concluding that 3–6 months after operation, QOL of life restores to preoperative values. We have not found information on QOL of elderly patients after lung surgery.

Keeping in mind these limitations of our study we can conclude that, in our series, advanced age and low predicted

postoperative FEV1% adversely influence the prognosis of completely resected NSCLC patients.

## Acknowledgements

The authors wish to express their gratitude to J.L. Fidalgo for reviewing the statistic analysis.

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