

Operative Mortality and Respiratory Complications After Lung Resection for Cancer: Impact of Chronic Obstructive Pulmonary Disease and Time Trends

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Background. Smoking is a common risk factor for chronic obstructive pulmonary disease (COPD), cardiovascular disease, and lung cancer. In this observational study, we examined the impact of COPD severity and time-related changes in early outcome after lung cancer resection.

Methods. Over a 15-year period, we analyzed an institutional registry including all consecutive patients undergoing surgery for lung cancer. Using the receiver-operating characteristic (ROC) curve, we analyzed the relationship between forced expiratory volume in 1 second (FEV₁) and postoperative mortality and respiratory morbidity. Multiple regression analysis has also been applied to identify other risk factors.

Results. A preoperative FEV₁ less than 60% was a strong predictor for respiratory complications (odds ratio [OR] = 2.7, confidence interval [CI]: 1.3 to 6.6) and 30-day mortality (OR = 1.9, CI: 1.2 to 3.9), whereas thoracic epidural analgesia was associated with lower mortality (OR = 0.4; CI: 0.2 to

0.8) and respiratory complications (OR = 0.6; CI: 0.3 to 0.9). Mortality was also related to age greater than 70 years, the presence of at least three cardiovascular risk factors, and pneumonectomy. From the period 1990 to 1994, to 2000 to 2004, we observed significant reductions in perioperative mortality (3.7% versus 2.4%) and in the incidence of respiratory complications (18.7% versus 15.2%), that was associated with a higher rate of lesser resection (from 11% to 17%, $p < 0.05$) and increasing use of thoracic epidural analgesia (from 65% to 88%, $p < 0.05$).

Conclusions. Preoperative FEV₁ less than 60% is a main predictor of perioperative mortality and respiratory morbidity. Over the last 5-year period, diagnosis of earlier pathologic cancer stages resulting in lesser pulmonary resection as well as provision of continuous thoracic epidural analgesia have contributed to improved surgical outcome.

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Surgery provides the best chance of prolonged survival for the early stages nonsmall-cell lung carcinoma [1]. However, given the failure of successful screening strategies and clinically silent progression of most cancer, only 15% to 25% of patients are selected to undergo curative pulmonary resection [2]. In addition, the risk of ventilatory failure precludes lung surgery in many patients with severe chronic obstructive pulmonary disease (COPD) [3, 4].

In this regard, pulmonary function tests remain the standard screening tests performed before pulmonary resection. It is generally agreed that a minimum value of forced expiratory volume in 1 second (FEV₁) is required preoperatively (2 L before pneumonectomy and 1.5 L lobectomy, respectively) and that further cardiopulmonary testing is needed in patients with marginal lung function [5–8]. Variable cutoff values of FEV₁ (ranging from 35% to 80%) have been arbitrarily chosen to assess the severity of COPD and to predict the risk for pulmonary complications [8–11].

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Over the last 2 decades, refinements in preoperative risk stratification and cancer staging along with advances in surgical and anesthetic approaches have allowed an increasing number of patients with compromised pulmonary function to undergo curative surgical resection [12]. Given these improvements, the relationship between preoperative functional assessment and postoperative outcome deserved a thorough reexamination. Accordingly, the main purpose of our observational study was to question whether a threshold value for FEV₁ was associated with increased mortality and pulmonary complications. Secondarily, we identified other perioperative risk factors and analyzed the time-related changes in the prevalence of COPD, the cancer stages, type of lung resection, and anesthetic management.

Patients and Methods

Patient Management

From January 1, 1990, to December 30, 2004, 1,239 consecutive thoracotomies for lung cancer (reinterventions, $n = 31$) were performed in two affiliated medical institutions: an academic center (Hôpitaux Universitaires de

Abbreviations and Acronyms

ASA	= American Society of Anesthesiologists
BMI	= body mass index
DL _{co}	= diffusion capacity of lung for carbon monoxide
FEV ₁	= forced expiratory volume in the first second
FVC	= forced vital capacity
PaCO ₂	= arterial carbon dioxide pressure tension
PaO ₂	= arterial oxygen pressure tension
VO ₂ max	= maximum volume of oxygen. FEV ₁ = forced expiratory volume in 1 second
FIO ₂	= inspired fraction of oxygen
ICU	= intensive care unit
IV	= intravenous
PaCO ₂	= arterial carbon dioxide pressure tension
PaO ₂	= arterial oxygen pressure tension
POD1	= first postoperative day.

Genève [HUG]) and a regional hospital (Centre Valaisan de Pneumologie [CVP]) that covered an area with approximately 680,000 inhabitants.

Preoperatively, patients with borderline spirometric results (FEV₁ lower than 60% of predicted), impaired exercise tolerance or cardiac risk factors underwent complementary investigations (diffusion capacity for carbon monoxide, maximal oxygen consumption, lung perfusion/ventilation scan, echocardiography, and myocardial thallium scintigraphy or coronary angiogram, or both). To assess the maximal possible exeresis, the predicted postoperative FEV₁ (ppoFEV₁) was calculated either by taking into account the function of the affected lung (perfusion lung scan) or by using the equation: ppoFEV₁= preoperative FEV₁ × (1-S × 0.0526), where S = number of resected pulmonary segments [13].

After anesthesia induction, a double-lumen tube was inserted and lung resection with systematic lymph node dissection was performed through an anterolateral muscle-sparing thoracotomy or a posterolateral approach (n = 64). Six patients underwent a combined unilateral lung volume reduction with tumor excision (2 lobectomies, 4 nonanatomical resections). In all patients, prophylactic antibiotics were administered (cefuroxime 1.5 g per 8 hours for 24 hours). At the discretion of the attending anesthesiologist, an epidural catheter was inserted preoperatively and thoracic epidural anesthesia (TEA) was continued for 2 to 4 days after surgery using low-dose bupivacaine and opiates.

After surgery, patients were monitored for at least 24 hours in the post-anesthesia care unit; admission in the intensive care unit was considered for high-risk patients and in case of intraoperative complications. Arterial blood was routinely sampled for gas exchange, electrolytes, and hemoglobin assessments at arrival in the intensive care unit or post-anesthesia care unit, on the first day after surgery, and in any case of clinical deteri-

oration. Chest radiograms were daily performed until chest drain removal and before hospital discharge.

Data Collection and Study Design

With Institutional Review Board approval, specific data on comorbidities, functional status, and results of complementary investigations were recorded on a standardized worksheet at the time of anesthetic consultation. All patients were prospectively monitored up to hospital discharge on a regular basis by a research fellow, and variables related to surgical and anesthetic management as well as postoperative events were prospectively collected. Case information spanning 80 perioperative variables was entered into a continually updated database. Internal audit was made to survey the validity of data and to verify correct transmission to the computer database. Recollection and reentry of data from 183 subjects (15%) selected at random revealed a data entry error rate of 1.5% and a data collection error rate of 2.9%. Outcome data were missing for 17 patients and were excluded from the analysis.

The severity of COPD was stratified into three groups using the European Respiratory Society criteria [14]: normal or mild impairment in pulmonary function tests (FEV₁ ≥70% of predicted values), moderate COPD (FEV₁ from 50% to <70%), and severe COPD (FEV₁ <50%). Pathologic staging was based on the revised TNM classification [15]. Binary data were obtained by identification of the presence or absence of relevant comorbidities and perioperative complications. The diagnosis of coronary artery disease was based on a history of myocardial infarct or angina, typical Q waves on the electrocardiogram, positive stress test, or evidence of coronary artery stenosis on the angiogram. Elevated blood pressure, arrhythmias, and diabetes mellitus requiring medications were considered significant comorbidities. Peripheral artery disease was defined by clinical evidence (claudication at exercise, past or current vascular surgery) or arteriography. The 5-grade classification of the American Society of Anesthesiologists (ASA) was used as a composite index of the patient's general status.

Potential operative risk factors were also considered: duration of surgery, surgical approach (anterolateral, posterolateral thoracotomy), extended resection (including adjacent structures), type of analgesia (intravenous opiate or TEA), and postoperative pathologic staging (early versus late stages).

Operative mortality was defined as any death occurring within 30 days of operation or during the hospital stay. Respiratory complications included prolonged chest drainage, reintubation, atelectasis, pneumonia, acute lung injury, and bronchopleural fistula (see Appendix).

Statistical Analysis

All analysis were performed using SPSS software (version 11.5; SPSS, Chicago, Illinois) and GraphPad Prism (version 4; San Diego, California). Continuous data were examined for normality with the Shapiro-Wilk test. Data are presented as mean and 95% confidence interval (CI), absolute numbers or percentages; statistical significance

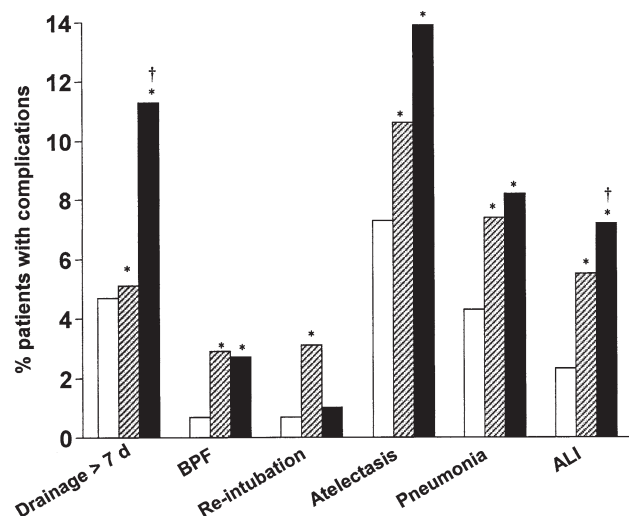


Fig 1. Incidence of respiratory complications after lung resection for cancer in three groups of patients with preoperative FEV₁ of 70% or more (white bars), FEV₁ of 5% to 70% (hatched bars), and FEV₁ of 50% or less (black bars). **p* less than 0.05, compared with patients FEV₁ of 70% or more; †*p* less than 0.05, compared with patients FEV₁ of 50% of 70%. (ALI = acute lung injury; BPF = bronchopleural fistula; d = days; FEV₁ = forced expiratory volume in 1 second.)

was set at the 0.05 level. The receiver-operator characteristic curve (ROC) analysis was used to detect the best threshold for FEV₁ (or ppoFEV₁) to predict pulmonary complications and sensitivity, specificity, positive predictive accuracy, and negative predictive accuracy were calculated. Differences between groups (below versus above the FEV₁ threshold) were examined using unpaired Student's *t* test or the Mann-Whitney test for continuous variables and Fisher's exact test for proportions. For time trends analysis, three consecutive periods were considered (from 1990 to 1994, from 1995 to 1999, and from 2000 to 2004), a χ^2 test for linear trend analyses (extension of Mantel) was applied followed by Duncan's multiple range test. After univariate analysis (χ^2 test for proportions and analysis of variance for continuous variables), multivariate logistic regression analysis was performed using backward elimination, taking perioperative outcome (30-day mortality or respiratory complications) as a dependent variable, and the explanatory clinical and surgical variables found to be significant in the univariate

analysis (*p* up to 0.25) as independent variables. To avoid multicollinearity, only one variable in a set of variables with a correlation coefficient greater than 0.5 was used in the multivariate analysis. Adjusted odds ratios (ORs) with 95% CI were calculated.

Results

From 1993 through 2004, completed data were obtained in 1,222 cases that were distributed in three groups: normal or mild impairment in pulmonary function tests (FEV₁ ≥ 70%: *n* = 728, 60%), moderate COPD (FEV₁ 50% to 70%: *n* = 397, 32%), and severe COPD (FEV₁ < 50%: *n* = 97, 8%).

Perioperative Outcome and Patient Characteristics

The overall mortality rate was 2.9% (1.1% in normal or mildly impaired pulmonary function tests, 5.8% in moderate COPD, and 3.1% in severe COPD); and it was primarily attributed to acute lung injury (41%), cardiovascular events (31%), hemorrhage (19%), or unknown causes (8%).

As shown in Figure 1, the incidence of respiratory complications was strongly related to preoperative functional lung impairment. Overall, at least one adverse respiratory events occurred in 10% of patients with normal-to-mild impairment in pulmonary function tests, in 25% of those with moderate COPD, and in 27% of those with severe COPD (*p* < 0.001). In the subset of patients with a ppoFEV₁ less than 35% of predicted value (*n* = 96), perioperative mortality and the incidence of respiratory complications were significantly higher (7.1% and 28.1%, respectively) than in patients with ppoFEV₁ greater than 35% (2.3% and 17.2%, respectively).

With a cutoff value of 60% for predicted FEV₁, the area under the ROC curve demonstrated a good model calibration and discriminatory power to predict respiratory complications, particularly in the subset of patients without thoracic epidural analgesia (0.74, 95% CI: 0.70 to 0.77). Using ppoFEV₁ with values ranging from 30% to 50% failed to achieve a better predictive risk model. Sensitivity, specificity, predictive accuracy (positive and negative), and ROC curve area are shown in Table 1.

Preoperative, intraoperative, and postoperative patient characteristics are described in Tables 2 and 3. The group with FEV₁ less than 60% was characterized by a higher prevalence of smoking habits, cardiovascular diseases

Table 1. Sensitivity, Specificity, Predictive Accuracy, and ROC Curve Area for Respiratory Complications

	FEV ₁ < 60%	FEV ₁ < 60% Without TEA	FEV ₁ < 60% With TEA	ppoFEV ₁ < 35%
Sensitivity, %	29	27	27	12
Specificity, %	88	93	87	92
Positive predictive accuracy, %	32	67	24	27
Negative predictive accuracy, %	86	70	88	82
ROC curve area	0.66	0.74	0.65	0.61

FEV₁ = forced expiratory volume in 1 second;
epidural analgesia.

ppo = predicted postoperative;

ROC = receiver operating characteristic;

TEA = thoracic

Table 2. Preoperative Characteristics of Study Population, Percent or Mean (95% Confidence Interval)

Variables	Number	FEV ₁ > 60% n = 1,036	FEV ₁ < 60% n = 186
Age, years	1,222	63 (61–65)	64 (62–66)
Patients > 70 years, %		29	30
Sex (male)		69	68
BMI, kg · m ⁻²	1,222	24.9 (24.5–25.4)	24.8 (24.1–25.3)
Cardiovascular diseases, %	1,222		
Hypertension		26	30 ^a
Diabetes mellitus		7.2	10.8
Hypercholesterolemia		8.7	9.4
Coronary artery disease		8.7	13.0
Peripheral artery disease		7.5	13.1 ^a
Smoking, %	1,222		
Current or < 6 months cessation		67	77 ^a
≥ 6 months cessation		9	10
No smoker		27	13 ^a
ASA class 3 and 4, %		36	74 ^a
Blood tests	1,209		
Hemoglobin (g/L)		145 (144–146)	147 (145–149)
Creatinine (mg/L)		90 (88–92)	87 (83–87)
Lung functional volume	1,222		
FVC (L)		3.6 (3.4–3.8)	2.7 (2.5–2.9) ^a
FVC (% predicted value)		101 (98–104)	77 (74–80) ^a
FEV ₁ (L)		3.4 (3.3–3.5)	1.4 (1.3–1.5) ^a
FEV ₁ (% predicted value)		88 (87–89)	49(48–50) ^a
FEV ₁ /FVC (%)		78 (77–79)	53 (42–54) ^a
Gas exchange	1,158		
PaCO ₂ (kPa)		4.7 (4.6–4.8)	5.1 (4.9–5.2) ^a
PaO ₂ (kPa)		11.5 (11.3–11.7)	10.1 (9.8–10.4) ^a
Exercise testing			
VO ₂ max (mL/min/kg)	259	19 (16–21)	15 (14–16) ^a
Diffusion capacity (DL _{co} , %)	223	56 (54–58)	35 (33–37) ^a

^a $p < 0.05$, compared with group FEV₁ > 60%.ASA = American Society of Anesthesiologists; BMI = body mass index; forced expiratory volume in the first second; FVC = forced vital capacity; tension; VO₂max = maximum volume of oxygen.DL_{CO} = diffusion capacity of lung for carbon monoxide; FEV₁ = forced expiratory volume in the first second; PaCO₂ = arterial carbon dioxide tension; PaO₂ = arterial oxygen

(hypertension, peripheral arterial disease), ASA classes 3 and 4, as well as limited aerobic exercise capacity and lung diffusion capacity.

Intraoperative and postoperative fluid balance as well as surgical and anesthetic durations did not differ regardless of preoperative FEV₁. Patients with FEV₁ less than 60% were more likely to undergo lesser extensive pulmonary resection stages as a result of earlier pathologic TNM stages; they also required more frequent admission in the intensive care unit and achieved lower oxygenation indices with higher arterial PCO₂ on the first postoperative day.

Risk Factors for Mortality and Respiratory Complications

Multiple logistic regression analysis showed that preoperative FEV₁ less than 60% of predicted was an independent risk factor of respiratory complications (OR = 2.7, CI: 1.3 to 6.6) and 30-day mortality (OR = 1.9, CI: 1.2 to

3.9) whereas TEA was associated with lower mortality (OR = 0.4, CI: 0.2 to 0.8) and respiratory complications (OR = 0.6, CI: 0.3 to 0.9). In addition, operative mortality was also strongly related to age greater than 70 years (OR = 1.9, CI: 1.1 to 6.2), the presence of at least three cardiovascular risk factors (OR = 2.4, CI: 1.1 to 5.7), and pneumonectomy (OR = 3.1, CI: 1.7 to 8.9).

As illustrated in Figure 2, TEA was associated with fewer operative deaths in the subgroup with FEV₁ less than 60% and with fewer respiratory complications, regardless of preoperative FEV₁ value.

Changing Patterns From 1990 to 2004

From 1990 to 1994, to 2000 to 2004, we observed a decline in operative mortality rate (3.7% versus 2.4%, $p < 0.05$) and in the incidence of respiratory complications (18.7% versus 15.2%, $p < 0.05$), whereas more patients with FEV₁ less than 60% (26.1% in 2000 to 2004 versus 14.8% in 1990 to 1994, $p < 0.05$), with cardiovascular diseases (more

Table 3. Perioperative Characteristics of Study Population, Percent or Mean (95% Confidence Interval)

	FEV ₁ > 60% n = 1,036	FEV ₁ < 60% n = 186
Type of surgery (% patients)		
Pneumonectomy, bilobectomy	28.8	26.8
Lobectomy	50.5	43.5
Lesser resection	14.0	22.7 ^a
Explorative thoracotomy	6.0	6.4
Pathologic stages (%)		
Ia and Ib	40	44
IIa and IIb	20	26 ^a
IIIa	19	15 ^a
IIIb and IV	13	12
Other	8	5
Intraoperative operative period		
Duration of surgery (min)	109 (106–12)	112 (114–120)
Duration of anesthesia (min)	160 (155–165)	168 (160–176)
Thoracic epidural anesthesia	76	85
Blood transfusion (% patients)	2.9	6.2
Intraoperative fluid balance (mL)		
IV crystalloids (mL)	1148 (1,108–1,188)	1121 (1,075–1,187)
IV colloids (mL)	389 (369–409)	405 (375–435)
Urine output (mL)	221 (211–231)	238 (226–240)
First 24 hours postoperative period		
IV crystalloids + colloids (mL)	1813 (1,768–1,858)	1787 (1,760–1,848)
Urine output (mL)	993 (965–1,024)	991 (955–1,028)
Chest drainage (mL)	422 (406–438)	463 (440–483)
Urine output (mL)	388 (375–401)	375 (365–385)
PaO ₂ /FIO ₂ at POD1	45.4 (44.9–45.9)	41.5 (41.0–42.0) ^a
PaCO ₂ at POD1	5.3 (5.0–5.6)	5.8 (5.6–6.0) ^a
Admission in ICU (%)	7	14 ^a
Hospital length of stay (days)	14.1 (13.7–14.5)	15.1 (14.6–15.6)

^a $p < 0.05$, compared with group FEV₁ > 60%.FEV₁ = forced expiratory volume in 1 second; FIO₂ = inspired fraction of oxygen; ICU = intensive care unit; IV = intravenous; PaCO₂ = arterial carbon dioxide pressure tension; PaO₂ = arterial oxygen pressure tension; POD1 = first postoperative day.

than three risk factors: 22.7% versus 13.8%, $p < 0.05$) and with early pathologic lung cancer stages (I and II: 70.1% versus 61.4%, $p < 0.05$) were selected for surgery (Table 4). Meanwhile, the use of TEA had increased (88.2% versus 64.6%, $p < 0.05$), and there was a higher rate of lesser resection (17% in 2000 to 2004 versus 10.7% in 1990 to 1996, $p < 0.05$) coupled with a decrease in exploratory thoracotomy (2.2% versus 8.5%, $p < 0.05$).

Comment

Over a 15-year period, retrospective analysis of 1,222 patients operated on for lung cancer demonstrated that (1) moderate-to-severe COPD was documented in 40% of surgical candidates, (2) preoperative FEV₁ below a threshold of 60% carried a twofold to threefold increased risk for operative mortality and respiratory complications whereas TEA was a predictor of better short-term outcome, and (4) over the last 5 years, a higher proportion of lesser resection due to diagnosis of earlier pathologic

TNM stages coupled with an increasing use of TEA have contributed to improve perioperative outcome despite the increasing prevalence of COPD and cardiovascular diseases.

COPD and Other Perioperative Risk Factors

In agreement with previous reports [16–23], we identified the extent of pulmonary resection (pneumonectomy), advanced age, and impairment of cardiopulmonary function (COPD, cardiovascular disorders) as independent predictors of operative deaths whereas pulmonary morbidity was mainly influenced by the degree of preoperative functional lung impairment. Since Gaensler and associates [24] in 1955 reported a 40% mortality among patients with a preoperative FEV₁ less than 70%, preset levels of relative/absolute values of FEV₁ have been arbitrarily chosen for preoperative risk stratification [5–11]. In this study, we determined a cutoff value at 60% for preoperative FEV₁ by using sensitivity analysis to discriminate subset of patients with different postoperative

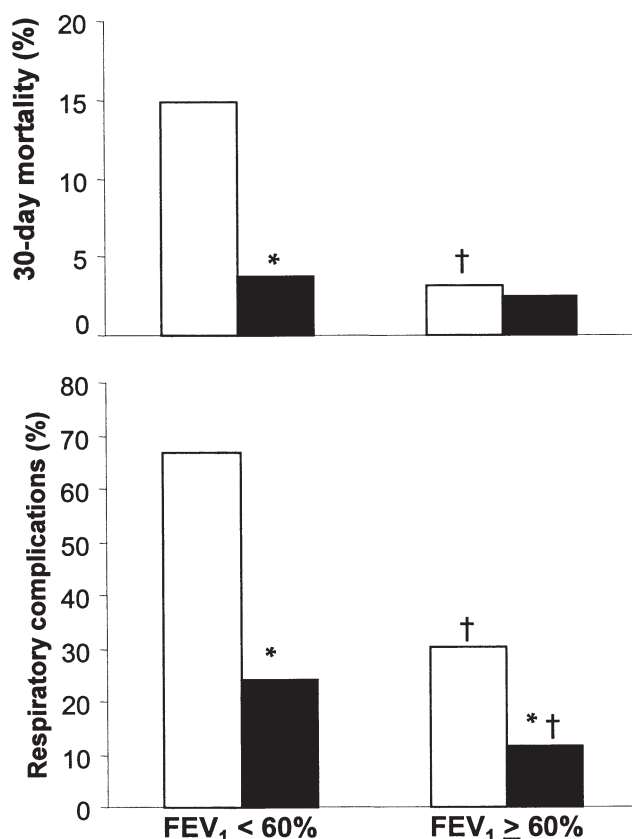


Fig 2. Thirty-day mortality rate (top) and incidence of respiratory complications (bottom) according to preoperative FEV₁ (<60% or ≥60%) and type of analgesic regimen: without thoracic epidural analgesia (white bars) or with thoracic epidural analgesia (black bars). **p* less than 0.05, compared with group without thoracic epidural analgesia; †*p* less than 0.05, compared with group FEV₁ ≥60%. (FEV₁ = forced expiratory volume in 1 second.)

respiratory morbidity. In any analysis, a test with a high specificity and a high positive predictive accuracy will identify patients at high risk of developing complication. In this context, FEV₁ less than 60% as a predictive index of pulmonary complications was most useful in the subset of patients who did not receive continuous TEA (specificity of 93%, positive prediction of 92%). Although ppoFEV₁ less than 35% was associated with higher mortality and respiratory complications, adding this factor in the multivariate analysis did not enhance the risk estimation, and the predictive power of ppoFEV₁ was not superior to the simple assessment of FEV₁ as evidenced by ROC curve areas.

Importantly, the risk of operative mortality and pulmonary complications was partially offset by providing continuous TEA, particularly in patients with FEV₁ less than 60%. These results are in line with two meta-analyses showing the effectiveness of central neuraxis blockade to reduce 30-day mortality as well as the incidence of pulmonary thromboemboli, deep vein thrombosis, respiratory depression, and pulmonary complications [25, 26]. In addition, besides its cardioprotective effects, TEA has

also been shown to improve ventilatory mechanics in patients with end-stage COPD as evidenced by decreased airway resistance and unchanged respiratory muscle force [27, 28]. Altogether, these beneficial effects of TEA have been attributed to the attenuation of the neuroendocrine response, modulation of the prothrombotic state, and improved diaphragmatic function.

Not surprisingly, cardiovascular diseases were more frequently diagnosed in COPD patients in relation to their greater propensity for smoking. Closer medical follow-up and radiologic examination of this high-risk group resulted in the detection of earlier lung cancer stages (screening bias) that required less extensive resection [29].

Time Trends From 1990 to 2004

During the latest period (2000 to 2004), despite aggravation of the preoperative cardiopulmonary risk profile, there was a reduction in operative mortality and pulmonary morbidity. The increasing use of TEA, diagnosis of earlier cancer stages and improvement in surgical techniques have likely contributed to better short-term outcome. More accurate preoperative staging has been achieved with the introduction of spiral computed tomography and positron emission tomography imaging, allowing the detection of patients with inoperable disease and those who could undergo complete tumor resection [30]. A certain number of “futile” exploratory thoracotomies have been avoided while curative resection has been afforded in a larger number of COPD patients with early lung cancer stages. As a result, there was an increasing prevalence of COPD and a shift from explorative thoracotomy toward more limited resections (eg, wedge resections or segmentectomies) aiming to preserve lung tissue and to permit a second or even a third curative resection over time. Finally, the feasibility and safety of curative cancer resection in these high-risk patients have been supported by the latest development of lung volume reduction for severe emphysema [31, 32]. Resecting nodules within hyperinflated and poorly perfused containing-segments has been shown to improve pulmonary function as a result of partial reexpansion of adjacent areas, increased elastic recoil, and improved chest mechanics [31, 32].

Currently, few studies have specifically examined the short-term outcome of patients with severely limited lung function (FEV₁ <50% of predicted) [33–37]. The large variability in mortality (1% to 20%) and in the incidence of respiratory complications (air leak, 11% to 22%; pneumonia, 3% to 25%; prolonged ventilation, 2% to 29% or new oxygen dependence 6% to 28%) can largely be explained by the lack of standard criteria to define outcome variables (eg, pneumonia) and by differences in the extent of resection (eg, pneumonectomy) and the type of incision (eg, muscle-sparing anterior thoracotomy, posterior and lateral thoracotomy, thoracoscopy).

Limitations of the Study

We are mindful of several limitations related to the observational and retrospective design of this single

Table 4. Time-Related Changes in Preoperative Cardiopulmonary Risk Profile, Type of Surgery, Pathologic Stages, Use of Thoracic Epidural Anesthesia, and Postoperative Outcome

	Period 1990–1994 n = 356	Period 1995–1999 n = 407	Period 2000–2004 n = 459
Age > 70 years	28.9	30.1	29.5
Female	24.9	26.7	33.0 ^a
FEV ₁ < 60%	16.3	20.3	26.1 ^a
At least 3 cardiovascular risk factors	13.8	14.8	22.7 ^a
Type of surgery			
Pneumonectomy or bilobectomy	28	30	28
Lobectomy	52	51	53
Lesser resection	11	13	17 ^a
Explorative thoracotomy	9	6	2 ^a
Pathologic TNM stages			
Ia and Ib	42	44	44
IIa and IIb	19	22	26 ^a
IIIa	20	20	19
IIIb and IV	18	14	11 ^a
Thoracic epidural anesthesia	65	77	88 ^a
Perioperative major complications			
Mortality (30-day)	3.7	2.9	2.4 ^a
At least one respiratory complication	18.7	16.9	15.2 ^a

Data shown as percent.

^a*p* < 0.05, compared with period 1990–1994.FEV₁ = forced expiratory volume in 1 second.

center report. First, although more than 80 items were prospectively entered in a local registry including 1,222 cases, the question of the impact of pulmonary function tests on surgical outcome was addressed a posteriori, precluding control of any confounding variables. Selection bias and length bias were unavoidable as the surgeon's choice to perform a major or minor resection was determined by both the pathologic stage and the severity of COPD that varied over a 15-year period owing to advances in diagnostic imaging technologies. Second, analysis of several potential risk factors such as preoperative bronchial hyperresponsiveness, interstitial lung disease, neoadjuvant chemoradiotherapy, and bronchoplastic procedures was inconclusive due to incomplete data and the small number of patients in these categories (type II error, false negative results). Third, maximal oxygen consumption and diffusion capacity of the lung for carbon monoxide are currently used in well-validated algorithms for preoperative risk assessment and postoperative residual function prediction [5, 6, 10]; these important variables obviously influenced the surgical decision without achieving statistical power because they were obtained in a minority of patients (FEV₁ < 60% or interstitial disease).

In conclusion, this observational study demonstrates that—besides age, cardiovascular diseases, and the extent of lung resection—a preoperative FEV₁ below 60% is a main predictor of perioperative mortality and respiratory morbidity whereas provision of continuous TEA is considered as a “protective” medical intervention.

Currently, given advances in diagnostic techniques, an

ever-larger number of COPD patients with early cancer stages are selected for curative surgery. To improve our selection criteria and to validate the therapeutic strategies (eg, major/minor lung resection, neoadjuvant therapy), multicentric follow-up studies should be focused on long-term respiratory function and quality of life.

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Appendix

Definitions of Respiratory Complications

- Prolonged drainage: For 7 days or more
- Hemothorax: Need for transfusion sanguine and chest drainage > 800 mL; Reoperation for hemostasis
- Bronchopleural fistula: Bronchoscopy and application of glue; Reoperation (direct closure, thoracocentesis, lavage)
- Reintubation: Ventilatory failure and need for mechanical ventilation
- Atelectasis: Lobar collapse (chest radiographs); Need for CPAP or bronchoscopy, or both
- Bronchopneumonia: Temperature greater than 38°C; Hyperleucocytosis (neutrophils); New lung infiltration (chest radiographs); Positive culture (bronchial secretions or alveolar fluid)
- Acute lung injury: Sudden onset of respiratory; Diffuse pulmonary infiltrates consistent with alveolar edema; Impaired oxygenation (PaO₂/FIO₂ ratio < 220); Absence of hydrostatic pulmonary edema due to cardiac insufficiency or fluid overload

INVITED COMMENTARY

The article by Licker and colleagues [1] describes the evolution of the surgical management of lung cancer in the perennial search of the functional Holy Graal (ie, the

single preoperative predictor of mortality and severe morbidity after pulmonary surgery). Indeed, the results of this rigorous observational study are important not so