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 (FEV_1) and postoperative mortality and respiratory morbidity. Multiple regression analysis has also been applied to identify other risk factors.

Results. A preoperative FEV_1 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 FEV_1less 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 (FEV_1) 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 FEV_1(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 FEV_1 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

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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_2max	= 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 (FEV_1 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 FEV_1 ($ppoFEV_1$) was calculated either by taking into account the function of the affected lung (perfusion lung scan) or by using the equation: $ppoFEV_1 =$ preoperative $FEV_1 \times$ (1-S $\times$ 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 deterioration. 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 (FEV_1 ≥70% of predicted values), moderate COPD (FEV_1 from 50% to <70%), and severe COPD (FEV_1 <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