

Pulmonary Complications Following Lung Resection*

A Comprehensive Analysis of Incidence and Possible Risk Factors

François Stéphan, MD, PhD; Sophie Boucheseiche, MD; Judith Hollande, MD; Antoine Flahault, MD, PhD; Ali Cheffi, MD; Bernard Bazelly, MD; and Francis Bonnet, MD

Study objectives: To assess the incidence and clinical implications of postoperative pulmonary complications (PPCs) after lung resection, and to identify possible associated risk factors.

Design: Retrospective study.

Setting: An 885-bed teaching hospital.

Patients and methods: We reviewed all patients undergoing lung resection during a 3-year period. The following information was recorded: preoperative assessment (including pulmonary function tests), clinical parameters, and intraoperative and postoperative events. Pulmonary complications were noted according to a precise definition. The risk of PPCs associated with selected factors was evaluated using multiple logistic regression analysis to estimate odds ratios (ORs) and 95% confidence intervals (CIs).

Results: Two hundred sixty-six patients were studied (87 after pneumonectomy, 142 after lobectomy, and 37 after wedge resection). Sixty-eight patients (25%) experienced PPCs, and 20 patients (7.5%) died during the 30 days following the surgical procedure. An American Society of Anesthesiology (ASA) score ≥ 3 (OR, 2.11; 95% CI, 1.07 to 4.16; $p < 0.02$), an operating time > 80 min (OR, 2.08; 95% CI, 1.09 to 3.97; $p < 0.02$), and the need for postoperative mechanical ventilation > 48 min (OR, 1.96; 95% CI, 1.02 to 3.75; $p < 0.04$) were independent factors associated with the development of PPCs, which was, in turn, associated with an increased mortality rate and the length of ICU or surgical ward stay.

Conclusions: Our results confirm the relevance of the ASA score in a selected population and stress the importance of the length of the surgical procedure and the need for postoperative mechanical ventilation in the development of PPCs. In addition, preoperative pulmonary function tests do not appear to contribute to the identification of high-risk patients.

(CHEST 2000; 118:1263–1270)

Key words: logistic regression analysis; mortality; nosocomial pneumonia; pulmonary complications; pulmonary function tests; risk factors; thoracic surgery

Abbreviations: ASA = American Society of Anesthesiology; CI = confidence interval; FEV₁-ppo = predicted postoperative FEV₁; NS = not significant; OR = odds ratio; PPC = postoperative pulmonary complication; PSB = protected specimen brush

Patients undergoing thoracotomy associated with lung resection are thought to be at high risk for the development of postoperative pulmonary complications (PPCs) during the perioperative period, and these

complications may lead to serious morbidity.¹ Despite advances in surgical technique, anesthesia, and perioperative care, mortality ranges from 2 to 12%.^{2,3} Although operative mortality following lobectomy or pneumonectomy has decreased over the past decade, PPCs continue to occur with incidence rates as high as 49%.⁴ Clinical studies have identified numerous patient- or procedure-related risk factors for PPCs following pulmonary resection, using various research designs and definitions. In most but not all studies, the most frequent risk factors were as follows: age,^{2,3,5–8} altered preoperative pulmonary function tests,^{4,5,9–12} cardiovascular comorbidity,^{2,4,7} and smoking status.^{4,8}

*From the Service d'Anesthésie-Réanimation chirurgicale (Drs. Stéphan, Boucheseiche, Hollande, Cheffi, and Bonnet), the Antenne de Biostatistiques et d'Informatique médicale (Dr. Flahault), and the service de Chirurgie thoracique et vasculaire (Dr. Bazelly), Hôpital Tenon 4 rue de la Chine, Paris, France. Manuscript received September 29, 1999; revision accepted April 19, 2000.

Correspondence to: François Stéphan, MD, PhD, département d'Anesthésie-Réanimation chirurgicale, Hôpital Henri Mondor 51 avenue du Maréchal de Lattre de Tassigny 94010 Créteil Cedex, France; e-mail: francois.stephan@hmn.ap-hop-paris.fr

However, there have been relatively few comprehensive overviews accurately describing the PPCs that may occur in these patients. Moreover, existing studies dealing with PPCs are difficult to interpret for several reasons. Firstly, definitions of PPCs varied widely and previous studies did not use explicit operational criteria. Secondly, although many risk factors for PPCs have been identified, many potential variables are often interrelated and it is difficult to extract which of these factors independently affect outcome. Unfortunately, the sample size of most studies was too small to apply a multivariate logistic regression model. Thirdly, few previous studies have included detailed clinical information, such as American Society of Anesthesiology (ASA) score, preoperative characteristics and pulmonary function tests, and postoperative analgesic treatment in their analysis.^{13,14}

The objectives of the present study were as follows: (1) to examine the incidence and clinical implications of PPCs after thoracic surgery in a tertiary-care center; and (2) to identify the preoperative or intraoperative factors that may predispose to the development of PPCs in this subset of patients.

MATERIALS AND METHODS

Patients

We (F.S., S.B., J.H.) reviewed the charts of all patients who had undergone pulmonary resection in our institution from January 1994 to December 1996. Operability was determined according to existing guidelines for pneumonectomy and lobectomy.¹⁵ We also regarded a preoperative PaO₂ > 60 mm Hg and a PaCO₂ < 45 mm Hg (resting, breathing room air) as requirements before surgery was undertaken. However, the final decision regarding operability was made by the attending surgeon, and some patients were accepted who did not meet the guidelines above. All pulmonary resections, from wedge resection to pneumonectomy, were performed by open thoracotomy by the same thoracic surgeon (B.B.). Emergency procedures were excluded from the analysis. All surgical procedures were performed under general anesthesia after premedication with midazolam, Etomidate, 0.3 to 0.4 mg/kg IV, and sufentanil, 0.5 mg/kg IV, were used for induction. Orotracheal intubation was facilitated by vecuronium, 0.1 mg/kg IV. Anesthesia was maintained by 50% N₂O in oxygen and isoflurane (1.0 to 1.5 minimum alveolar concentration). At the end of surgery, neuromuscular block was systematically reversed with neostigmine, 2.5 mg IV, preceded by atropine, 1 mg IV, when two responses to the train-of-four nerve stimulation were present. Left-sided or right-sided double-lumen endotracheal tubes were never used during the surgical procedure. Unless otherwise indicated, all patients were scheduled for extubation in the recovery room at the end of the operation. When discharged from the recovery room, patients were managed in the thoracic ward unless complications required their admission to the ICU. Postoperative pain control was mainly achieved by systemic opioids (parenteral administration or IV patient-controlled administration) combined with acetaminophen. Some patients received epidural analgesia and intercostal blocks. The choice of analgesic technique was made at the convenience of the anesthesiologist. All patients had an active

program of physiotherapy including deep-breathing exercises and incentive spirometry during the postoperative period.

Postoperative Evaluation

Charts were evaluated according to the method of Feinstein et al.¹⁶ The following data were abstracted from all charts by means of a standardized form: age, sex, body mass index, smoking history (pack-year history), comorbid cardiovascular conditions (preexisting history of myocardial infarction, angina pectoris, hypertension, arrhythmia, stroke), preoperative pulmonary function tests, ASA class,¹⁷ presence or absence of lung malignancy, preoperative chemotherapy, type and duration of pulmonary resection, quantification of blood loss during the perioperative period (perioperative period and during the first 24 h after the end of surgery), and postoperative analgesic therapies. The ASA classification system¹⁷ is based on the presence or absence of systemic disturbances: absent (class 1), mild (class 2), moderate (class 3), severe (class 4), or almost certain to cause death (class 5). We used the ASA status recorded in the anesthesiologist's preoperative note once its validity was reassessed according to the data found in the medical record of each patient. Extended resections were defined as those requiring either chest wall resection or other extended resection, including sleeve, tracheal, atrial, intrapericardial, aortic and diaphragmatic resection, or extrapleural pneumonectomy. Complications, both pulmonary and nonpulmonary, were ascertained by detailed chart review according to the operational definitions reported below. It is acknowledged that retrospective identification of PPCs depends on the detail and completeness of the medical record. To minimize this factor, the analysis was limited to postoperative complications thought to be clinically significant (see below) and thus unlikely to be omitted from the medical record.

Definitions of Postoperative Complications

Postoperative complications were defined as those occurring within 30 days of thoracotomy. Death was analyzed as a separate complication.

Pulmonary Complications

(1) Nosocomial pneumonia: In patients receiving mechanical ventilation, the diagnosis of nosocomial pneumonia was considered when patients developed a new and persistent lung infiltrate and had purulent tracheal secretions confirmed by a bacterial culture of the protected specimen brush (PSB) > 10³ cfu/mL or of the BAL > 10⁴ cfu/mL.¹⁸ When bacterial culture was < 10³ cfu/mL for PSB or < 10⁴ cfu/mL for BAL, the diagnosis of bronchitis was retained. In patients breathing spontaneously, the diagnosis was considered if they had a compatible chest radiograph and purulent sputum with Gram's stain and sputum culture documenting the presence of microorganisms. (2) Lobar or whole-lung atelectasis evidenced on chest radiograph and requiring bronchoscopy. (3) Acute respiratory failure: Postoperative ventilator dependence > 24 h or reintubation for controlled ventilation. (4) Prolonged air leak: Air leak requiring > 7 days of postoperative chest tube drainage. (5) Pulmonary embolism documented by pulmonary arteriogram or autopsy, or supported by a ventilation/perfusion radioisotope scan showing "high probability" of pulmonary embolism. (6) ARDS: Acute onset with a PaO₂/fraction of inspired oxygen ≤ 200 mm Hg and bilateral infiltrates seen on frontal chest radiograph, with no clinical evidence of left atrial hypertension.¹⁹ (7) Pneumothorax evidenced on chest radiograph or CT scan and requiring chest tube placement. (8) Bronchospasm: wheezing, increased airway pres-

sure during positive-pressure ventilation, or prolonged expiratory phase. (9) Aspiration pneumonia, defined as either the presence of bilious secretion or particulate matter in the tracheobronchial tree or, in patients who did not have their tracheobronchial airways directly examined after regurgitation, a postoperative chest radiograph with infiltrates not identified by preoperative radiograph.

Other Complications

Bleeding through the chest tubes was considered to be a significant complication when a reoperation was required, or when three or more RBC packs were transfused.

Cardiovascular complications were defined as follows: (1) symptomatic cardiac arrhythmia requiring treatment, (2) acute myocardial infarction (ECG and elevation of creatine phosphokinase or cardiac troponin I) or unstable angina, and (3) stroke. The criteria for sepsis have been previously reported.²⁰ Shock was defined as a decrease in systolic BP (< 90 mm Hg) despite adequate vascular filling, or the need for vasoactive drugs (dopamine > 5 µg/kg/min, dobutamine, epinephrine, or norepinephrine). Finally, analysis of the results shows that some patients had more than one complication.

Predicted Postoperative FEV₁

Unfortunately, not all the patients had been explored with a lung perfusion scan or any other lateralizing test. Therefore, the predicted postoperative FEV₁ (FEV₁-ppo) was estimated by the formula published by Juhl and Frost²¹: FEV₁-ppo = preoperative FEV₁ × (1 - [S × 5.26]/100), where S is the number of bronchopulmonary segments removed. A right pneumonectomy was considered to cause a 55% decrement in preoperative FEV₁, and a left pneumonectomy to cause a 45% decrement. In patients undergoing wedge resections, each wedge resection was assumed to account for one bronchopulmonary segment. The right and left lower lobes were considered to have five bronchopulmonary segments, the right middle lobe to have two bronchopulmonary segments, the right upper lobe to have three bronchopulmonary segments, and the left upper lobe to have four bronchopulmonary segments. The postoperative values obtained by this method of calculation have a good agreement with postoperative values calculated from preoperative regional lung function tests using ¹³³Xe.²¹

Statistical Analysis

Data were computerized and analyzed using BMDP statistical packages (BMDP Statistical Software; Los Angeles, CA). Categorical variables were compared using the χ^2 test or Fisher's Exact Test, and continuous variables were compared using the Student's *t* test or Mann-Whitney *U* test when appropriate. The risk of PPCs associated with selected factors was evaluated using stepwise logistic regression analysis to estimate odds ratios (ORs) and their 95% confidence intervals (CIs). Continuous variables

were dichotomized by using the median as the cutoff value. A *p* value ≤ 0.05 by univariate analysis was chosen as the criterion for submitting variables to the model. As quantification of blood loss was available for only 158 patients, and despite a significant statistical association on univariate analysis, this variable was not taken into account in the multivariate analysis. Goodness of fit was assessed by the Hosmer and Lemeshow χ^2 test.²² The relative risk, defined as the ratio of incidence among exposed to that among nonexposed subjects,²³ was used to summarize the strength of the association between risk factors and death; the 95% CI of the relative risk was calculated using Miettinen's test-based approach.²³ Unless otherwise stated, results are expressed as mean ± SD for continuous variables and as percent for categorical variables.

RESULTS

Study Population

Two hundred sixty-six patients (mean age, 59 ± 14 years; 205 men and 61 women) underwent pulmonary resections. Lobectomy, the most common operation, was performed in 142 cases (53%), while 87 patients (33%) underwent pneumonectomy, and 37 patients (14%) underwent wedge resections (Table 1). There was no significant relationship between the complication rate and the operative procedure. Extended resections were performed in 51 patients (19%). Two hundred fifteen patients (81%) had malignant neoplasms as their final diagnosis. Tumor type included squamous cell carcinoma in 113 patients (53%), adenocarcinoma in 59 patients (27%), small cell carcinoma in 7 patients (3%), and other types in 16 patients (7%). Staging was as follows: stage I (n = 73; 37%), stage II (n = 28; 14%), stage IIIa (n = 48; 25%), stage IIIb (n = 38; 20%), stage IV (n = 8; 4%). Twenty patients had pulmonary metastases (10%). Benign lung diseases (51 patients) were most often caused by pulmonary tuberculosis (n = 17) and bronchiectasis (n = 12). One hundred six patients (40%) had a comorbid cardiovascular condition as previously defined, and 64 patients (24%) were classified as ASA 3 or 4 by the anesthesiologist.

PPCs

Sixty-eight patients (25%) developed a total of 97 PPCs (Table 2). There was no significant difference

Table 1—Incidence of Postoperative Complications According to Type of Surgical Procedure*

Extent of Surgery	Type of Complication		
	Death	Respiratory	Cardiovascular and Miscellaneous
Pneumonectomy (n = 87)	6 (7)	20 (23)	10 (11)
Lobectomy (n = 142)	11 (8)	41 (29)	17 (12)
Wedge resections (n = 37)	3 (8)	7 (19)	3 (8)

*Data are presented as No. (%). No significant statistical difference was found.

Table 2—Types and Incidence of Pulmonary Complications (n = 97) and Respective Percentages in Total Patients (n = 266)

Complications	No.	Total Patients, %
Prolonged air leak, bronchopleural fistula*	22	8.3
Bacterial pneumonia	17	6.4
Acute respiratory failure	16	6.0
Postoperative hemorrhage	11	4.0
Atelectasis	8	3.0
Pneumothorax	5	2.0
Bronchospasm	4	1.5
Pulmonary embolism	3	1.0
ARDS	3	1.0
Bronchitis	3	1.0
Aspiration pneumonia	2	0.7
Pleural effusion	1	0.4
Acute pulmonary edema	1	0.4
Purulent pleuritis	1	0.4
Total	97	—

*Bronchopleural fistula in five cases (4 right pneumonectomies and 1 left pneumonectomy) and prolonged air leak in the remaining cases (15 lobectomies and 2 wedges).

between the pulmonary complication rate and the operative procedure (Table 1). When looking at the overall pulmonary complications, prolonged air leak and bronchopleural fistula were the most prevalent complications recorded (23%), followed by bacterial pneumonia (17%) and acute respiratory failure (16%).

Gram-negative bacilli were recovered in 16 of the 17 episodes of pneumonia (94%). The distribution pattern of Gram-negative bacilli isolated strains was as follows: *Pseudomonas aeruginosa* (n = 4; 22%); *Enterobacter cloacae*, *Escherichia coli*, and *Haemophilus influenzae* (n = 3; 17% for each); *Klebsiella pneumoniae* (n = 2); others (Enterobacteriaceae sp, n = 2; and *Acinetobacter baumannii*, n = 1). *Staphylococcus aureus* was recovered in six episodes (35%; 50% were methicillin resistant). Twelve episodes (70%) of nosocomial pneumonia occurred while patients were receiving mechanical ventilation. Seven episodes of pneumonia were associated with polymicrobial infection (40%), and five episodes were related to both Gram-negative bacilli and Gram-positive cocci.

Twelve patients required early postoperative mechanical ventilation > 24 h (4.5%). The duration of mechanical ventilation ranged from 1 to 30 days. Four patients had tracheotomy. The interval between surgery and the diagnosis of the first pulmonary complication was 3.8 ± 4.4 days. Mechanical complications (air leak, atelectasis, hemorrhage) occurred 2.3 ± 2.8 days (range, 1 to 19 days) after surgery, while infectious pulmonary complications occurred after 9.9 ± 7.1 days (range, 2 to 28 days; $p = 0.0003$).

Thirty patients (11.2%) experienced 39 complications other than respiratory complications, including 21 cardiovascular complications (15 arrhythmias, 3 myocardial infarctions/unstable anginas, and 3 strokes); 10 septic complications other than pneumonia (6 sepsis and septic shock, 2 peritonitis, and 2 endocarditis); and 8 miscellaneous (2 upper-GI hemorrhages, 2 acute renal failures, 2 undetermined shock, 1 hypernatremia, and 1 psoas hematoma).

Risk Factors for Postoperative Pulmonary and Overall Complications

Perioperative historical data for patients with and without pulmonary complications are reported in Table 3. Variables predictive of pulmonary complications on univariate analysis include smoking history, associated comorbid cardiovascular conditions, ASA physical status ≥ 3 , a longer operating time, a higher blood loss, and a longer duration of immediate postoperative mechanical ventilation.

Preoperative pulmonary function tests, available only for 243 patients, are shown in Table 4. After univariate analysis, FEV₁ and FEV₁-ppo (expressed either as a percentage of the predicted normal value or in absolute units) were predictive of pulmonary complications. Patients with a preoperative FEV₁ < 2 L experienced an increased pulmonary complication rate. Pulmonary complications occurred in 30 of 74 patients (40%) with FEV₁ < 2 L vs 33 of 169 patients (19%) with a preoperative FEV₁ > 2 L ($p < 0.001$). In contrast, patients with FEV₁-ppo < 1 L did not have an increased pulmonary complication rate. Thirty-three patients had FEV₁-ppo < 1 L, and 12 patients (36%) had a respiratory complication (not significant [NS]).

Stepwise logistic regression analysis was then used to identify perioperative variables independently associated with PPCs. Because FEV₁ and FEV₁-ppo were collinear, two models were constructed to see whether FEV₁ or FEV₁-ppo further contributed to the model. Three independent risk factors were associated with the development of PPCs: an ASA score ≥ 3 (OR, 2.11; 95% CI, 1.07 to 4.16; $p = 0.02$), operating time > 80 min (OR, 2.08; 95% CI, 1.09 to 3.97; $p < 0.02$), and need for mechanical ventilation for > 48 min during the immediate postoperative period (OR, 1.96; 95% CI, 1.02 to 3.75; $p = 0.04$). However, the alteration of pulmonary function tests (expressed by either FEV₁ or FEV₁-ppo) was not identified as a variable independently associated with PPCs ($p = 0.4$). The goodness-of-fit χ^2 of this model remained nonsignificant during the three steps ($p = 0.93$ at the last step). This model explained 10% of the variance in the data ($R^2 = 0.10$).

Stepwise logistic regression analysis was also used

Table 3—Characteristics of Patients With and Without Pulmonary Complications*

Variables	Patients With Pulmonary Complications (n = 68)	Patients Without Pulmonary Complications (n = 198)	p Value
Sex ratio, M/F (% M)	53/15 (78)	151/47 (76)	NS
Age, yr	62 ± 13	58 ± 14	0.02
Age > 60 yr	39 (57)	99 (50)	NS
Body mass index, kg/m ²	23.3 ± 4.7	23.9 ± 3.7	NS
Smoking history, pack-yr	50.4 ± 34.6	39.0 ± 28.7	0.009
Comorbid cardiovascular conditions	34 (50)	72 (36)	< 0.05
ASA physical status			0.001
ASA 1, 2	42 (62)	160 (81)	
ASA 3, 4	26 (38)	38 (19)	
Type of procedure			NS
Pneumonectomy	20 (30)	67 (34)	
Lobectomy	41 (60)	101 (51)	
Wedge resection	7 (10)	30 (15)	
Chest wall resections	14 (21)	37 (19)	NS
Lung malignancy	57 (84)	158 (80)	NS
Preoperative chemotherapy	11 (16)	41 (15)	NS
Operating time, min	101 ± 44	82 ± 34	0.0003
Blood loss,† mL	988 ± 528	715 ± 454	< 0.002
Duration of immediate postoperative mechanical ventilation, h	46 ± 139	1.2 ± 2.4	< 0.0001
Mechanical ventilation > 24 h	11 (16)	1 (0.5)	< 0.0001
Postoperative analgesia‡			NS
Conventional systemic opioid	28 (41)	66 (33)	
PCA of opioid	36 (53)	112 (57)	
Thoracic epidural analgesia	2 (3)	13 (7)	
Intercostal block	2 (3)	7 (3)	
Deaths, No. (%)	16 (23)	4 (2)§	< 0.0001

*Data are presented as No. (%) or mean ± SD unless otherwise indicated. M = male; F = female; PCA = patient-controlled administration.

†Quantification of blood loss during the perioperative period (perioperative period and during the first 24 h after the end of surgery) was available in 158 patients only.

‡Comparison of conventional systemic opioid administration with other analgesic therapies was statistically nonsignificant.

§Deaths were related to undetermined shock in two patients, peritonitis in one patient, and hypernatremia with generalized convulsions after hypertonic saline solution for hydatid cyst in one patient.

to identify perioperative variables independently associated with all complications. Two independent risk factors were associated with the development of any kind of complications: operating time > 80 min (OR, 2.2; 95% CI, 1.2 to 4.1; $p = 0.01$), and need for mechanical ventilation > 48 min during the immediate postoperative period (OR, 1.94; 95% CI, 1.1 to 3.56; $p = 0.03$). However, an ASA score ≥ 3 was not identified as a variable independently associated with overall complications ($p = 0.1$). The goodness-of-fit χ^2 of this model remained nonsignificant during the three steps ($p = 0.89$ at the last step). This model explained 11% of the variance in the data ($R^2 = 0.11$).

Outcome

Twenty deaths (mortality rate, 7.5%) occurred within 30 days after the operation. Table 1 shows that pneumonectomies, lobectomies, and wedge resections were associated with similar in-hospital postoperative mortality rates.

Among the several factors studied, the develop-

ment of PPCs was the sole factor associated with an increased risk of death (Table 3). The relative risk was 14.9 (95% CI, 4.76 to 26.9). Multivariate analysis was not performed to assess death as a dependent variable, owing to the small number of cases.

The median (25th to 75th percentiles) duration of postoperative stay in the surgical ward was 10.0 days (8.7 to 13.0 days) for patients without PPCs, 11.0 days (9.0 to 17.0 days) for patients with PPCs who were kept in the ward ($p < 0.004$), and 14.0 days (8.5 to 29.0 days) for patients with PPCs who required ICU admission ($p = 0.03$).

DISCUSSION

This retrospective study documents a 25% pulmonary complication rate in this series of patients scheduled for thoracotomy. The present study demonstrates that ASA physical status, operating time, and need for prolonged mechanical ventilation were associated with a twofold increase in PPCs. PPCs

Table 4—Preoperative Pulmonary Function Tests in 243 Patients*

Parameters	Patients With Pulmonary Complications (n = 63)	Patients Without Pulmonary Complications (n = 180)	p Value
FEV ₁ , L (range)	2.11 ± 0.71 (0.88–3.89)	2.51 ± 0.73(0.98–5.59)	0.0002
FEV ₁ , % predicted, (range)	0.76 ± 0.22 (0.31–1.27)	0.85 ± 0.20 (0.30–1.36)	0.006
FEV ₁ -ppo, L (range)	1.48 ± 0.57 (0.55–2.89)	1.74 ± 0.68 (0.70–4.70)	0.006
FEV ₁ -ppo, % predicted, (range)	0.53 ± 0.18 (0.17–1)	0.59 ± 0.21 (0.22–1.26)	0.04
FVC, L (range)	3.19 ± 0.96 (1.18–6.05)	3.51 ± 0.92 (1.44–7.20)	0.02
FVC, % predicted, (range)	0.86 ± 0.24 (0.36–1.47)	0.94 ± 0.19 (0.25–1.47)	0.01
FEV ₁ /FVC, (range)	0.69 ± 0.13 (0.38–0.98)	0.71 ± 0.1 (0.39–0.94)	NS
PaO ₂ at FIO ₂ 0.21, mm Hg	80.4 ± 12.9	83.0 ± 13.5	NS
Paco ₂ , mm Hg	40.0 ± 4.6	36.9 ± 4.7	<0.001
PaCO ₂ > 45 mm Hg, No. (%)	7 (11)	8 (4)	0.08

*FIO₂ = fraction of inspired oxygen.

were also strongly associated with an increased risk of death and a prolonged hospital stay.

Our study is probably limited by its retrospective design.¹⁶ Firstly, pulmonary complications were determined by chart review, and a primary concern is the sensitivity and specificity of data scoring. However, all severe complications—particularly pneumonia and ventilatory failure—should have been detected, as they would greatly affect the postoperative prognosis. Secondly, the sensitivity of data scoring may have been increased in patients perceived as presenting an increased risk (*eg*, patients planned to be admitted to ICU). However, the analysis was limited to postoperative complications thought to be clinically significant, even in the ICU setting. Thirdly, important new parameters like split-function studies or transfer factor for carbon monoxide were not taken into account.¹⁵

The overall incidence of PPCs following thoracic surgery is approximately 30%.^{7,24–27} However, estimations vary widely in the literature, from 7 to 49%.^{4,5,28} This variability is primarily due to the type of pulmonary complications studied, the clinical criteria used in the definition, the type of surgery, and the use of different regimens of preoperative chemotherapy. In this study, the incidence of PPCs was 25% using restrictive definitions. The most frequent PPC was bronchopleural fistula and the consequent prolonged air leak, as previously reported by two studies.^{11,29} The incidence of air leaks ranges from 4%⁴ to 26%.¹¹ The bronchopleural fistula rate of 5.7% after pneumonectomy compares with the 3.1 to 15% rates reported by other authors.^{4,7,10,30} Bronchopleural fistula is one of the most difficult complications to manage following pneumonectomy, and it is associated with a high mortality rate.^{4,10,30} In contrast, prolonged air leak following lobectomy or wedge resection carries a low mortality rate, but is associated with prolonged hos-

pitalization.¹¹ Moreover, the presence of pleural air leaks may further deteriorate pulmonary gas exchange by increasing the amount of wasted ventilation and the work of breathing.

Nosocomial pneumonia is the most important risk factor for morbidity and mortality after thoracotomy.³ The incidence of nosocomial pneumonia in our study (6.4%) is lower than the previously reported rates of 15 to 22%.^{4,10,12,25,31} Although a number of factors may influence the incidence of pneumonia in this setting (*eg*, patient population, isolation procedures, and so forth), it should be emphasized that all previous studies were based on clinical criteria for the diagnosis of pneumonia. Previous studies have shown that reliance on clinical criteria alone leads to a substantial overdiagnosis of pneumonia.³² In contrast, the current study used objective diagnostic criteria based on bronchoscopic techniques to obtain PSB and BAL specimens, with a high overall accuracy in the diagnosis of nosocomial pneumonia and the microorganisms responsible.¹⁸

Acute respiratory failure was the third most common PPC, with an incidence rate of 6%. Other studies have reported an incidence between 2.4%⁷ and 17%,¹¹ for a mean incidence rate estimate of 9.0% when main studies are pooled.^{4,6,10,33} One of the most striking features is the high mortality rate associated with this complication.^{4,6,10,12,33} In fact, the prognosis is probably more closely related to the severity of the underlying pulmonary complication leading to mechanical ventilation, rather than to mechanical ventilation itself. However, prolonged mechanical ventilation has also been associated with the risk of acquired nosocomial pneumonia³² and bronchopleural fistula.^{10,30}

As previously reported in several studies,^{3–6,10,12,25,34} we found that PPCs were associated with significant mortality with a relative risk of death of 14.9 (95% CI, 4.76 to 26.9), which could be mainly attributed to

nosocomial pneumonia.³ The mortality rate of 7.5% is in the range of those previously reported (1.3 to 10.1%) according to the type of procedure.^{2-4,28} Moreover, the stage and histology of the tumor play an important role in the assessment of the surgical risk in lung cancer patients. Like other authors, we also found that PPCs led to a prolonged postoperative hospital stay,^{8,11,26,27} which has a significant economic impact. Physicians therefore use a variety of strategies to reduce the risk of pulmonary complications in patients at high risk after a thorough clinical evaluation and review of risk factors.¹

In our study, the major predictors for PPCs were ASA physical status, operation time, and duration of postoperative mechanical ventilation. ASA physical status is the commonest risk factor for postoperative complications regardless of the circumstances. Higher ASA physical status has been associated with postoperative pneumonia³¹ and prolonged postoperative intubation³⁵; therefore, it is not surprising that a high grade of ASA physical status would be associated with PPCs after thoracic surgery.¹⁴ Another study of geriatric patients undergoing elective abdominal and noncardiac thoracic surgery also found ASA class to be a powerful univariate predictor of both cardiac and pulmonary complications.¹³ However, in our study, high-grade ASA physical status seemed not to be a powerful predictor of overall complications. As previously suggested, this clinical index did not predict cardiac morbidity well.¹⁷ A potential deficiency of the ASA classification is that it is based on the subjective evaluation of patients and is therefore open to observer variability. However, in our study, we found that the ASA determination performed prior to surgery by the attending anesthesiologists provided critical information. Finally, ASA physical status is the best single risk factor for PPCs in this study, probably because it includes both pulmonary and nonpulmonary factors. Consequently, pulmonary complications are more strongly related to coexisting conditions than to chronologic age¹; therefore, advanced age alone does not appear to be a powerful predictive risk factor.^{4,9,11,25,28,29}

Regarding the intraoperative period, longer operations carried a higher risk of PPCs, as previously suggested.^{31,34,36} Finally, the last risk factor identified was the inability to rapidly wean the patient from mechanical ventilation after the surgical procedure. We have already outlined the possible harmful effect of prolonged mechanical ventilation in these patients.

Preoperative assessment of pulmonary function has been the most extensively studied factor for predicting morbidity and mortality of pulmonary resection. Previous studies have yielded conflicting results regarding the use of preoperative pulmonary function tests as predictors of PPCs. Some studies have identified FEV₁

and/or FVC results (either expressed as absolute values or percentage) as possible risk factors,^{4-6,9,28} while others did not.^{8,11-13,25,27,37} More interestingly, several studies have confirmed the value of the FEV₁-ppo in predicting PPCs and mortality after lung resection.^{10,12,24,28,37} Difference between conclusions of these studies and ours could be explained in part by the lack of any kind of "lateral test" or lung perfusion scans to correct FEV₁-ppo.²¹ These calculations may not provide a reliable estimate of the actual postresection measurements.²⁴ However, clinical findings are generally more predictive of PPCs than spirometric results in the few studies that have evaluated both factors.^{13,14} Hypercapnia has often been cited as a contraindication to thoracotomy, but it has been reported that it is possible to operate safely on patients with a PaCO₂ > 45 mm Hg.^{15,37} Therefore, even patients with impaired respiratory function can undergo surgery with an acceptable risk of PPCs. A modern approach should probably include pulmonary function tests, predicted postoperative function, and exercise variables.¹⁵ However, one has to remember that many lung resection candidates can undergo resections up to a pneumonectomy without any sophisticated tests, which are costly and not universally available.¹⁵

This retrospective investigation can only help to identify those variables associated with PPCs. There are two types of prognostic variables: those that can be altered to decrease risk (*eg*, operation time) and those that cannot be altered (*eg*, ASA score). However, even a strong statistical association does not necessarily indicate a cause-and-effect relation. Therefore, shortening surgery and anesthesia durations and avoiding prolonged conventional mechanical ventilation may not actually decrease the incidence of PPCs.

In conclusion, an ASA physical status ≥ 3 , which is a subjective global rating of comorbid disease burden, indicated an increased pulmonary risk in this study. Consistent with a growing body of evidence, preoperative spirometry did not help to identify patients at increased risk of PPCs. Pulmonary complications are mainly responsible for mortality of patients undergoing thoracotomy; surgeons and anesthesiologists must actively participate in the development of more effective preventive strategies.

REFERENCES

- 1 Smetana GW. Preoperative pulmonary evaluation. *N Engl J Med* 1999; 340:937-944
- 2 Romano PS, Mark DH. Patient and hospital characteristics related to in-hospital mortality after lung cancer resection. *Chest* 1992; 101:1332-1337
- 3 Wada H, Nakamura T, Nakamoto K, et al. Thirty-day operative mortality for thoracotomy in lung cancer. *J Thorac Cardiovasc Surg* 1998; 115:70-73

- 4 Patel RL, Townsend ER, Fountain SW. Elective pneumonectomy: factors associated with morbidity and operative mortality. *Ann Thorac Surg* 1992; 54:84–88
- 5 Nagasaki F, Flehinger BJ, Martini N. Complications of surgery in the treatment of carcinoma of the lung. *Chest* 1982; 82:25–29
- 6 Keagy BA, Lores ME, Starek PJK, et al. Elective pulmonary lobectomy: factors associated with morbidity and operative mortality. *Ann Thorac Surg* 1985; 40:349–352
- 7 Deslauriers J, Ginsberg RJ, Piantadosi S, et al. Prospective assessment of 30-day operative morbidity for surgical resections in lung cancer. *Chest* 1994; 106:329S–330S
- 8 Harpole DH Jr, Liptay MJ, DeCamp MM Jr, et al. Prospective analysis of pneumonectomy: risk factors for major morbidity and cardiac dysrhythmias. *Ann Thorac Surg* 1996; 61:977–982
- 9 Dales RE, Dionne G, Leech JA, et al. Preoperative prediction of pulmonary complications following thoracic surgery. *Chest* 1993; 104:155–159
- 10 Mitsudomi T, Mizoue T, Yoshimatsu T, et al. Postoperative complications after pneumonectomy for treatment of lung cancer: multivariate analysis. *J Surg Oncol* 1996; 61:218–222
- 11 Abolhoda A, Liu D, Brooks A, et al. Prolonged air leak following radical upper lobectomy: an analysis of incidence and possible risk factors. *Chest* 1998; 113:1507–1510
- 12 Ribas J, Barbera JA, Mateu M, et al. Invasive exercise testing in the evaluation of patients at high-risk for lung resection. *Eur Respir J* 1998; 12:1429–1435
- 13 Gerson MC, Hurst JM, Hertzberg VC, et al. Prediction of cardiac and pulmonary complications related to elective abdominal and non cardiac thoracic surgery in geriatric patients. *Am J Med* 1990; 88:101–107
- 14 Kroenke K, Lawrence VA, Theroux JF, et al. Postoperative complications after thoracic and major abdominal surgery in patients with and without obstructive lung disease. *Chest* 1993; 104:1445–1451
- 15 Bolliger CT, Perruchoud AP. Functional evaluation of the lung resection candidate. *Eur Respir J* 1998; 11:198–212
- 16 Feinstein AR, Pritchett JA, Schimpff CR. The epidemiology of cancer therapy: IV. The extraction of data from medical records. *Arch Intern Med* 1969; 123:571–590
- 17 Dripps RD, Lamont A, Eckenhoff JE. The role of anesthesia in surgical mortality. *JAMA* 1961; 178:261–266
- 18 Chastre J, Fagon J-Y, Trouillet JL. Diagnosis and treatment of nosocomial pneumonia in patients in intensive care units. *Clin Infect Dis* 1995; 21(suppl 3):S226–S237
- 19 Bernard GR, Artigas A, Brigham KL, et al. The American-European consensus conference on ARDS: definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med* 1994; 149:818–824
- 20 American College of Chest Physicians/Society of Critical Care Medicine Consensus Committee. Definitions for sepsis and organ failures and guidelines for the use of innovative therapies in sepsis. *Crit Care Med* 1992; 20:864–874
- 21 Juhl B, Frost N. A comparison between measured and calculated changes in the lung function after operation for pulmonary cancer. *Acta Anaesth Scand* 1975; Suppl 57:39–45
- 22 Hosmer DW, Lemeshow S. *Applied logistic regression*. New York, NY: John Wiley, 1989; 140–145
- 23 Kirkwood BR. *Essential of medical statistics*. Cambridge, MA: Blackwell Scientific Publications, 1988; 173–183
- 24 Markos J, Mullan BP, Hillman DR, et al. Preoperative assessment as a predictor of mortality and morbidity after lung resection. *Am Rev Respir Dis* 1989; 139:902–910
- 25 Bush E, Verazin G, Antkowiak JG, et al. Pulmonary complications in patients undergoing thoracotomy for lung carcinoma. *Chest* 1994; 105:760–766
- 26 Korst RJ, Humphrey CB. Complete lobar collapse following pulmonary lobectomy: its incidence, predisposing factors, and clinical ramifications. *Chest* 1997; 111:1285–1289
- 27 Melendez JA, Carlon VA. Cardiopulmonary risk index does not predict complications after thoracic surgery. *Chest* 1998; 114:69–75
- 28 Wahi R, McMurtey MJ, DeCaro, et al. Determinants of perioperative morbidity and mortality after pneumonectomy. *Ann Thorac Surg* 1989; 48:33–37
- 29 Cerfolio RJ, Allen MS, Trastek VF, et al. Lung resection in patients with compromised pulmonary function. *Ann Thorac Surg* 1996; 62:342–351
- 30 Wright CD, Wain JC, Mathisen DJ, et al. Postpneumonectomy bronchopleural fistula after sutured bronchial closure: incidence, risk factors, and management. *J Thorac Cardiovasc Surg* 1996; 112:1367–1371
- 31 Garibaldi RA, Britt MR, Coleman ML, et al. Risk factors for postoperative pneumonia. *Am J Med* 1981; 70:877–880
- 32 Fagon JY, Chastre J, Hance AJ, et al. Detection of nosocomial lung infection in ventilated patients: use of a protected specimen brush and quantitative culture techniques in 147 patients. *Am Rev Respir Dis* 1988; 138:110–116
- 33 Hirschler-Schulte CJW, Hylkema BS, Meyer RW. Mechanical ventilation for acute postoperative respiratory failure after surgery for bronchial carcinoma. *Thorax* 1985; 40:387–390
- 34 Pedersen T, Eliassen K, Henriksen E. A prospective study of risk factors and cardiopulmonary complications associated with anesthesia and surgery: risk indicators of cardiopulmonary morbidity. *Acta Anaesthesiol Scand* 1990; 34:144–155
- 35 Forrest JB, Redher K, Cahalan MK, et al. Multicenter study of general anesthesia: III. Predictors of severe perioperative adverse outcomes. *Anesthesiology* 1992; 76:3–15
- 36 Kroenke K, Lawrence VA, Theroux JF, et al. Operative risk in patients with severe obstructive pulmonary disease. *Arch Intern Med* 1992; 152:967–971
- 37 Kearney DJ, Lee TH, Reilly JJ, et al. Assessment of operative risk in patients undergoing lung resection: importance of predicted pulmonary function. *Chest* 1994; 105:753–759