

# Prediction of Postoperative Pulmonary Complications in a Population-based Surgical Cohort

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## ABSTRACT

**Background:** Current knowledge of the risk for postoperative pulmonary complications (PPCs) rests on studies that narrowly selected patients and procedures. Hypothesizing that PPC occurrence could be predicted from a reduced set of perioperative variables, we aimed to develop a predictive index for a broad surgical population.

**Methods:** Patients undergoing surgical procedures given general, neuraxial, or regional anesthesia in 59 hospitals were randomly selected for this prospective, multicenter study. The main outcome was the development of at least one of the following: respiratory infection, respiratory failure, bronchospasm, atelectasis, pleural effusion, pneumothorax, or aspiration pneumonia. The cohort was randomly divided into a development subsample to construct a logistic regression model and a validation subsample. A PPC predictive index was constructed.

**Results:** Of 2,464 patients studied, 252 events were ob-

served in 123 (5%). Thirty-day mortality was higher in patients with a PPC (19.5%; 95% [CI], 12.5–26.5%) than in those without a PPC (0.5%; 95% CI, 0.2–0.8%). Regression modeling identified seven independent risk factors: low preoperative arterial oxygen saturation, acute respiratory infection during the previous month, age, preoperative anemia, upper abdominal or intrathoracic surgery, surgical duration of at least 2 h, and emergency surgery. The area under the receiver operating characteristic curve was 90% (95% CI, 85–94%) for the development subsample and 88% (95% CI, 84–93%) for the validation subsample.

**Conclusion:** The risk index based on seven objective, easily assessed factors has excellent discriminative ability. The index can be used to assess individual risk of PPC and focus further research on measures to improve patient care.

### What We Already Know about This Topic

- ❖ Postoperative pulmonary complications result in major morbidity and mortality, but risk factors for such complications are not described in a large, heterogeneous population.

### What This Article Tells Us That Is New

- ❖ In a prospective, multicenter study of nearly 2,500 patients, seven factors provided a sensitive and specific prediction of risk for postoperative pulmonary complications.
- ❖ Application of these data can stratify patients for risks in both research and clinical practice.

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**P**OSTOPERATIVE pulmonary complications (PPCs) account for a substantial proportion of risk related to surgery and anesthesia and are a major cause of postoperative morbidity, mortality, and longer hospital stays.<sup>1,2</sup> In one

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systematic review of studies of noncardiac surgery, the incidence of PPCs was found to vary from 2 to 19%.<sup>3</sup> Identifying patients at risk is an important first step toward improving surgical care, yet research on PPCs to date has been subject to sampling bias. For example, two important studies of risk that analyzed data from the National Veterans Affairs Quality Improvement Program in order to derive indices for predicting risk of pneumonia<sup>4</sup> and respiratory failure<sup>5</sup> after noncardiac surgery included mostly male veterans. Systematic review has detected many studies with such bias-introducing limitations as small sample size; narrow selection of patients, comorbidities, and operations; and retrospective or non-blinded outcome assessment. In addition, PPC definitions have differed.<sup>2</sup> Nonetheless, despite the limitations of such studies, groups still seek to establish risk-mitigating guidelines; the most ambitious attempt to date to marshal current knowledge on this clinical problem is the American College of Physicians guidelines for preventing PPCs in patients undergoing noncardiac surgery.<sup>2</sup> In this context, it is clear that it would be very useful to be able to predict the likelihood of PPCs from a reduced perioperative set of variables. Furthermore, an index would be most useful if applicable across a wide range of surgical settings.

We sought to reduce sampling bias by basing our analysis of risk factors on prospectively gathered data from a large population undergoing a broad range of surgical procedures. The population-based sample used was broadly representative of patients from a southern European territory that includes several large cities as well as rural areas. The participating hospitals were also representative of all levels of care. Our goals were to assess the incidence and characteristics of PPCs in this population and to build a scoring system with a reduced number of significant variables that would identify PPC risk in most clinical settings.

## Materials and Methods

### Design

We conducted a prospective, multicenter, observational study of a random-sample cohort of patients undergoing nonobstetric in-hospital surgical procedures with general, neuraxial, or regional anesthesia.

### Setting

The 59 participating Spanish hospitals (community, intermediate referral, or major tertiary care facilities) included all of the hospitals providing public health services in the autonomous community of Catalonia (7.36 million inhabitants) plus one center in Valencia. Throughout Spain, the entire population has full free access to National Health Service care such as these hospitals provide. The participating centers are known to perform 63% of all in-hospital anesthetic procedures that could provide the patients for the study. Non-participant centers in the area were private, and, according to a cross-sectional survey of anesthetic practices in Catalonia completed in 2003, their patients were younger, more fre-

quently women, and had lower American Society of Anesthesiologists physical status and surgical complexity.<sup>6,7</sup> Recruitment was carried out throughout a full year from January 10, 2006, to January 9, 2007. Follow-up ended in April 2007.

### Sampling

To reflect the seasonal, weekly, and daily distribution of the surgical caseload, patients were randomly selected using methods similar to those used in previous surveys.<sup>6-8</sup> Each center was notified of seven randomly assigned days of the year, one for each day of the week. Two restrictions were imposed: (1) each day of the study period should have a minimum of 1 and a maximum of 2 centers recruiting patients; and (2) for the 20 highest-volume centers, a minimum interval of 15 days should occur between two sampling days.

### Inclusion and Exclusion Criteria

On each assigned day, each participating center considered eligible all patients who underwent scheduled or emergency surgery with general, neuraxial, or regional anesthesia. The exclusion criteria were as follows: (1) younger than 18 yr of age; (2) obstetric procedures or any procedure during pregnancy; (3) procedures in which only local or peripheral nerve anesthesia was used; (4) procedures outside the operating room; (5) procedures related to a previous surgical complication; (6) patients who were reoperated on during the 90-day follow-up; (7) organ transplantation; (8) patients with preoperatively intubated trachea; and (9) outpatient procedures, defined as those requiring less than a 1-day stay for a patient alive at discharge.

### Ethical Considerations

The ethics committee of each participating center approved the study, and patients or significant others signed informed consent statements for data collection and follow-up telephone contact. If eligible patients were unable to provide consent, relatives or legal representatives were asked to consent. All patients received routine care; no research-related intervention was introduced.

### Data Collection

Each local research team consisted of anesthesiologists or was led by anesthesiologists. General and local training sessions were held to instruct the investigators on how to complete the structured questionnaire and how to identify the PPC outcomes recorded in the charts. Questionnaire variables and definitions are shown in Supplemental Digital Content 1, <http://links.lww.com/ALN/A646>. A short questionnaire on demographic characteristics, smoking status, and type of surgery (scheduled *vs.* emergency) was completed for patients who declined to take part in the study. Responses were uniformly recorded without regard to severity or whether an intervention was a scheduled or an emergency procedure. Local teams used a hot-pursuit approach (*i.e.*, regularly and assiduously checking records to ensure completeness of data

collection in real time and starting from admission). A centralized database and specific applications for remote data recording incorporated quality control algorithms to validate online data entry and identify missing data. A data manager checked entries and asked local teams to confirm completeness of records. An expert on the *International Classification of Diseases, Ninth Revision, Clinical Modification*, coded all diagnoses and procedures at the end of the study. To assess 30- and 90-day mortality, a structured survey was carried out by telephone operators who were blinded to perioperative variables and outcomes. All patients' names were also checked in the National Health Service Death Register for confirmation and date of death. If the date in our records differed from the date in the register, we considered the officially registered date to be valid.

### Outcomes

The main outcome, a PPC, was a composite of the in-hospital fatal or nonfatal postoperative events, as defined<sup>4,9-15</sup> in table 1. Although PPCs were recorded throughout the in-hospital postoperative period, the investigators—usually anesthesiologists—did not modify a center's customary management of patients. Patients with PPCs were identified by consulting medical records in real time, when they were being created, to find events that fulfilled any PPC definition. Any such event occurring during the hospital stay, regardless of postoperative day, was considered a PPC outcome. The secondary outcomes were postoperative length of stay (LOS) and 30-day and 90-day mortality rates.

### Sample Size

In a pilot study, we detected a PPC incidence of 4.1% in 172 patients, similar to previous studies.<sup>4,10</sup> According to a cross-sectional survey of anesthetic practices in Catalonia,<sup>7</sup> it was expected that the 59 participating centers would be able to recruit at least 2,500 eligible patients in a year and observe 100 patients with at least one PPC.

### Statistical Analysis

From the set of questionnaire variables (see table, Supplemental Digital Content 1, <http://links.lww.com/ALN/A646>), we selected potential PPC predictors, according to the investigators' consensus on measurable preoperative variables or the results of previous studies.<sup>2,4,5,10</sup> Independent continuous variables (age, oxygen saturation as measured by pulse oximetry [SpO<sub>2</sub>], and duration of surgery) were previously grouped into categories based on the investigators' clinical understanding. The unadjusted association of all these variables was evaluated for categorical (chi-square test and Fisher exact test) variables. Bivariate odds ratios and 95% CI values were also estimated. To assess collinearity between categorical variables, the relationships between them was tested by the Cramer V test (between nominal variables) and Kendall tau ( $\tau$ )  $\beta$  coefficient (between ordinal variables).

Before constructing the predictive logistic regression model, we randomly divided the sample into two parts: a

**Table 1.** Definitions of Postoperative Pulmonary Complications

Complication	Definition
Respiratory infection	When a patient received antibiotics for a suspected respiratory infection and met at least one of the following criteria <sup>4,9,10</sup> : new or changed sputum, new or changed lung opacities, fever, leukocyte count $>12,000/\mu$
Respiratory failure	When postoperative Pao <sub>2</sub> $<60$ mmHg on room air, a ratio of Pao <sub>2</sub> to inspired oxygen fraction $<300$ or arterial oxyhemoglobin saturation measured with pulse oximetry $<90\%$ and requiring oxygen therapy
Pleural effusion	Chest x-ray demonstrating blunting of the costophrenic angle, loss of the sharp silhouette of the ipsilateral hemidiaphragm in upright position, evidence of displacement of adjacent anatomical structures, or (in supine position) a hazy opacity in one hemithorax with preserved vascular shadows <sup>11</sup>
Atelectasis	Lung opacification with a shift of the mediastinum, hilum, or hemidiaphragm toward the affected area, and compensatory overinflation in the adjacent nonatelectatic lung <sup>12,13</sup>
Pneumothorax	Air in the pleural space with no vascular bed surrounding the visceral pleura <sup>14</sup>
Bronchospasm	Newly detected expiratory wheezing treated with bronchodilators
Aspiration pneumonitis	Acute lung injury after the inhalation of regurgitated gastric contents <sup>15</sup>

Pao<sub>2</sub> = partial pressure of oxygen in arterial blood.

development and a validation subsample. The development subsample (66.6% of patients) was used to construct the model and the validation subsample (33.3%) to confirm the model's discriminatory capability.

The logistic regression model was constructed using a backward stepwise selection procedure in which the presence of a PPC was the dependent variable. Independent predictors were entered into the model on the basis of the bivariate analysis ( $P < 0.05$ ) and correlation coefficients between variables lower than 0.4. Potential predictors were sequentially removed if this exclusion did not result in a significant change in the log-likelihood ratio test. The cutoff for variable removal was set at a significance level of 0.05. We then calculated the adjusted odds ratios and the corresponding 95% CI values. The calibration of the logistic regression model was assessed by the Hosmer-Lemeshow goodness-of-fit statistic. To avoid overfitting the data for the development sample, a bootstrap method was used to find the best subset of factors. One thousand computer-generated samples, each in-

cluding 1,623 individuals (*i.e.*, study subsample less one patient), were derived from the development subsample by random selection with replacement. Within each bootstrap sample, the  $\beta$  coefficient was calculated using all selected independent variables. The reliability of predictor variables in the final regression model was estimated by the 80% CI of the  $\beta$  coefficient in the bootstrap samples. Reliable predictors were expected to be retained if the 80% CI of bootstrap samples indicated statistical significance ( $P < 0.05$ ). The model's discriminative performance was assessed by the c-statistic.

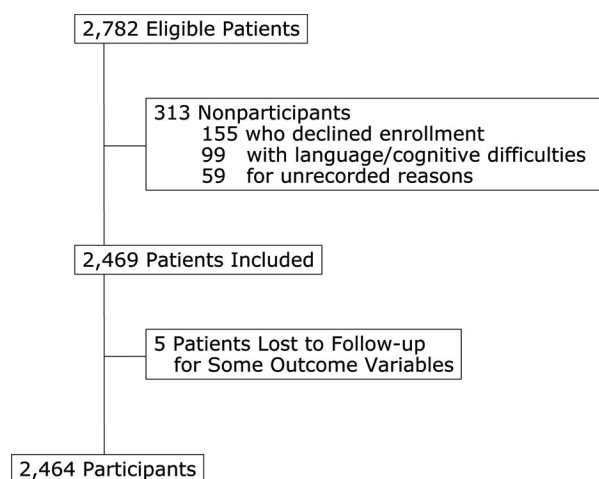
A simplified predictive risk score was then calculated by multiplying each logistic coefficient of regression ( $\beta$ ) by 10 and rounding off its value. The simplified scores for development subsample cases were added together to produce an overall PPC risk score for each patient. To evaluate the ability of the model to predict increasing rates of PPC, we used that score and the minimum description length principle<sup>16</sup> to divide the subsample into three ranges reflecting low, medium, and high risk for PPC, each containing a similar number of patients with a PPC. Finally, to assess the discriminative performance of this risk score in both the development and validation subsamples, we used the c-statistic, which was also displayed graphically as the area under the receiver operating characteristic (ROC) curve. The Mann-Whitney U test was used to compare postoperative LOS between patients with and without a PPC. The Kruskal-Wallis test was used to compare postoperative LOS between groups according to the number of PPCs (0, 1, 2–3, or 4 or more). The Mantel-Haenszel test was used to analyze trend in mortality rates between groups formed according to the number of PPCs. Statistical analyses were performed using the SPSS software package (IBM SPSS Statistics 18, Chicago, IL); this version includes algorithms for performing bootstrapping procedures.

### Quality Assurance

To evaluate the quality of recruitment and data collection, independent observers audited the medical records of a random sample of 150 patients (5% of the sample) from 12 randomly selected centers (4 community, 4 intermediate, and 4 major tertiary care hospitals). In every center, the number of patients audited was proportional to the number of patients recruited. It was found that the eligibility criteria were properly applied in all the audited centers. The data sample check included 130 items for each patient, encompassing all variables directly involved in the predictive model plus others; this data check found 379 instances of error or missing data (1.9% of the data audited), primarily involving time variables.

### Results

Of 2,782 eligible patients, 313 were nonresponders or refused to participate, and 5 were lost to follow-up for the recording of outcome variables; thus, of those recruited, 88.6% participated. Nonparticipants were more likely than



**Fig. 1.** Recruitment flowchart. Communication difficulties were related mainly to a language barrier or cognitive disorders. Patients lost to follow-up for outcome were those with unknown outcome information in the postoperative period (one appendectomy, one herniorrhaphy, and three minor peripheral orthopedic procedures).

participants to have undergone emergency surgery (34% *vs.* 14%,  $P < 0.001$ ) and to be current smokers (29% *vs.* 22%,  $P = 0.013$ ) and older (mean [SD], 61 [20] yr *vs.* 58 [18] yr,  $P = 0.004$ ). The final sample included in the statistical analysis, therefore, consisted of 2,464 inpatients (fig. 1). The characteristics of patients and procedures are detailed in table 2.

### PPCs, LOS, and Mortality

A total of 242 PPCs were recorded in 123 patients (5.0% of the 2,464 studied patients). Postoperative respiratory failure developed in 63 patients (2.6%), bronchospasm in 44 (1.8%), pleural effusion in 43 (1.7%), respiratory infection in 40 (1.6%), atelectasis in 35 (1.4%), aspiration pneumonia in 9 (0.4%), and pneumothorax in 8 (0.3%).

The median postoperative LOS was longer in patients with at least one PPC (12 days; 10–90th percentile, 4–36.8 days) than in those without a PPC (3 days; 10–90th percentile, 1–11 days). Thirty-five patients died within 30 days; 24 of these patients had at least one PPC (19.5% of the 123 patients with a PPC; 95% CI, 12.5–26.5%) and 11 had no PPC (0.5% of the 2,341 with no PPC; 95% CI, 0.2–0.8%). At 90 days, mortality was 24.4% (95% CI, 16.8–32.0%) of the 123 patients with at least one PPC and 1.2% (95% CI, 0.8–1.6%) of the 2,341 without a PPC ( $P < 0.001$  for all comparisons).

The highest PPC rate was after cardiac surgery (39.6%), followed by thoracic (31.4%), abdominal (7.2%), and vascular procedures (5.8%). In absolute terms, the largest contribution came from abdominal surgery. Table 3 shows detailed information on the characteristics of PPCs, mortality, and postoperative ventilation management by specialties. Six of 1,336 patients who received general anesthesia required postoperative reintubation. Table 4 shows postoperative LOS and mortality by number of PPCs. Both of

**Table 2.** Demographic and Clinical Characteristics

Total No. (%) of patients	2,464 (100)
Male sex, n (%)	1,251 (50.8)
Age, median (10–90th percentile), yr	60 (31.6–80.0)
Education, median (10–90th percentile), yr	9 (0–16)
Smoking status, n (%)	
Never smoker	1,230 (49.9)
Former smoker	729 (29.6)
Current smoker	505 (20.5)
Preoperative SpO <sub>2</sub> , median (10–90th percentile), %	97 (94–99)
Body mass index, median (10–90th percentile), kg/m <sup>2</sup>	26.3 (21.5–29.4)
COPD, n (%)	281 (11.4)
Respiratory infection in the last month, n (%)	146 (5.9)
ASA physical status, n (%)	
1	653 (26.5)
2	1,304 (52.9)
3	454 (18.4)
4	53 (2.2)
Emergency surgery, n (%)	349 (14.2)
Anesthesia, n (%)	
General	1,336 (54.2)
Neuraxial/regional	1,128 (45.8)
Surgical specialty, n (%)	
Orthopedic	799 (32.4)
General and digestive	726 (29.5)
Urology	276 (11.2)
Gynecology	174 (7.1)
ENT	133 (5.4)
Vascular	104 (4.2)
Breast	93 (3.8)
Cardiac	53 (2.2)
Thoracic	35 (1.4)
Neurosurgery	26 (1.1)
Other	45 (1.7)
Duration of surgery, median (10–90th percentile), h	1.8 (0.8–3.9)
Preoperative LOS, median (10–90th percentile), d	1 (0–2)
Postoperative LOS, median (10–90th percentile), d	3 (1–12)
30-day mortality, n (%)	35 (1.4)
90-day mortality, n (%)	59 (2.4)

ASA = American Society of Anesthesiologists; COPD = chronic obstructive pulmonary disease; ENT = ear, nose, and throat; LOS = length of stay; SpO<sub>2</sub> = oxyhemoglobin saturation by pulse oximetry breathing air in supine position.

these outcomes increased significantly as the number of PPCs increased.

### Risk Factors and PPC Scoring

The results for independent variables that were entered into the logistic regression model are shown in table 5, along with significant variables that were rejected because of high collinearity with other independent variables (smoking status and chronic obstructive pulmonary disease). Alcohol intake, snoring, sleepiness, obesity, diabe-

tes, immunosuppression, intraoperative fluid therapy, and postoperative pain were unrelated ( $P \geq 0.05$ ) to the presence of a PPC.

Multivariable logistic regression selected nine independent predictors of PPC: age, male sex, low preoperative SpO<sub>2</sub>, acute respiratory infection during the month before surgery, preoperative anemia (hemoglobin concentration lower than 10 g/dl), positive cough test, upper abdominal or intrathoracic surgery, duration of procedure, and emergency surgery. Bootstrap validation (1,000 subsamples of 1,623 cases) indicated that 7 of those 9 independent predictors were present in more than 80% of bootstrap samples and thus were retained in the final model. The raw and adjusted odds ratios for the seven variables are shown in table 6, which also shows the simplified risk score derived from the  $\beta$  coefficient for each variable. This seven-variable regression model had good discrimination (c-statistic, 0.90) and calibration (Hosmer-Lemeshow  $P = 0.45$ ) values. The ROC curves and the c-statistics for both the development and validation subsamples are presented in figure 2 (for the model using  $\beta$  coefficients) and figure 3 (for the model using the simplified risk score).

Table 7 shows the incidence of PPCs by risk score. The most relevant cut point was a simplified risk score of 26 (sensitivity 87.3% [95% CI, 77.7–94.0%], specificity 79.1% [95% CI, 77.0–81.1%]), which indicated moderate risk; a score greater than 45 indicated high risk (sensitivity 61.9% [95% CI, 49.7–73.2%], specificity 96.5% [95% CI: 95.5–97.4%]).

### Discussion

The 5% incidence of PPCs that we observed in a broad, heterogeneous surgical population fell within the range reported.<sup>3,5</sup> One of 5 patients who developed a PPC died within 30 days of surgery. Seven independent risk factors were finally selected in building a predictive score for PPC. Four patient-related factors (low preoperative SpO<sub>2</sub>, recent respiratory tract infection, age, and low hemoglobin concentration) accounted for approximately 55% of the total risk score. The remaining three predictors were related to the surgical procedure (intrathoracic or upper abdominal surgery, duration of procedure, and emergency surgery) and accounted for 45% of the score. Good discriminative power for identifying patients at risk of a PPC was indicated by an area under the ROC curve of 90% for the simplified score. Three risk factors identified by our procedure, but not included in the evidence-based American College of Physicians guidelines,<sup>2</sup> were low preoperative SpO<sub>2</sub>, recent respiratory infection, and preoperative anemia.

### Predictors of PPC

Preoperative SpO<sub>2</sub> breathing room air in supine position was the strongest patient-related PPC risk factor. We consider this to be a highly useful finding because SpO<sub>2</sub> is an easily recorded objective measure. To our knowledge, this is the

**Table 3.** Characteristics of PPCs and Postoperative Mechanical Ventilation According to Surgical Specialties

	General and Digestive	Cardiac	Orthopedic	Thoracic	Other	Total
Patients, n	726	53	799	35	851	2,464
Patients with at least 1 PPC, n (%)	52 (42.3)	21 (17.1)	19 (15.4)	11 (8.9)	20 (16.3)	123 (100)
Incidence of patients with at least 1 PPC within specialty, %	7.2	39.6	2.4	31.4	2.4	5.0
Patients with at least 1 PPC dead at 30 days, n (% of patients with PPC)	18 (34.6)	0 (0)	1 (5.3)	2 (18.2)	3 (15.0)	24 (19.5)
Patients with at least 1 PPC dead at 90 days, n (% of patients with PPC)	20 (38.5)	1 (4.8)	2 (10.5)	2 (18.2)	5 (25.0)	30 (24.4)
Patients with prolonged mechanical ventilation after surgery, n	27	50	7	2	31	117
Patients with prolonged mechanical ventilation >24 h, n (%)	11 (40.7)	9 (18.0)	0 (0)	0 (0)	7 (22.6)	27 (23.1)

PPC = postoperative pulmonary complication.

first time that preoperative SpO<sub>2</sub> has been tested as a predictor. We found a strong association between PPCs and respiratory disease (respiratory symptoms), smoking (lifetime exposure), and heart failure (table 5), consistent with previous studies.<sup>2</sup> However, these factors were not selected as independent predictors on multivariable analysis, probably because SpO<sub>2</sub> is a reflection of both respiratory and cardiovascular functional status.

A history of respiratory infection in the month before surgery, with fever and antibiotic treatment, encompasses both upper and lower airway infections. Each may have a different effect on morbidity.<sup>18–20</sup> Recent respiratory infections can cause local changes in airway reactivity, pulmonary function, and residual impairment of immunity induced by the infection itself or by antibiotic use. An increased risk of intraoperative respiratory events after an upper respiratory tract infection can persist for 4–6 weeks in children, especially if the trachea is intubated.<sup>18,19</sup> The ease with which such a history can be obtained from the patient and its high clinical value in predicting risk according to our findings suggest that it should be included in preoperative assessment. It might even be cause for postponing nonemergency surgery in some cases.

Age is a consistently reported predictor of PPCs,<sup>10,20</sup> and our findings confirm this. Furthermore, we found a clear deflection point (80 yr) at which the PPC rate increased

markedly (odds ratio of 5.6 after this age). This observation is particularly relevant in Western countries where the population is aging and where surgery is being extended to patients who had formerly been excluded.

Preoperative anemia (hemoglobin concentration lower than 10 g/dl) raised the risk for PPCs almost 3-fold, in agreement with recent studies identifying anemia as a predictor of poor outcome in critical and postoperative patients. Even minimal degrees of anemia are associated with a significant increase in the risk of 30-day postoperative mortality and cardiac events,<sup>22</sup> although so far, there is no clear evidence that preoperative transfusion would reduce risk.

We confirmed that surgery-related risk factors are highly relevant.<sup>2,5</sup> Those identified as independent predictors—namely anatomical site (upper abdomen or intrathoracic incisions), duration of surgery longer than 2 h, and emergency surgery—are factors that, to some extent, can be controlled by surgeons in patients at high risk.

Many studies identify smoking and chronic obstructive pulmonary disease as risk factors for PPC.<sup>2</sup> However, in our study, both showed a high level of collinearity with other factors. Current smokers had the lowest PPC rate in our study, whereas former smokers had the highest (see table 5). The reason for this finding might be that current smokers were on average 17 yr younger than former smokers. Lifetime exposure to smoking was chosen to enter the analysis because

**Table 4.** Postoperative LOS and Mortality According to the Number of PPCs

	No. of PPCs				Total No. of Patients
	0	1	2–3	≥4	
No. (%) of patients	2,341 (95.0)	66 (2.7)	37 (1.5)	20 (0.8)	2,464 (100)
Postoperative LOS, median (10–90th percentile), d*	3 (1–11)	10 (3–26.5)	11 (3.8–27.8)	27 (10.4–105.1)	3 (1–12)
30-day mortality, n (%)†	11 (0.5)	6 (9.1)	11 (29.7)	7 (35.0)	35 (1.4)
90-day mortality, n (%)†	29 (1.2)	7 (10.6)	12 (32.4)	11 (55.0)	59 (2.4)

\* Kruskal-Wallis test for comparing means,  $P < 0.0001$ . † Mantel-Haenszel test for mortality trend,  $P < 0.0001$ .

LOS = length of stay; PPC = postoperative pulmonary complication, a composite outcome in which 1 or more PPCs might be observed.

**Table 5.** Distribution of Results of Independent Variables in the Total Study Population of 2,464 Patients and the 123 Patients with at Least 1 PPC

	No. of Patients	Missing Patients	No. (%) of Patients with $\geq 1$ PPC	<i>P</i> Value
Variables entered into the multiple regression model				
Hospital type		0		<0.001
Community	641		14 (2.2)	
Intermediate referral	1,083		51 (4.7)	
Major tertiary care	740		58 (7.8)	
Sex		0		<0.001
Male	1,251		86 (6.9)	
Female	1,213		37 (3.0)	
Age, yr		0		<0.001
$\leq 50$	804		17 (2.1)	
51–80	1,410		75 (5.3)	
$> 80$	250		31 (12.4)	
Education, yr		2		0.002
$\leq 12$	1,836		106 (5.8)	
$> 12$	626		17 (2.7)	
Functional status		0		<0.001
Independent	2,212		99 (4.5)	
Partially or totally dependent	252		24 (9.5)	
Smokers: lifetime pack-year, n		2		<0.001
0	1,230		46 (3.7)	
1–40	935		38 (4.1)	
$> 40$	297		39 (13.1)	
Respiratory symptoms (cough, sputum, dyspnea, wheezing), n		1		<0.001
0	1,364		44 (3.2)	
1–2	833		44 (5.3)	
3–4	266		35 (13.2)	
Asthma		0		0.033
No	2,315		110 (4.8)	
Yes	149		13 (8.7)	
Other respiratory diseases		0		<0.001
No	2,322		99 (4.3)	
Yes	142		24 (16.9)	
Cough test*		8		<0.001
Negative	2,019		81 (4.0)	
Positive	437		38 (8.7)	
Respiratory infection in the last month		1		<0.001
No	2,317		97 (4.2)	
Yes	146		26 (17.8)	
Preoperative SpO <sub>2</sub> , %		2		<0.001
$\geq 96$	1,887		56 (3.0)	
91–95	519		51 (9.8)	
$\leq 90$	56		16 (28.6)	
Active oncologic disease in the last 5 yr		0		<0.001
No	2,069		83 (4.0)	
Yes	395		40 (10.1)	
Heart failure		0		<0.001
No	2,273		89 (3.9)	
Yes	191		34 (17.8)	
Coronary artery disease		0		<0.001
No	2,289		101 (4.4)	
Yes	175		22 (12.6)	
Hypertension		0		<0.001
No	1,591		61 (3.8)	
Yes	873		62 (7.1)	
Renal failure†		0		0.003
No	2,378		112 (4.7)	
Yes	86		11 (12.8)	
Neurologic disease		0		0.047
No	2,371		114 (4.8)	
Yes	93		9 (9.7)	
Liver disease		0		0.037
No	2,356		113 (4.8)	
Yes	108		10 (9.3)	

(continued)

Table 5. Continued

	No. of Patients	Missing Patients	No. (%) of Patients with $\geq 1$ PPC	P Value
Preoperative anemia†		0		<0.001
No	2,305		105 (4.6)	
Yes	159		18 (11.3)	
Preoperative nasogastric tube		0		<0.001
No	2,378		105 (4.4)	
Yes	86		18 (20.9)	
Preoperative length of stay, d		0		<0.001
<2	2,156		81 (3.8)	
$\geq 2$	308		42 (13.6)	
Type of surgery		0		<0.001
Scheduled	2,115		93 (4.4)	
Emergency	349		30 (8.6)	
Anesthesia		0		<0.001
Regional (neuraxial or plexus)	1,128		23 (2.0)	
General	1,336		100 (7.5)	
Surgical incision		0		<0.001
Peripheral	2,013		45 (2.2)	
Upper abdominal	361		44 (12.2)	
Intrathoracic	90		34 (37.8)	
Surgical invasiveness§		0		<0.001
1–2 (low)	1,605		24 (1.5)	
3 (intermediate)	711		54 (7.6)	
4–5 (high)	148		45 (30.4)	
Intraoperative nasogastric tube		0		<0.001
No	2,074		55 (2.7)	
Yes	390		68 (17.4)	
Intraoperative bladder catheter		1		<0.001
No	1,524		27 (1.8)	
Yes	939		96 (10.2)	
Preoperative prophylaxis with antibiotics		1		<0.001
No	669		12 (1.8)	
Yes	1,794		111 (6.2)	
Intraoperative blood transfusion		3		<0.001
No	2,348		100 (4.3)	
Yes	113		22 (19.5)	
Intraoperative pulmonary complications		0		<0.001
No	2,213		81 (3.7)	
Yes	251		42 (16.7)	
Intraoperative cardiovascular complications		0		<0.001
No	2,022		72 (3.6)	
Yes	442		51 (11.5)	
Duration of surgery, h		0		<0.001
$\leq 2$ h	1,958		48 (2.5)	
>2 to 3 h	272		25 (9.2)	
>3 h	234		50 (21.4)	
Significant variables not entered into the multiple regression model due to high collinearity				
ASA physical status		0		<0.001
1	653		10 (1.5)	
2	1,304		29 (2.2)	
3	454		64 (14.1)	
4	53		20 (37.7)	
Smoking status		0		<0.001
Never smoker	1,230		46 (3.7)	
Former smoker	729		65 (8.9)	
Current smoker	505		12 (2.4)	
COPD		0		<0.001
No	2,183		77 (3.5)	
Yes	281		46 (16.4)	

\* In the cough test, the patient is asked to take a deep breath and cough once. A positive test is defined by repeated coughing after the first cough.<sup>10</sup> † Renal failure, defined as serum creatinine >2.5 mg/dl. ‡ Preoperative anemia, defined as hemoglobin <10 g/dl. § Scoring as described by Holt and Silverman.<sup>17</sup>

ASA = American Society of Anesthesiologists; COPD = chronic obstructive pulmonary disease; PPC = postoperative pulmonary complication; SpO<sub>2</sub> = peripheral arterial oxygen saturation breathing room air in supine position measured by pulse oximetry.

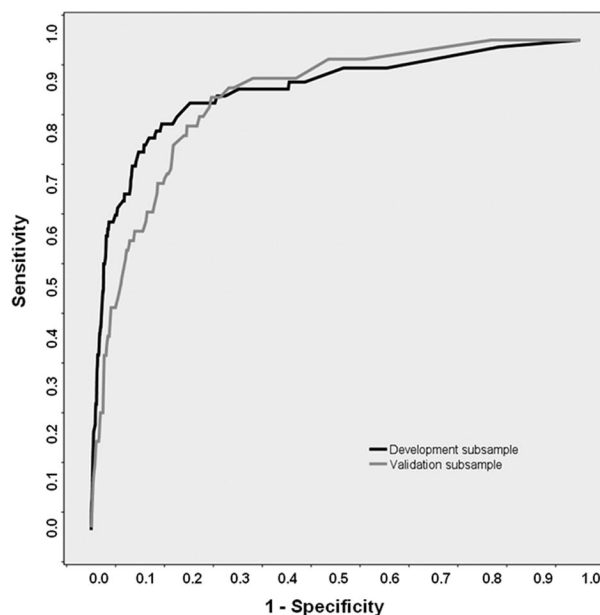
**Table 6.** Independent Predictors of Risk for PPCs Identified in the Logistic Regression Model

	Multivariate Analysis OR (95% CI) n = 1,624*	$\beta$ Coefficient	Risk Score†
Age, yr			
≤50	1		
51–80	1.4 (0.6–3.3)	0.331	3
>80	5.1 (1.9–13.3)	1.619	16
Preoperative SpO <sub>2</sub> , %			
≥96	1		
91–95	2.2 (1.2–4.2)	0.802	8
≤90	10.7 (4.1–28.1)	2.375	24
Respiratory infection in the last month	5.5 (2.6–11.5)	1.698	17
Preoperative anemia (≤10 g/dl)	3.0 (1.4–6.5)	1.105	11
Surgical incision			
Peripheral	1		
Upper abdominal	4.4 (2.3–8.5)	1.480	15
Intrathoracic	11.4 (4.9–26.0)	2.431	24
Duration of surgery, h			
≤2	1		
>2 to 3	4.9 (2.4–10.1)	1.593	16
>3	9.7 (4.7–19.9)	2.268	23
Emergency procedure	2.2 (1.0–4.5)	0.768	8

\* Because of a missing value for some variables, three patients were excluded. Logistic regression model constructed with the development subsample, c-index = 0.90; Hosmer-Lemeshow chi-square test = 7.862;  $P = 0.447$ . † The simplified risk score was the sum of each  $\beta$  logistic regression coefficient multiplied by 10, after rounding off its value.

CI = confidence interval; OR = odds ratio; PPC = postoperative pulmonary complications; SpO<sub>2</sub> = oxyhemoglobin saturation by pulse oximetry breathing air in supine position.

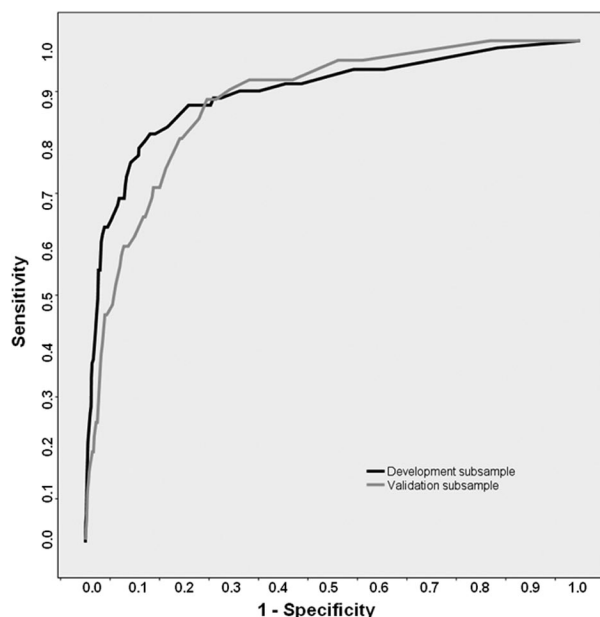
exposure in excess of 40 pack-years was associated with higher risk in the bivariate analysis; nonetheless, the independence of this factor was not confirmed, so it was removed. With regard to chronic obstructive pulmonary disease, it is important to take into account that when this disease is mentioned in a patient's chart, it is often based on clinical criteria rather than a confirmed spirometric diagnosis.<sup>23</sup> For this reason, we considered that respiratory symptoms, which are easily recorded during the pre-anesthetic consultation by means of the Medical Research Council questionnaire,<sup>24</sup> would perhaps provide a better candidate for inclusion in the regression analysis. Furthermore, there is some suggestion in the literature that the larger the number of abnormal clinical findings present, the more severe the obstructive lung disease will probably be.<sup>25,26</sup> However, respiratory symptoms also failed to emerge as an independent factor on multivariable analysis.



**Fig. 2.** Receiver operating characteristic (ROC) curve drawn for the model built using  $\beta$  coefficients. Development subsample, c-statistic for the area under the ROC curve (AUC) = 0.90 (95% confidence interval [CI], 0.85–0.94); validation subsample, c-statistic for the AUC = 0.88 (95% CI, 0.84–0.93).

### Study Strengths and Limitations

A strength of the current study was its prospective, population-based, multicenter design. We collected data for a representative random sample of surgical patients undergoing



**Fig. 3.** Receiver operating characteristic (ROC) curve drawn using the simplified risk score. Development subsample, c-statistic for the area under the ROC curve (AUC) = 0.89 (95% confidence interval [CI], 0.83–0.93); validation subsample, c-statistic for the AUC = 0.84 (95% CI, 0.77–0.90). The simplified risk score was obtained by multiplying the logistic regression  $\beta$  coefficient by 10 and rounding off its value.

**Table 7.** PPC Risk Score: Distribution of Patients and Rates by Intervals

	Risk Score Intervals*		
	Low Risk <26 Points	Intermediate Risk 26–44 Points	High Risk ≥45 Points
Development subsample, No. (%) of patients†	1,238 (76.2)	288 (17.7)	98 (6.0)
Validation subsample, No. (%) of patients	645 (77.1)	135 (16.1)	57 (6.8)
PPC rate, development subsample, % (95% CI)	0.7 (0.2–1.2)	6.3 (3.5–9.1)	44.9 (35.1–54.7)
PPC rate, validation subsample, % (95% CI)	1.6 (0.6–2.6)	13.3 (7.6–19.0)	42.1 (29.3–54.9)

\* Risk intervals were based on division of the development subsample into optimal risk intervals, according to the simplified risk score and applying the minimum description length principle. † Three patients were excluded because of a missing value in some variable. CI = confidence interval; PPC = postoperative pulmonary complication.

routine anesthetic procedures for each type of surgery during the course of a year and throughout an extensive geographic area that included rural, semirural, and urban populations with wide-ranging health and social status. We decided to include patients undergoing cardiac surgery because they make up a substantial part of the surgical caseload and have both procedure-related and other risk factors common to all surgical patients (see table 3). A recent study of a large general surgical population reported a mortality rate for cardiac surgery that was lower than the average for all surgical procedures,<sup>27</sup> suggesting that it need not be singled out as a special higher-risk setting *a priori*. We did exclude patients undergoing procedures of very low complexity, performed on an outpatient basis, or involving only peripheral or local anesthesia. We consider that by applying these inclusion and exclusion criteria, we accomplished our goal of taking an approach that would be relevant to the real world of anesthetics and surgery in which PPCs are a serious threat.

A limitation of our study was that the sample size was not large enough to develop adequately a multivariable regression model in which 33 predictors were entered. For this reason, after performing the multivariable analysis, we re-sampled the development subsample using a bootstrapping technique. The purpose was to avoid overfitting and to estimate the stability of the dataset. As a result, seven of nine variables initially identified by multivariable regression were retained in the model. Only those seven variables were then used to build up the predictive index. Alternatively, based on the performance of the model in the validation subsample, it would also be possible to propose a parsimonious model with only three factors because such a reduced model would preserve much of the predictive power of the seven-factor model. In fact, the three most powerful variables (*i.e.*, SpO<sub>2</sub>, surgical incision, and duration of surgery) give an area under the ROC curve of more than 0.87. However, various other combinations of three risk factors would likewise give high c-statistics such that the clinical utility of one three-factor model would not be clearly greater than the utility of another

one. We, therefore, chose to emphasize the clinical interest of the full range of seven relevant variables identified in the development subsample, given the ease with which information on all these factors can be obtained in most settings and because some of them can be preoperatively managed. The use of this seven-variable model also allowed us to stratify PPC risk on three levels (table 7).

Another possible limitation is our definition of PPC. A more stringent definition would probably have increased the impact of PPC on mortality and postoperative LOS. However, we chose to follow the approach of most PPC studies to date in which risk is established for a composite outcome,<sup>2</sup> one that can occur in the presence of any of several or all of a list of complications. We observed that removing individual PPCs from the composite did not have an appreciable effect on the prediction capacity. For example, if we were to remove bronchospasm from the composite outcome, the area under the ROC curve would change only slightly, from 0.90 to 0.89 in the development subsample. Furthermore, it is worth noting that even the appearance of a single PPC among those that comprise the composite was independently associated with increased LOS and mortality (table 4).

A third potential limitation of the study was the participation of more than 200 recorders of data in 59 hospitals. However, we took measures to avoid inconsistencies and designed a questionnaire that addressed major medical conditions. We also conducted training sessions for the investigators and checked for and ruled out an effect of center. A fourth potential limitation was that in some centers, the observers were also the anesthesiologists in charge of patient care. We, therefore, included a quality assurance step in which medical records were checked by independent auditors to assure compliance with instructions. A fifth limitation was that the characteristics of nonresponders suggest that the PPC incidence may have been underestimated in patients who were older, who were smokers, or who underwent emergency surgery. The high response rate, however, means that

the effect of this unavoidable methodological problem would be minimal.

Finally, we must also be concerned about possible imprecision in the definition of some preexisting conditions, given that diagnoses were established from the medical records or patient interviews. We felt that, for the purpose of this study, the recorded clinical data would suffice in the interest of convenience. In relation to this limitation, there is a possible concern that we deliberately excluded laboratory or spirometric tests, although certain abnormalities have been associated with PPCs.<sup>2</sup> We did so because such tests (notably spirometry) would be difficult to undertake systematically in all clinical settings. In the example of spirometry, most of the patients this test would identify as high risk can be found preoperatively equally well by clinical evaluation of symptoms,<sup>23</sup> which are readily evaluated with the Medical Research Council respiratory questionnaire<sup>24</sup> we used.

### Possible Usefulness of the Score

We sought a clinically convenient, as well as statistically defensible, scoring system. The American Society of Anesthesiologists physical status classification is a patient-related factor that is consistently reported to be associated with PPCs.<sup>2</sup> We decided *a priori* to exclude it from the model so as not to mask other factors; furthermore, great variability in an American Society of Anesthesiologists physical status assessment has been reported,<sup>28</sup> and we considered it preferable to include objective factors that might be more easily and confidently assessed by clinicians. In this regard, three of the variables included in the risk index we propose ( $\text{SpO}_2$ , age, and hemoglobin concentration) are easily quantifiable and verifiable, and the three surgical risk factors can be anticipated. In some cases, the risk index may guide strategies to avoid or allay possible PPCs and to prompt the consideration of nonsurgical alternatives or the advisability of postponing surgery for some time. In selected high-risk patients, the preoperative quantification of surgical risk may be of help in explaining risk objectively to patients before scheduling and in encouraging adherence to measures to reduce risk for PPCs, such as preoperative respiratory physiotherapy, among others.<sup>29</sup>

Given the conspicuous importance of the duration of surgery and the location of the surgical incision in the development of PPCs, special attention should be given to modifying procedures, whenever possible, to shorten them and take tissue-sparing approaches.

In summary, our study identified seven straightforward, objective, and easily assessed factors associated with the appearance of PPCs. A simple risk score based on these factors predicted the development of PPCs in a broad and diverse surgical population sample and allowed us to stratify that sample by level of risk. To test the clinical value of the risk index, we propose to validate it in other geographic areas. Research could also consider the predictive power of preoperative  $\text{SpO}_2$  and the advisability of postponing surgery if a

recent respiratory infection is reported, as well as test the effect of treating preoperative anemia.

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## ANESTHESIOLOGY REFLECTIONS

### Erdmann's Life Membership No. 1 in the ASA



In 1905 Adolph Frederick Erdmann, M.D. (1867–1953), gathered eight medical colleagues and founded the Long Island Society of Anesthetists, a group which evolved successively into the New York Society of Anesthetists (1911), the American Society of Anesthetists (1935), and finally the American Society of Anesthesiologists (ASA) (1945). A teetotaling nonsmoker, Erdmann invented an ether dropper and promoted use of perioperative music for relaxing patients. After "Fred" Erdmann retired in 1937 from active practice, the Society's secretary, Paul M. Wood, M.D., signed a wallet-sized "Silver Certificate" (above) that declared that Erdmann was "a member in good standing for the year life" and "Active Member No. 1." In 1947 the ASA honored Erdmann with its third Distinguished Service Award. (Copyright © the American Society of Anesthesiologists, Inc. This image appears in color in the *Anesthesiology Reflections* online collection available at [www.anesthesiology.org](http://www.anesthesiology.org).)

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