

# Multifactorial Risk Index for Predicting Postoperative Respiratory Failure in Men After Major Noncardiac Surgery

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## Objective

To develop and validate a preoperative risk index for predicting postoperative respiratory failure (PRF).

## Summary Background Data

Respiratory failure is an important postoperative complication.

## Method

Based on a prospective cohort study, cases from 44 Veterans Affairs Medical Centers (n = 81,719) were used to develop the models. Cases from 132 Veterans Affairs Medical Centers (n = 99,390) were used as a validation sample. PRF was defined as mechanical ventilation for more than 48 hours after surgery or reintubation and mechanical ventilation after postoperative extubation. Ventilator-dependent, comatose, do not resuscitate, and female patients were excluded.

## Results

PRF developed in 2,746 patients (3.4%). The respiratory failure risk index was developed from a simplified logistic regression model and included abdominal aortic aneurysm repair, thoracic surgery, neurosurgery, upper abdominal surgery, peripheral vascular surgery, neck surgery, emergency surgery, albumin level less than 30 g/L, blood urea nitrogen level more than 30 mg/dL, dependent functional status, chronic obstructive pulmonary disease, and age.

## Conclusions

The respiratory failure risk index is a validated model for identifying patients at risk for developing PRF and may be useful for guiding perioperative respiratory care.

Postoperative pulmonary complications greatly contribute to the death and complication rates of surgery. It has

been reported that 5% to 10% of all surgical patients and 9% to 40% of those undergoing abdominal surgery experience postoperative pulmonary complications.<sup>1</sup> In prior studies, the definition of what constitutes a postoperative pulmonary complication varied greatly. Atelectasis,<sup>2,3</sup> postoperative pneumonia,<sup>2–4</sup> acute respiratory distress syndrome,<sup>4,5</sup> and postoperative respiratory failure<sup>6,7</sup> have all been classified as postoperative pulmonary complications. Although the clinical significance of each of these complications varies, they are often grouped together in studies of risk factors for postoperative pulmonary complications.<sup>8</sup>

Postoperative respiratory failure (PRF) is among the most serious of the postoperative pulmonary complications. It is most commonly defined as the inability to be extubated 48

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**Table 1. VARIABLE DEFINITIONS**

Age	Patient's age in years on date of surgery.
Functional health status	Corresponding level of self-care demonstrated by the patient on admission to the hospital, reflecting patient's prehospitalization functional status.
Independent	Patient is independent in activities of daily living, and does not require assistance of nursing care, equipment, or devices (includes a person who is able to function independently with a prosthesis).
Partially dependent	Patient requires use of equipment or devices coupled with assistance from another person for some activities of daily living. Any patient coming from a nursing home setting who is not totally dependent would fall into this category, as would any patient who requires kidney dialysis or home ventilator support, yet maintains some independent functions.
Totally dependent	Patient cannot perform any activities of daily living for him/herself (includes a patient in an ICU/floor who is totally dependent upon nursing care, or a dependent nursing home patient).
Diabetes mellitus	Metabolic disorder of the pancreas whereby the patient requires daily dosages of exogenous parenteral insulin or an oral hypoglycemic agent to prevent hyperglycemia or metabolic acidosis. Three categories:
No diabetes	Patient has no diagnosis of diabetes mellitus or diabetes is controlled by diet alone.
Oral therapy	Patient has a diagnosis of diabetes mellitus requiring therapy with an oral hypoglycemic agent (e.g., glyburide or glipizide) in the 2 weeks before surgery.
Insulin therapy	Patient has a diagnosis of diabetes mellitus requiring daily insulin therapy within the 2 weeks before surgery.
Alcohol use	Patient admits to drinking >2 oz. hard liquor or >2 beers per day in the 2 weeks before admission for surgery.
Weight loss	Greater than 10% weight decrease in body weight in the immediate 6-month period before surgery, as manifested by serial weights in the chart, as reported by the patient, or as evidenced by change in clothing size or severe cachexia. Patients who had intentionally lost weight as part of a weight reduction program were excluded.
Disseminated cancer	Patient has cancer that has spread to more than one site in addition to the primary site, and the presence of multiple metastases indicate that the cancer is widespread, fulminant, or near-terminal.
Smoking	Current smoker within 2 weeks of index surgery.
Preoperative pneumonia	Documentation of an infiltrate on chest x-ray, and/or positive sputum cultures with the initiation of appropriate antibiotic therapy.
History of COPD	Patient has COPD resulting in any one or more of the following: functional disability, hospitalization in the past for treatment of COPD, requiring bronchodilator therapy, and FEV <sub>1</sub> of less than 75% of predicted. Patients excluded from this category included those in whom the only pulmonary disease was acute asthma, an acute and chronic inflammatory disease of the airways resulting in bronchospasm.
Dyspnea	The patient describes difficult, painful, or labored breathing. The dyspneic patient is subjectively aware of difficulty with breathing. Patients categorized based on the patient's subjective experience coupled with study nurse's assessment:
No dyspnea	No dyspnea is present.
Dyspnea on minimal exertion	The patient becomes dyspneic upon modest exertion, e.g., is unable to climb one flight of stairs without shortness of breath.
Dyspnea at rest	The patient is dyspneic at rest, e.g., the resting respiratory rate is >30 respirations/min.
Impaired sensorium	Patient is acutely confused and/or delirious and responds to verbal and/or mild tactile stimulation; patients with mental status changes, and/or delirium in the context of the current illness. Patients with chronic mental status changes secondary to chronic mental illness or chronic dementing illnesses were excluded from this category.
Neuromuscular degenerative disease	Any of a number of congenital, hereditary, or acquired diseases resulting in chronic neurologic deficits, including muscular dystrophy, amyotrophic lateral sclerosis, multiple sclerosis, and poliomyelitis.
History of CVA with residual neurological deficit	History of CVA (embolic, thrombotic, or hemorrhagic) with persistent motor, sensory, or cognitive dysfunction.
Tumor involving the central nervous system	Space-occupying lesions of the brain which may be benign or primary or secondary malignancies.
History of myocardial infarction	History of a non-Q wave or a Q-wave infarct in the 6 months before surgery as diagnosed in the patient's medical record.
History of PTCA	Patient has undergone PTCA at any time (does not include valvuloplasty procedures).
History of angina	Within 1 month before surgery, patient experiences pain or discomfort between the diaphragm and the mandible resulting from myocardial ischemia.
History of congestive heart failure	Patient experiences related manifestations within 1 month before surgery, including abnormal limitation in exercise tolerance due to dyspnea or fatigue, orthopnea, paroxysmal nocturnal dyspnea, increased jugular venous pressure, pulmonary rales on physical exam, cardiomegaly, pulmonary vascular engorgement.
History of cardiac operation requiring cardiopulmonary bypass	Cardiac operations requiring use of cardiopulmonary bypass; includes coronary artery bypass graft surgery, valve replacement or repair, repair of atrial or ventricular septal defects, etc.
Preoperative renal failure	Clinical condition associated with rapid, steadily increasing azotemia (increase in BUN), with a urinary output of <500cc/24-hr period, and a rising creatinine of above 3 mg/dL.
Transfusion	Preoperative loss of blood necessitating a minimum of 4 units of whole blood/packed red cells transfused during the present admission, including any transfused in the emergency room.

(continues)

**Table 1 VARIABLE DEFINITIONS** (continued)

Emergency surgery	A surgical procedure which must be performed as soon as possible and no later than 12 hours after the patient has been admitted to the hospital or after the onset of related preoperative symptomatology.
Type of anesthesia	The principal anesthesia technique used: general (including IV anesthesia with intubation), spinal, epidural, regional, local or monitored anesthesia.
Cardiac arrest requiring cardiopulmonary resuscitation	Any cardiac arrest requiring external or open cardiopulmonary resuscitation of any duration, occurring in the operating room, intensive care unit, ward, or out-of-hospital after the chest has been completely closed and within 30 days after surgery.
Systemic sepsis	Patient is noted to be acutely ill, usually febrile, resulting from the presence of microorganisms or their poisonous products in the blood stream. Patient has one or more positive blood cultures and antibiotic therapy was instituted.
Postoperative pneumonia	Patient had positive sputum cultures and was being treated with antibiotics, or had an infiltrate on a chest x-ray diagnosed as pneumonia or pneumonitis.
Postoperative pulmonary edema	Patient developed respiratory distress with evidence of fluid accumulation in the lungs by clinical exam, chest x-ray, or invasive monitoring that was treated with intravenously administered diuretic therapy.

BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; CVA, cerebral vascular accident; FEV<sub>1</sub>, forced expiratory volume in 1 second; PTCA, percutaneous transluminal coronary angioplasty.

hours after surgery,<sup>6</sup> although some investigators have used 5 days.<sup>7</sup> Among patients undergoing abdominal aortic aneurysm repair, the rate of PRF is 5% to 21%, depending on the type of aneurysm.<sup>7</sup> More importantly, the in-hospital death rate for patients with PRF is 40% to 42% versus 6% for those without PRF.<sup>7</sup>

Prior studies have suggested that the risk factors for PRF include those that are patient-specific and those that are operation-specific. The patient-specific risk factors can be divided into those related to the patient's general health status (*e.g.*, age,<sup>3</sup> functional status, diabetes mellitus, cancer, alcohol use), pulmonary status (*e.g.*, smoking,<sup>3,4-6</sup> chronic obstructive pulmonary disease [COPD],<sup>9,10</sup> increased body mass index,<sup>3</sup>), neurologic status (*e.g.*, impaired sensorium<sup>3</sup>), cardiac status (*e.g.*, myocardial infarction<sup>6</sup>), and renal and fluid status (*e.g.*, renal failure,<sup>6,7</sup> blood transfusion<sup>11</sup>). The operation-specific risk factors include the location of the incision in relation to the diaphragm,<sup>3,7</sup> emergent operation, and the type of anesthesia used (*e.g.*, general vs. spinal).

The main objective of this study was to determine the preoperative predictors of PRF in a large multicenter observational cohort of subjects undergoing major noncardiac surgery. Specific goals included identifying predictors of PRF that are easily obtained and commonly accessible to care providers before surgery. Using these predictors, a risk assessment model and scoring system analogous to risk assessment models for postoperative cardiac complications<sup>12-14</sup> was developed and validated.

## METHODS

Subjects were selected from the National Veterans Affairs Surgical Quality Improvement Program (NSQIP). A detailed description of the study methods has been published previously and is briefly summarized here.<sup>15-17</sup>

## Participating Hospitals

Phase I of the study included patients enrolled between Oct. 1, 1991, and Dec. 31, 1993, and was conducted at 44 Veterans Affairs Medical Centers (VAMCs) that were closely affiliated with university medical centers and offered both cardiac and noncardiac surgery. Phase II of the study included patients enrolled between Jan. 1, 1994, and Aug. 31, 1995, and was conducted at all 132 VAMCs that perform major surgery.

## Selection of Subjects

All noncardiac operations performed under general, spinal, or epidural anesthesia were eligible for inclusion as index operations. Based on a review of the surgical death rates from the Veterans Affairs administrative discharge database for 1988 and 1989, selected operations with very low death rates such as dental procedures, central line insertions, dressing changes, and endoscopic procedures were excluded from the NSQIP.<sup>18</sup> Major transplantation procedures and cases entered into the study within the previous 30 days were also excluded. Because the data were obtained from veterans undergoing surgery in VAMCs, most of the patients were men. Female patients tended to be much younger and healthier than male patients and had better outcomes in the NSQIP. Specifically for this study, operations performed on patients who were female, ventilator-dependent, or comatose or had a do-not-resuscitate (DNR) order were excluded from analysis. All eligible operations were included at low-volume centers (<140 eligible operations per month). At high-volume centers (>140 eligible operations per month), the first 36 consecutive eligible operations were entered in each consecutive 8-day period, beginning with a different day each period. Only the first five transurethral resections of the prostate and tumors of the bladder performed in each 8-day cycle were

**Table 2. CLASSIFICATION OF SURGERY BY TYPE OF SURGERY AND LOCATION OF INCISION**

Type of Surgery	Specific Surgery/Location of Incision
Thoracic surgery	Includes: esophagus resection, esophageal repair, mediastinoscopy, pleural biopsy, pneumocentesis, chest wall excision, incision and drainage of neck and thorax, excision of neck and thorax, repair of fractured ribs, diaphragmatic hernia repair, bronchoscopy, catheterization of trachea, trachea repair, thoracotomy, pericardium, pacemaker placement, heart wound repair, valve repair, thoracic or abdominal-thoracic aortic aneurysm repair, and pulmonary artery procedures.
Peripheral vascular surgery	Any surgery related to the arteries or veins except central nervous system aneurysm or abdominal aortic aneurysm repair.
Upper abdominal surgery	Includes: gastrectomy, vagotomy, intestinal surgery, partial hepatectomy, subfascial abdominal excision, splenectomy, excision of abdominal masses, laparoscopic appendectomy and cholecystectomy, shunt insertion, ventral, umbilical and spigelian hernia repair; surgery related to the liver, gallbladder, and pancreas.
Abdominal aortic aneurysm	Includes: repair of ruptured or unruptured aortic aneurysm involving only abdominal incisions.
Neurosurgery	Includes: application of a halo, central nervous system injection, central nervous system drainage, burr hole, craniectomy, craniotomy, arteriovenous malformation or aneurysm repair, stereotaxis, neurostimulator placement, skull repair, and cerebral spinal fluid shunt.
Neck Surgery	Surgeries related to the thyroid, parathyroid, and larynx. Includes: tracheostomy; cervical and axillary lymph node excision; cervical and axillary lymphadenectomy.
Other Surgery	These categories were grouped together as "other surgery" and were found to have the lowest associated risk for postoperative respiratory failure in univariate analyses:
Extremities	Nonvascular surgery related to the humerus, elbow, forearm, wrist, hand, fingers, pelvis, hip, femur, knee, tibia, fibula, ankle, or foot; arthroscopy.
Eye, ear, nose, and mouth surgery	Surgery related to the lips, tongue, vestibule and floor of mouth, dentoalveolar area, palate, uvula, salivary glands, pharynx, adenoids, tonsils, auditory canal, mandibular, dental bone, nose, or sinuses; ophthalmological surgery; laryngeal endoscopy.
Lower abdomen	Femoral or inguinal hernia repair; radical perineal procedure; lymphadenectomy of pelvic, paraaortic, or renal nodes; urologic surgeries related to kidney, ureter, bladder; male and female genital surgery; surgery related to appendix, rectum, anus.
Skin	Superficial incision and drainage, all dermatology operations.
Spine and back	Excision of tumor from back, surgery related to spine, laminectomy, intraspinal lesion excision, and nerve blocks.

included because of the large number of these procedures that were performed.

## Data Collection

A surgical risk assessment nurse was assigned at each center to collect the data. These nurses completed in-depth training on the protocol and study definitions. Annual meetings and regular conference calls were conducted, and two traveling nurse coordinators performed site visits to maintain data reliability.

Generic preoperative, intraoperative, and postoperative variables were chosen on the basis of clinical relevance, reliability of data collection, and availability of data. Relevant variable definitions are given in Table 1.<sup>18</sup> Preoperative data were obtained by the study nurse from the medical chart or a surgical risk assessment profile that was completed by the surgical resident caring for the patient and was later verified by the study nurse from the medical chart. Preoperative laboratory values within 30 days of the index operation and closest to the time of operation were acquired automatically from the laboratory software in each center's computer system. Intraoperative variables were collected from the surgical log and anesthesia record for the index

operation. The index operation was defined as the first eligible operation performed on the patient. Other operations performed under the same anesthetic by the same or a different surgical team were also recorded. Specifically for this study, the type of surgery was primarily classified by the anatomical location of the surgical incision (Table 2).

Patients were followed for 30 days after surgery. Thirty-day surgical death was defined as death from any cause inside or outside the hospital within 30 days of surgery. Patients were defined as having respiratory failure if the total duration of ventilator-assisted respiration during the postoperative hospital stay exceeded 48 hours. Patients were defined as having unplanned intubation if they required placement of an endotracheal tube and mechanical or assisted ventilation because of respiratory or cardiac failure manifested by severe respiratory distress, hypoxia, hypercarbia, or respiratory acidosis subsequent to extubation after general anesthesia. For the analysis reported in this study, patients with respiratory failure or unplanned intubation were combined into the primary outcome variable of PRF.

The study nurse obtained outcomes information by chart review, interviews with care providers, reports from morbidity and mortality conferences, and communication with

each patient on the 30th postoperative day by letter or by telephone. The nurse input all data into a surgical risk assessment module in each center's computer system. A summary of the entire data record on each patient was forwarded to the chief of the surgical service 30 days after surgery for inspection. No later than 45 days after surgery, the case records were transmitted automatically to the statistical coordinating center for editing and analysis.

## Missing Data

All data were greater than 99% complete, with the exception of the preoperative laboratory variables, the completeness of which depended on whether the specific laboratory tests had been ordered. The logistic regression models were run with missing laboratory values being assigned normal values (albumin = 40 g/L, blood urea nitrogen [BUN] = 10 mg/dL, creatinine = 1.0 mg/dL). This is based on the assumption that these relatively routine laboratory tests were not obtained in healthier patients, who would likely have normal values. The models were also analyzed using dummy variables to designate the group of patients with missing values. The  $\beta$ -coefficients for these dummy variables were not significantly different from the reference groups for each laboratory test. A regression procedure was also used to estimate missing values based on values of variables that were present, and the final models were evaluated using these generated values.<sup>19</sup> The  $\beta$ -coefficients of the models did not change significantly with any of these three methods, so the results reported are from the models run with missing values being assigned normal values.

## Statistical Analysis

Data were analyzed using the SAS for UNIX software package (SAS, Cary, NC). Using patients from phase I, the univariate relationship between each variable and PRF was tested using a chi-square test for categorical variables and a Student *t* test for continuous variables. All variables were entered into a logistic regression model with PRF as the dependent variable. Continuous variables were categorized into ranges suggested by their relationship to PRF in univariate analyses. Dummy variables were created for each range, and all such dummy variables were used in the logistic regression models. Potential predictor variables that were not statistically significant at the  $P < .05$  level were sequentially deleted from the base model until only predictor variables that were significant remained. All two-way interactions were analyzed, with none being statistically significant. The resulting model was designated model 1.

Model 1 was then used as the basis for developing a simplified model. Variables with multiple ranges in model 1 (e.g., albumin, BUN) were categorized into dichotomous variables. Starting with the variables that had the lowest odds ratios (OR), variables were sequentially eliminated

from model 1. If the deletion of a variable resulted in a decrease in the c-index of less than 0.005, then that variable was excluded. Excluded variables were reintroduced into the model at various stages of model development to reassess their contribution to the explanatory power of the model. If the reintroduction of a previously deleted variable resulted in an increase in the c-index of less than 0.005, then that variable was excluded. The resulting model was designated model 2.

## Development of Scoring System

Using the methodology of Le Gall et al.,<sup>20</sup> point values were assigned to each predictor by multiplying the  $\beta$ -coefficients from model 2 by 10 and rounding off to the nearest integer. The point total for each patient was designated as the respiratory failure risk index and was used in a multiple logistic regression equation designed to convert the risk index to a probability of PRF. The risk index scores were highly skewed, so a shrinking power transformation,  $\ln$  (respiratory failure risk index + 1), where  $\ln$  indicates the natural logarithm, was incorporated into the model.<sup>20</sup>

## Model Performance

To assess the calibration of the models, formal goodness-of-fit (Hosmer-Lemeshow) tests<sup>21</sup> were performed on patients from both phase I (development set) and phase II (validation set). The Hosmer-Lemeshow test compares the expected and observed events in 10 equal subgroups defined by the deciles of predicted probabilities of PRF. The inclusion of the shrinking power transformation resulted in improved model calibration, reflected by a statistically nonsignificant goodness-of-fit statistic.

The c-index was used in the two datasets to evaluate discrimination. The c-index is the proportion of all possible pairs of patients with and without PRF for which the predicted probability of PRF in the patient with PRF is greater than that of the patient without PRF.<sup>22</sup> A c-index of 0.5 means no predictability; a c-index of 1.0 means perfect predictability.

## RESULTS

### Patient Characteristics and PRF Rates

Of the 87,078 patients enrolled in phase I, 5,359 (6.2%) were excluded as noted above, leaving 81,719 for model development. Of the 107,241 patients enrolled in phase II, 7,851 (7.3%) were excluded, leaving 99,390 for model validation.

Table 3 displays the baseline characteristics of patients with and without PRF. There were 2,746 patients (3.4%) with PRF in phase I. Patients with PRF had a mean age of  $65.8 \pm 10.1$  years versus  $60.0 \pm 13.4$  years for those without PRF. In bivariate analysis, patients with PRF were

Table 3. PATIENT CHARACTERISTICS, PHASE I

Characteristics*	Postoperative Respiratory Failure (n = 2,746, 3.4%)	No Postoperative Respiratory Failure (n = 78,973, 96.6%)
Age (years ± SD)	65.8 ± 10.1	60.0 ± 13.4
Albumin (mean g/L ± SD)	35 ± 7.4	39 ± 4.7
Functional status		
Independent	1,920 (70%)	68,588 (87%)
Partially dependent	551 (20%)	8,517 (11%)
Totally dependent	275 (10%)	1,868 (2%)
Diabetes mellitus		
No diabetes or diet-controlled	2,251 (82%)	68,040 (86%)
Oral hypoglycemic therapy	218 (8%)	5,298 (7%)
Insulin therapy	277 (10%)	5,635 (7%)
Alcohol >2 drinks/day	508 (19%)	12,258 (16%)
Greater than 10% weight loss in 6 months before surgery	312 (11%)	3,392 (4%)
Disseminated cancer	163 (6%)	2,667 (3%)
Respiratory status		
Recent smoking	1,223 (45%)	32,328 (41%)
History of COPD	872 (32%)	10,845 (14%)
Dyspnea		
No dyspnea	1,921 (68%)	68,486 (86%)
Minimal exertion	739 (26%)	10,545 (13%)
At rest	161 (6%)	940 (1%)
Preoperative pneumonia	137 (5%)	576 (1%)
Cardiac status		
History of CPB operation	324 (12%)	6,248 (8%)
History of angina	269 (10%)	4,476 (6%)
History of CHF	261 (10%)	2,205 (3%)
History of MI	77 (3%)	784 (1%)
History of PTCA	71 (3%)	1,665 (2%)
Neurologic status		
History of CVA	320 (12%)	4,705 (6%)
Impaired sensorium	287 (10%)	3,300 (4%)
Tumor involving CNS†	44 (2%)	1,065 (1%)
Neuromuscular disease‡	41 (1%)	972 (1%)
Renal and fluid status		
Transfusion >4 units	194 (7%)	781 (1%)
Preoperative renal failure	80 (3%)	348 (<1%)
Blood urea nitrogen (mean mg/dL ± SD)	22.5 ± 17.4	16.4 ± 9.4
Creatinine (mean mg/dL ± SD)	1.6 ± 1.5	1.2 ± 0.9
Type of surgery		
Upper abdominal	858 (31%)	10,685 (14%)
Thoracic	518 (19%)	5,567 (7%)
Peripheral vascular	389 (14%)	7,232 (9%)
Extremity	249 (9%)	17,291 (22%)
AAA repair	232 (8%)	1,323 (2%)
Lower abdominal	158 (6%)	16,814 (21%)
Neurosurgery	103 (4%)	1,907 (2%)
Back and spine	81 (3%)	7,850 (10%)
Neck§	71 (3%)	2,118 (3%)
Dermatologic	46 (2%)	3,279 (4%)
Eye, nose, mouth, other	41 (1%)	4,907 (6%)
Total	2,746 (100%)	78,973 (100%)
General anesthesia	2,506 (91%)	59,926 (76%)
Emergency surgery	872 (32%)	6,736 (9%)
Postoperative complications		
Pneumonia	1,119 (41%)	1,472 (2%)
Pulmonary edema	745 (27%)	907 (1%)
Systemic sepsis	710 (26%)	686 (1%)
Cardiac arrest requiring CPR	582 (21%)	472 (1%)
30-day postoperative deaths	752 (27%)	1,080 (1%)

AAA, abdominal aortic aneurysm; CHF, congestive heart failure; CNS, central nervous system; CPB, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty.

\*  $P < .001$  for all variables except CNS tumor, neuromuscular disease, and neck surgery.

†  $P = .26$  for CNS tumor.

‡  $P = .22$  for neuromuscular disease.

§  $P = .76$  for neck surgery.

significantly more likely to be classified as having dependent functional status and had lower baseline albumin levels. They were significantly more likely to report treatment for diabetes mellitus and to have a history of recent smoking, dyspnea, COPD, and preoperative pneumonia. Patients with PRF were significantly more likely to have characteristics related to cardiac, neurologic, and renal disease. Patients with PRF underwent significantly more upper abdominal, thoracic, peripheral vascular, abdominal aortic aneurysm repair, and neurosurgical operations than did patients without PRF. The most common postoperative complications associated with PRF included pneumonia, pulmonary edema, systemic sepsis, and cardiac arrest. Overall, the 30-day death rate was 27% in patients with PRF versus 1% in those without PRF.

### Multivariable Analysis

It is possible that a significant proportion of the 1,080 patients who died and were classified in our analysis as not having PRF may have died within the first 48 hours after surgery while receiving mechanical ventilation. These early deaths represent potential cases of PRF that were unobserved (censored). To address this possibility, the number of deaths that occurred within 48 hours after surgery was determined. Of these 211 patients who died early, 39 had unplanned intubation and were included in our definition of PRF. The multivariable models were reanalyzed assuming that all the remaining 172 patients with early death would have developed PRF. The significant predictors and  $\beta$ -coefficients in these revised models were essentially identical to the original models; therefore, the results of the original models are presented.

Table 4 displays the results of the initial logistic regression model (model 1), which included all the significant preoperative predictors of PRF. Potential predictors that were excluded from model 1 included preoperative creatinine level, disseminated cancer, neuromuscular disease, central nervous system tumor, angina, myocardial infarction, angioplasty, and operation involving cardiopulmonary bypass. Significant predictors of PRF related to general health status included serum albumin level, age, dependent functional status, weight loss of greater than 10% in the 6 months before surgery, alcohol use, and insulin therapy for diabetes. The OR for developing PRF increased with decreasing serum albumin levels, especially with levels of less than 30 g/L. Increasing age was associated with increased odds of PRF, particularly for patients older than 60. Patients designated as having a totally dependent functional status had an OR of 2.2 (95% confidence interval [CI], 1.9–2.7) compared with those with an independent functional status; the OR was 1.5 (95% CI, 1.3–1.7) for those designated as having a partially dependent functional status.

Significant predictors related to renal and fluid status included BUN, preoperative renal failure, and preoperative transfusion of more than 4 units. Patients with a preopera-

**Table 4. PREOPERATIVE PREDICTORS OF POSTOPERATIVE RESPIRATORY FAILURE (MODEL 1)**

Variable	Odds Ratio (95% Confidence Interval)
General health status	
Albumin (g/L)	
<20	4.33 (3.39–5.52)
20–30	2.16 (1.86–2.51)
31–40	1.17 (1.05–1.31)
>40	1.00 (reference)
Age (years)	
≥70	2.60 (2.21–3.05)
60–69	1.99 (1.70–2.33)
50–59	1.50 (1.25–1.79)
<50	1.00 (reference)
Functional status	
Totally dependent	2.24 (1.88–2.66)
Partially dependent	1.50 (1.34–1.68)
Independent	1.00 (reference)
Greater than 10% weight loss in 6 months before surgery	1.37 (1.19–1.57)
Alcohol >2 drinks/day	1.19 (1.07–1.33)
Diabetes mellitus	
Insulin therapy	1.15 (1.00–1.33)
No diabetes, diet-controlled, or oral therapy	1.00 (reference)
Renal and fluid status	
Blood urea nitrogen (mg/dL)	
>40	2.35 (2.00–2.76)
31–40	2.09 (1.78–2.45)
21–30	1.31 (1.18–1.46)
≤20	1.00 (reference)
Preoperative renal failure	1.67 (1.23–2.27)
Transfusion >4 units	1.56 (1.28–1.91)
Respiratory status	
Preoperative pneumonia	1.70 (1.35–2.13)
Dyspnea	
At rest	1.69 (1.36–2.09)
On minimal exertion	1.21 (1.09–1.34)
No dyspnea	1.00 (reference)
History of COPD	1.58 (1.44–1.75)
Recent smoking	1.24 (1.14–1.36)
Cardiac status: history of CHF	1.25 (1.07–1.47)
Neurologic status	
Impaired sensorium	1.22 (1.04–1.43)
History of CVA	1.20 (1.05–1.38)
Type of surgery	
AAA	11.0 (9.2–13.1)
Thoracic	5.91 (5.15–6.78)
Peripheral vascular	3.40 (2.96–3.91)
Upper abdomen	3.36 (2.96–3.80)
Neurosurgery	2.96 (2.35–3.73)
Neck	2.13 (1.63–2.77)
Other surgery*	1.00 (reference)
Emergency surgery	2.81 (2.54–3.11)
Type of anesthesia	
General anesthesia	1.91 (1.64–2.21)
Spinal or epidural anesthesia	1.00 (reference)

AAA, abdominal aortic aneurysm; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident.

\* Other surgeries include ophthalmologic, ear, nose, mouth, lower abdominal, extremity, dermatological, spine and back surgeries.

**Table 5. PREOPERATIVE PREDICTORS OF POSTOPERATIVE RESPIRATORY FAILURE (MODEL 2)**

Variable	Odds Ratio (95% Confidence Interval)
Type of surgery	
Abdominal aortic aneurysm	14.3 (12.0–16.9)
Thoracic	8.14 (7.17–9.25)
Neurosurgery, upper abdominal, or peripheral vascular	4.21 (3.80–4.67)
Neck	3.10 (2.40–4.01)
Other surgery†	1.00 (reference)
Emergency surgery	3.12 (2.83–3.43)
Albumin (<30 g/L)	2.53 (2.28–2.80)
Blood urea nitrogen (>30 mg/dL)	2.29 (2.04–2.56)
Partially or fully dependent status	1.92 (1.74–2.11)
History of COPD	1.81 (1.66–1.98)
Age (years)	
≥70	1.91 (1.71–2.13)
60–69	1.51 (1.36–1.69)
<60	1.00 (reference)

COPD, chronic obstructive pulmonary disease.  
 \* Other surgeries include ophthalmologic, ear, nose, mouth, lower abdominal, extremity, dermatologic, spine, and back surgeries.

tive BUN of more than 40 mg/dL had an OR of 2.4 (95% CI, 2.0–2.8) compared with those with a BUN less than 20 mg/dL. Among the significant factors related to respiratory status, preoperative pneumonia had the highest OR, 1.7 (95% CI, 1.4–2.1). Among several potential predictors related to cardiac status, only a history of congestive heart failure was a significant predictor of PRF, with an OR of 1.3 (95% CI, 1.1–1.5). Impaired sensorium and a history of prior cerebrovascular accident with a residual neurologic deficit were the only factors related to neurologic status that were significant in multivariable analysis.

Operation-specific factors had the highest associated OR for developing PRF, particularly the type of surgery performed. The type of surgery performed was classified primarily by the location of the incision (Table 2). The reference group for type of surgery, designated as “other surgery,” included ophthalmologic, ear, nose, mouth, lower abdominal, extremity, dermatologic, spine, and back surgeries. These groups were chosen as the reference category because they had the lowest associated rates of PRF in univariate analysis. Patients undergoing surgery related to an abdominal aortic aneurysm had the greatest risk of developing PRF of any surgical category. Patients undergoing emergency surgery or surgery using general anesthesia were also found to have an increased risk of developing PRF.

Model 2 includes 11 predictors of PRF and is shown in Table 5. Patients undergoing abdominal aortic aneurysm surgery had an OR of 14.3 (95% CI, 12.0–16.9) compared with those undergoing “other surgery.” Patients undergoing thoracic surgery had an OR of 8.1 (95% CI, 7.2–9.3), and

those undergoing neurosurgical, upper abdominal, or peripheral vascular surgery had an OR of 4.2 (95% CI, 3.8–4.7). Patients undergoing neck surgery had an OR of 3.1 (95% CI, 2.4–4.0), and patients undergoing emergency surgery had an OR of 3.1 (95% CI, 2.8–3.4). Patients with an albumin level less than 30 g/L had an OR of 2.5 (95% CI, 2.3–2.8), and patients with a BUN more than 30 mg/dL had an OR of 2.3 (95% CI, 2.0–2.6). The OR for patients with a partially or totally dependent functional status was 1.9 (95% CI, 1.7–2.1). For patients with a history of COPD, the OR was 1.8 (95% CI, 1.7–2.0). Compared with patients younger than 60, patients older than 70 had an OR of 1.9 (95% CI, 1.7–2.1), and patients 60 to 69 years old had an OR of 1.5 (95% CI, 1.4–1.7).

### Model Calibration and Discrimination

Model 1 applied to patients from phase I resulted in a c-index of 0.846, indicating excellent discrimination. The Hosmer-Lemeshow goodness-of-fit statistic was 13.5 with 8 *df* ( $P > .095$ ), indicating good fit of model 1 to the data. When model 1 was applied to patients from phase II, the c-index was essentially unchanged ( $c = 0.843$ ) and the Hosmer-Lemeshow goodness-of-fit statistic was 8.16 with 8 *df* ( $P > .41$ ), indicating that the model continued to have excellent discrimination and good fit in an independent dataset.

Model 2 had a slightly lower c-index than model 1 ( $c = 0.834$ ). The Hosmer-Lemeshow goodness-of-fit statistic was 3.37 with 6 *df* ( $P > .76$ ), indicating good fit of the model to the data. When model 2 was applied to phase II data, the c-index was essentially unchanged ( $c = 0.828$ ) and the Hosmer-Lemeshow goodness-of-fit statistic was 0.97 with 6 *df* ( $P > .98$ ), indicating that model 2 also had excellent discrimination and good fit in an independent dataset.

### Respiratory Failure Risk Index

Point values were assigned to each predictor by multiplying the  $\beta$ -coefficients from model 2 by 10 and rounding off to the nearest integer.<sup>20</sup> Table 6 displays the point values assigned to each preoperative predictor used in calculating the respiratory failure risk index score. Based on the predicted probability associated with various scores, patients were categorized into five risk classes. Table 7 displays the number of phase I patients in each risk class, the associated predicted probability of PRF based on model 2, and the actual incidence of PRF in phase I and phase II patients.

The respiratory failure risk index predicted the incidence of PRF well for phase I patients across all risk classes, with a Pearson chi-square goodness-of-fit statistic of 3.86 ( $P > .10$ ). It also predicted the incidence of PRF well in risk classes 1 and 2 for phase II patients, but it appeared to overestimate the risk of PRF in classes 3, 4, and 5 in phase

**Table 6. RESPIRATORY FAILURE RISK INDEX**

Preoperative Predictor	Point Value
Type of surgery	
Abdominal aortic aneurysm	27
Thoracic	21
Neurosurgery, upper abdominal, or peripheral vascular	14
Neck	11
Emergency surgery	11
Albumin (<30 g/L)	9
Blood urea nitrogen (>30 mg/dL)	8
Partially or fully dependent functional status	7
History of chronic obstructive pulmonary disease	6
Age (years)	
≥70	6
60–69	4

II. Overall, the incidence of PRF decreased from 3.4% in phase I to 2.8% in phase II.

## DISCUSSION

This study confirmed several preoperative predictors of PRF. Operation-specific risk factors, particularly the type of surgery, had the highest ORs. Prior studies have examined risk factors for PRF after high-risk operations, including abdominal aortic aneurysm repair,<sup>6,7,9</sup> thoracotomy,<sup>2,10</sup> colon resection,<sup>3,5,10</sup> and head and neck surgery.<sup>4</sup> All of these types of operations were associated with an increased risk of PRF in this study.

In some patients, the operation cannot be significantly modified, making operation-specific risk factors less reasonable targets for clinical intervention to decrease the rate of PRF. Prior studies consistently identified patient-specific risk factors similar to those in our respiratory failure risk index, such as age older than 60,<sup>3,9,23</sup> low albumin level,<sup>5</sup> renal insufficiency,<sup>5–7</sup> and prior history of COPD<sup>9,10</sup> or smoking.<sup>4</sup> The respiratory failure risk index points to several potentially treatable or correctable factors that may

decrease the risk for PRF. Proper perioperative fluid management as reflected by a normal BUN, correction of possible malnutrition as reflected by a low albumin level, and performance of high-risk surgeries electively rather than waiting until an emergency surgery becomes necessary may all decrease the risk of PRF. Pulmonary rehabilitation, smoking cessation, and maximizing pharmacologic treatments to optimize the respiratory status of patients with COPD, asthma, and congestive heart failure may also decrease the risk for respiratory failure. Chumillas et al<sup>24</sup> found that preoperative and postoperative respiratory rehabilitation protected against postoperative pulmonary complications in moderate-risk and high-risk patients undergoing upper abdominal surgery.

The respiratory failure risk index provides a useful guide to evaluating preoperative risk for developing PRF. One major advantage of this study is that patient characteristics and outcomes were obtained prospectively with a level of clinical detail not found in administrative databases. Most prior studies examining risk factors for PRF depended on a retrospective review of administrative databases or medical chart review.<sup>4,5,7,9,10</sup> Missing data, inconsistencies in the use of variable definitions, and lack of clinical detail are some of the limitations encountered when using retrospectively obtained or administrative data. Another weakness of prior studies is the lack of validation of the models in independent datasets.<sup>25,26</sup> The NSQIP provided a unique opportunity to develop models on more than 80,000 patients and to validate the models on a separate set of more than 99,000 patients. The models developed in this study performed well in validation testing, maintaining almost all of their explanatory power.

The models developed in this study may be useful in future studies aimed at reducing PRF rates. In this study, we determined the preoperative risk factors for developing PRF. There are many intraoperative and postoperative factors that probably influence the risk of developing PRF as well, such as intraoperative ventilator and cardiovascular management, use of intravenous versus inhalation anesthetic maintenance, and use of intraoperative and early postoperative analgesia and sedation. Our models may be

**Table 7. RESPIRATORY FAILURE RISK INDEX SCORES FOR PHASE I AND PHASE II PATIENTS**

Class	Point Total	n (%)*	Predicted Probability of PRF	Phase I (% RF)	Phase II (% RF)
1	≤10	39,567 (48%)	0.5%	0.5%	0.5%
2	11–19	18,809 (23%)	2.2%	2.1%	1.8%
3	20–27	13,865 (17%)	5.0%	5.3%	4.2%
4	28–40	7,976 (10%)	11.6%	11.9%	10.1%
5	>40	1,502 (2%)	30.5%	30.9%	26.6%

PRF, postoperative respiratory failure.

\* Number of phase I subjects in each risk class.

used to control for preoperative patient-specific and operation-specific risk factors in future studies designed to evaluate interventions in intraoperative and postoperative management. The models may also be used for case-mix adjustment in studies examining variation in PRF rates between hospitals.

The most common postoperative complications in phase I were postoperative pneumonia (3.6%), urinary tract infection (3.5%), and respiratory failure (3.4%). Notably, two of the top three postoperative complications were pulmonary complications. The 30-day death rate for patients with PRF was 27% versus 1% for patients without PRF. In contrast, cardiac arrest requiring cardiopulmonary resuscitation occurred in 1.5% of total patients; myocardial infarction occurred in only 0.7% of patients. The development and clinical use of preoperative cardiac risk assessment models<sup>12–14</sup> may have focused greater attention on maximizing cardiac status before surgery, as well as possible cancellation of surgery if the cardiac risk was deemed to be high. These results from the NSQIP raise concerns that similar attention needs to be given to postoperative pulmonary complications.

Some controversy exists over the best definition for PRF. PRF is most commonly defined as the inability to be extubated 48 hours after surgery,<sup>6</sup> although other investigators have used 5 days after surgery as their definition.<sup>7</sup> The definition of PRF used in this study was a combination of two separately measured outcomes from the NSQIP: unplanned intubation and inability to be extubated 48 hours after surgery. Thirty-seven percent of patients with PRF had the inability to be extubated, 29% had unplanned intubation, and 34% had both. For all three groups, the most commonly associated postoperative complications were pneumonia, pulmonary edema, systemic sepsis, and cardiac arrest. The 30-day death rate was 31% for reintubation patients and 23% for patients with the inability to be extubated. Initially, logistic regression models were developed for each of these groups separately. The significant predictors and  $\beta$ -coefficients in these initial models were essentially identical, and therefore these groups were combined.

There are several limitations to our study. Because veterans cared for at VAMCs have a high level of comorbid conditions, these models may not generalize to other, healthier populations. Another limitation was that women were excluded because of the caseload of the source hospitals. Patient-specific factors such as age and albumin level are likely to be relevant in women, but the associated ORs may be different. Future studies are needed to validate these models in other populations including women.

Another limitation was that other potentially important preoperative risk factors for PRF were not included in the NSQIP. During the planning stages of the NSQIP, a pilot study examining the feasibility of including pulmonary function test results revealed that it would be extremely difficult to obtain reliable information consistently across multiple institutions. The lack of pulmonary function test

data did not allow assessment of the severity of underlying pulmonary diseases such as asthma, COPD, or restrictive lung disease. The definition of COPD used in the NSQIP was fairly broad and may have resulted in an underestimation of the risk associated with severe COPD. Body mass index, which has been shown to be associated with respiratory failure, was not recorded in the NSQIP.<sup>3</sup> Therefore, the respiratory failure risk index does not include an assessment of the importance of obesity or increased body mass index as risk factors for PRF.

Despite these limitations, the respiratory failure risk index may be helpful to clinicians and researchers in targeting perioperative testing and respiratory care to high-risk patients. Prior studies have been limited to patients undergoing specific types of operations<sup>2–7,9,10</sup> or patients with particular risk factors.<sup>1,10</sup> The respiratory failure risk index is unique in that it includes several patient-specific and operation-specific risk factors simultaneously, allowing for an accurate assessment of the preoperative risk of PRF associated with each individual risk factor. We found that the type of surgery performed has the highest associated risk for developing PRF and that the major patient-specific risk factors are related to general health status, renal and fluid status, and respiratory status. We hope that an increased awareness of the importance of postoperative pulmonary complications will develop through the clinical use of the respiratory failure risk index. We also hope that by using the models developed in this study, researchers will be able to evaluate future interventions aimed at reducing the rate of PRF.

## APPENDIX 1: Participants in the National Veterans Administration Surgical Quality Improvement Program

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