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Critical Respiratory Events in the Postanesthesia Care Unit

Patient, Surgical, and Anesthetic Factors

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Background: **Previous studies have noted a high incidence of adverse outcomes in the postanesthesia care unit (PACU), but few have examined associated factors and patient outcomes. To determine the frequency of acute, unanticipated respiratory problems and to examine the associated patient, surgical, and anesthetic factors, we prospectively collected preoperative, intraoperative, and postoperative data on 24,157 consecutive PACU patients who received a general anesthetic during a 33-month period.**

Methods: **A PACU critical respiratory event (CRE), was defined as any unanticipated hypoxemia (hemoglobin oxygen saturation < 90%), hypoventilation (respiratory rate < 8 breaths/min or arterial carbon dioxide tension > 50 mmHg) or upper-airway obstruction (stridor or laryngospasm) requiring an active and specific intervention (ventilation, tracheal intubation, opioid or muscle relaxant antagonism, insertion of oral/nasal airway or airway manipulation). These problems were documented by PACU nurses whereas data on case-mix, surgical factors, and intraoperative management were retrieved from the anesthetic record. Significant patient, surgical, and anesthetic factors were identified by logistic regression analysis. Other morbidity experienced by patients with a CRE was also noted.**

Results: **For patients given general anesthesia the risk of a CRE was 1.3% (hypoxemia 0.9%, hypoventilation 0.2%, airway obstruction 0.2%). Preoperative factors that increase risk were age > 60 yr, male gender, diabetes, and obesity ($P < 0.05$). Patients who underwent operative procedures on an emergency basis and whose operation was longer than 4 h were also at increased risk, but those undergoing perineal procedures were at lower risk ($P < 0.05$). Anesthetic risk factors ($P < 0.05$) included opioid premedication (relative odds 1.8), sedatives preoperatively (2.0), fentanyl > 2.0 $\mu g \cdot kg^{-1} \cdot h^{-1}$ as the sole opioid (1.9), fentanyl used in combination with morphine (1.6) and atracurium ≥ 0.25 $mg \cdot kg^{-1} \cdot h^{-1}$ (2.2). Patients in whom anesthesia was induced with thiopental (relative odds 2.5), compared with those who received propofol for induction, were also at increased risk of a CRE. Patients with a CRE stayed longer in PACU, had higher rates of unanticipated admissions to the intensive care unit and were more likely to have PACU cardiac problems ($P < 0.01$).**

Conclusions: **A CRE is relatively rare. Multiple patient and surgical factors and specific aspects of anesthetic management are associated with the occurrence of a CRE in the PACU. (Key words: Complications: airway obstruction; hypoventilation; hypoxemia; postoperative. Statistics: numerical data.)**

RECENT epidemiologic studies of adverse events associated with anesthesia have described low mortality but strikingly high morbidity during the perioperative period.[1–3] These large prospective studies have concentrated on general complications, many without explicit or objective parameters, in the operating room, in postanesthesia care unit (PACU), and in the early postoperative period. Few studies have focused on acute respiratory problems in the PACU.[4–6] Although the etiology of respiratory complications has been ascribed to multiple preoperative patient and surgical factors, the relation between these respiratory problems and aspects of anesthetic management is poorly understood.

The first objective of this study was to determine the rate of critical respiratory events (CREs) in the PACU among general surgical patients after general anes-

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thesia. The second objective was to examine the association between preoperative patient characteristics, surgical factors, anesthetic management, and CREs in the PACU. In this manner, anesthesiologists can be alerted to potential risk factors under their direct control. Other adverse outcomes occurring in patients with a CRE also were identified.

Materials and Methods

Data Collection and Patient Population

After approval from the Human Ethics Committee, consecutive patients admitted to the PACU who received a general anesthetic during a 33-month period (January 1, 1991 through September 30, 1993; n = 24,157) were followed and the incidence and treatment of CREs in the PACU were determined. The definition of CREs in this study refers to major unanticipated ventilation problems (desaturation, hypoventilation, airway obstruction) in the PACU requiring a physical or pharmacologic intervention (ventilation, tracheal intubation, opioid antagonism, muscle relaxant antagonism, oral/nasal airway insertion, or airway manipulation) (table 1). The occurrence of an adverse event in the PACU did not imply an error by the attending health care professional.

Data on patient, surgical, and anesthesia factors and on adverse events were collected from specially designed operating room and PACU records.[7] Anesthesiologists and PACU nurses used a check-box format to record preoperative patient illnesses, medication used, anesthetic techniques, anesthetic drug choices, and PACU airway management. Both the PACU record and the operating room anesthetic record contained an extensive list of observations or adverse events defined on the record. The occurrence of any of these events in the operating room was documented by the anesthesiologist at the completion of the surgical procedure and in the PACU by the nurse when the patient was discharged from the PACU. Carbon copies of all records were reviewed the day after surgery by a designated anesthetic research nurse and a clinical anesthesiologist to ensure accuracy and completeness. When information was unclear or missing, whenever possible, these data were retrieved from a retrospective chart review or by direct consultation with the anesthesiologist who completed the case. All information was entered into a customized dBase program, and data were analyzed with use of statistical software (version 6.04, SAS, Cary, NC).[7]

Table 1. Critical Respiratory Events in the Post Anesthesia Care Unit

Event	n	% GA Patients
Any critical respiratory event	325	1.3
Hemoglobin desaturation	228	0.9
Hypoventilation	41	0.2
Airway obstruction	56	0.2

All patients following general anesthesia n = 24,157.

Hemoglobin desaturation = $SpO_2 < 90\%$ on post anesthesia care unit (PACU) arrival requiring an active intervention (ventilation, tracheal intubation, opioid antagonism, muscle relaxant antagonism, oral/nasal airway insertion, or airway manipulation; Hypovenilation = respiratory rate ≤ 8 or $PaCO_2 \geq 50$ mmHg requiring an active intervention on arrival in PACU (ventilation, tracheal intubation, opioid antagonism, muscle relaxant antagonism, oral/nasal airway insertion, or airway manipulation) excluding those above in whom hemoglobin desaturation occurred; Airway obstruction = stridor, obstruction or laryngospasm on arrival in PACU (requiring ventilation, tracheal intubation, muscle relaxant antagonist, oral/nasal airway insertion) excluding those above who desaturate or hypoventilate.

The data collected on each patient included physical status score, gender, age, and weight. Preoperative medical data included information on specific illnesses, concurrent medications, and preoperative sedation given. Details of the intraoperative anesthetic management included the anesthetic technique, monitors used, patient position, mode of ventilation, and the type of airway used. Codes for all drugs (and total doses per kilogram body weight per hour of anesthesia) given by the anesthesiologist were included in the data collection. Similar data on PACU management was available from the PACU record. Surgical procedures were classified according to the International Classification of Diseases codes (ninth revision) and further classified into 19 "families" of surgical procedures according to the anatomic site of the surgery and the degree of anesthetic trespass.[8] The categories were digestive intraabdominal; endoscopy; extremity—bone; extremity—skin, fat, or joint; eye; ear, nose, and throat; gynecologic intraabdominal; intracranial; intrathoracic; major vascular; minor vascular; head and neck; perineal; major renal; minor renal; spine; therapeutic or diagnostic; and trunk. A final category, multiple, was added for procedures that involved more than one of these operative sites. Duration of anesthesia and prolonged PACU stay (15 min longer than the anticipated time: the lesser of surgical time or 2 h) were also noted. In-hospital mortality was retrieved from other hospital databases.

Criteria for appropriateness of tracheal extubation in the operating room and timing of transfer to the PACU were at the discretion of each individual anesthesiol-

ogist. Oxygen (40% by face tent) was routinely administered on PACU arrival, and patient hemoglobin oxygen saturation was monitored during the entire PACU stay. Nursing patient ratio was 1:1 on admission and 1:2 for the remainder of the stay. Patients whose lungs were electively ventilated and who required overnight admission to an intensive care unit (ICU) were not admitted to the PACU and are not part of this study. Patients in whom the tracheal tube was in place on arrival in PACU (to avoid unanticipated airway problems) were excluded (n = 462). Thus, the final database included all patients who had a general anesthetic and were admitted to the PACU and in whom a tracheal tube was not in place (n = 24,157 during the 33-month period).

As a reliability check, 18 variables relevant to the study were reviewed on a random sample of 50 records (900 data points). Only 13 errors of a possible 900 entries were noted; most of these (7) were missing documentation of minor PACU events. Other errors involved demographic data and anesthetic management and were corrected.

Statistical Analysis

The frequency of CREs by type of CRE, and the specific interventions required to treat the CREs were determined. The definition of CRE included (1) all patients whose hemoglobin oxygen saturation decreased to less than 90%; (2) patients remaining who had inadequate ventilation (respiratory rate ≤ 8 breaths/min or arterial carbon dioxide tension ≥ 50 mmHg but no desaturation); and (3) patients remaining in whom neither hemoglobin desaturated or hypoventilation, by our definition, occurred but did have an episode of upper-airway obstruction.

The risk of a CRE with various preoperative patient, surgical, or anesthetic factors present and the risk of a CRE if the factor was not present were compared first by univariate analysis using the chi-squared statistic; crude relative risks and 95% confidence intervals then were determined.[9] Because various categorizations of continuous variables did not affect the overall results, categorical variables were used to aid interpretation. To identify the variables, not controlled by the anesthesiologist, that were independent risk factors predictive of a CRE, we included patient and surgical factors found significant by univariate analysis at the $P \leq 0.05$ level into a multiple logistic regression model. This procedure involved choosing a reference category for each variable that best reflected clinical practice so that the least invasive or commonest factor had an adjusted relative odds equal to 1.

All nineteen categories of surgical procedures were tested for an association with having a CRE. Only those that were significant at the $P < 0.05$ level were included in the multivariate analysis. All others were grouped as "other surgical procedures." To determine if there were multicollinearity concerns (variables highly correlated with one another), correlation coefficients were determined between all variables found to have a significant association with a CRE.[10] For each such "cluster" of highly correlated variables, those with the most clinical importance were retained. For example, ASA physical status was highly correlated with preoperative medical conditions. Specific preoperative medical conditions were more informative than ASA physical status, so that ASA physical status was not included in the multivariate analysis.

To determine the important anesthetic management factors that may have affected outcome, we next included patient and surgical risk factors that were significant at the $P < 0.05$ level and all significant anesthetic management variables into a multiple logistic regression model. The results of the multiple logistic regression are presented as adjusted relative odds for each risk factor relative to the reference group. These are interpreted as follows. If the relative odds for a risk factor has a numerical value less than one, then that factor is associated with a lower risk for a CRE (risk of CRE will be less among those patients with that factor). If the relative odds for a particular risk factor has a numerical value greater than 1, then this indicates an increased likelihood of occurrence of a CRE for patients with that factor. For the multiple logistic regression model, a 20% random sample of patients who did not have a CRE and all patients who had a CRE were included. A second random sample of a different 20% of patients who did not have a CRE was used to confirm the initial results. Because the results were virtually identical, we present the results from the initial model.

Finally, the relation of specific intraoperative problems and occurrence of CRE in PACU was determined. The importance of CREs on overall patient outcome also was assessed by determining the incidence of other adverse events for those who had CREs as compared with those who did not have a CRE. Statistical significance for both the associated variables and other outcomes was determined by the chi-squared test or Fisher's exact test ($P < 0.01$).

Table 2. Treatment of Patients with Critical Respiratory Events in the Post Anesthesia Care Unit

	Hemoglobin Desaturation (n = 228)	Hypoventilation (n = 41)	Airway Obstruction (n = 56)	Any Critical Respiratory Event (n = 325)
Manual ventilation	30.7	14.6	7.1	24.6
Tracheal intubation	7.5	2.4	7.1	6.8
Opioid antagonism	18.9	87.8	0	24.3
Relaxant antagonism	7.5	17.1	5.4	8.3
Insertion of oral/ nasal airway	57.0	29.2	92.8	59.7
Jaw manipulation	57.0	21.9	28.5	47.6

Data are percentages.

* Total treatments may add up to greater than 100% because of multiple interventions used for many individual patients with critical respiratory events.

Results

There were 24,157 patients who received a general anesthetic and were admitted to the PACU without a tracheal tube during a 33-month period. Of these patients, 49%, 38.5%, 11.5%, and 1% were ASA physical status 1, 2, 3, and 4, respectively. Thirty-six percent were men, and 22.4% were older than 60 yr. Preoperative medical conditions of note included diabetes in 4.6% of patients, chronic obstructive pulmonary disease 2.9%, (long-standing symptoms of respiratory disability), renal disease 2.8% (serum creatinine > 140 μM). The proportion of current smokers was 25.6%.

Incidence of Critical Respiratory Events and Treatment

A CRE occurred in 325 patients admitted to the PACU (1.3% of 24,157 patients who had a general anesthetic) (table 1). The commonest interventions used to treat CREs (table 2) were insertion of oral/nasal airway (59.7%) and airway manipulation (47.6%). Although only 22 patients (0.1% of all these PACU admissions) required emergency tracheal intubation in the PACU, 80 patients required manual ventilation of their lungs. In only four of these patients in whom the trachea was intubated, was the trachea extubated before PACU discharge.

Patient and Surgical Factors

Older patients (>60 yr) and men were at increased risk for a CRE (table 3). Other significant patient factors that increased risk include obesity (>120 kg for men or >100 kg for women) and diabetes. Patients with chronic obstructive pulmonary disease and renal disease (variables significant in univariate analysis) were no longer significant after controlling for other factors such as age and sex. Patients whose operative procedures were longer than 4 h or performed on an emergency basis were at increased risk (table 4). Among

Table 3. Patient Factors and Critical Respiratory Events after General Anesthesia

Factors	n	Rate of Critical Respiratory Events (%)	Relative Risk	95% Confidence Interval	Adjusted Relative Odds*	95% Confidence Interval
Age >60 yr	5,400	2.1	1.92	(1.54–2.42)	1.54	(1.19–1.99)
Male	8,738	1.9	1.82	(1.46–2.26)	1.36	(1.07–1.74)
Obese (>120 kg males, >100 kg females)	570	3.0	2.28	(1.40–3.70)	2.14	(1.25–3.65)
Diabetics	1,078	2.7	2.08	(1.42–3.04)	1.60	(1.05–2.45)
Chronic obstructive pulmonary disease	666	3.0	2.30	(1.46–3.60)	1.45	(0.87–2.42)
Renal disease	670	3.0	2.30	(1.47–3.60)	1.37	(0.80–2.35)
Smokers	5,952	1.5	1.20	(0.94–1.52)	1.11	(0.85–1.45)

* Adjusted for all factors in the table, as well as surgical factors.

Table 4. Surgical Factors and Critical Respiratory Events After General Anesthesia

Factor	n	Rate of Critical Respiratory Events (%)	Relative Risk	95% Confidence Interval	Adjusted Relative Odds*	95% Confidence Interval
Emergency	2,159	1.9	1.51	(1.10–2.09)	1.63	(1.14–2.33)
OR > 4 h	1,287	3.4	3.30	(2.38–4.59)	2.25	(1.53–3.31)
OR > 2, ≤ 4 h	5,960	1.8	1.72	(1.35–2.19)	1.26	(0.97–1.63)
OR ≤ 2 h+	16,910	1.0	1.00	—	1.00	—
Surgical Procedures						
Perineal	3,150	0.3	0.21	(0.11–0.40)	0.30	(0.15–0.60)
Extremity—fat/skin/joint	2,087	0.9	0.62	(0.39–1.00)	0.68	(0.41–1.13)
Intraabdominal—digestive	1,340	2.1	1.51	(1.02–2.23)	1.13	(0.73–1.74)
Intracranial	820	2.3	1.67	(1.05–2.66)	1.16	(0.69–1.94)
Major renal	395	2.8	1.82	(1.10–3.65)	0.93	(0.44–1.98)
Ocular	1,581	2.3	1.64	(1.15–2.34)	1.40	(0.95–2.06)
All others†	14,784	1.4	1.00	—	1.00	—

* Adjusted for all factors in the table as well as patient factors.

†Reference group.

surgical procedures only perineal surgery was shown to be associated with a CRE (decreased risk).

Anesthetic Factors

Anesthetic management factors (after controlling for patient and surgical factors) examined for an association with CREs are shown in table 5. The choice of inhalational agent was not a significant factor in the univariate analysis. Four anesthetic choices associated with a significantly increased risk for a CRE were identified by the logistic regression model. These factors were premedications, induction agents, opioids, nondepolarizing neuromuscular relaxants. Premedication with opioids (codeine, morphine, or meperidine) alone or in combination with sedatives (diazepam, midazolam, lorazepam, perphenazine, dimenhydrinate, or promethazine) or use of these sedatives alone increased risk. Patients who received thiopental for induction of anesthesia compared with those who received propofol also were at increased risk of a CRE. Although not statistically significant, it was noted that when propofol was given as a continuous infusion without inhalational agents or opioids for maintenance (n = 92), no CREs were noted in PACU. Use of intraoperative fentanyl in larger dosages as the sole opioid agent (>2.0 $\mu g \cdot kg^{-1} \cdot h^{-1}$) and the use of any fentanyl dosage in combination with morphine were identified as risk factors compared with the choice of fentanyl alone in lower dosages (<1.0 $\mu g \cdot kg^{-1} \cdot h^{-1}$, the reference group). Atracurium, used intraoperatively in patients whose lungs were mechanically ventilated (>0.25 $mg \cdot kg^{-1} \cdot h^{-1}$) was associated with increased risk of CREs compared with similar patients who received no nondepolarizing neuromuscular relaxants or a lower dosage (vecuronium < 0.04 $mg \cdot kg^{-1} \cdot h^{-1}$, atracurium < 0.25 $mg \cdot kg^{-1} \cdot h^{-1}$, or pancuronium < 0.02 $mg \cdot kg^{-1} \cdot h^{-1}$). For all patients whose lungs were mechanically ventilated who received nondepolarizing muscle relaxants the rate of use of anticholinesterase antagonism was similar (atracurium ≥ 0.25 $mg \cdot kg^{-1} \cdot h^{-1}$, 94.5%; vecuronium ≥ 0.04 $mg \cdot kg^{-1} \cdot h^{-1}$, 95.7%; pancuronium > 0.02 $mg \cdot kg^{-1} \cdot h^{-1}$, 95.2%; and the smaller-dosage group, excluding those who received none, 92.0%). Intraoperative use of any benzodiazepine (midazolam or diazepam) or droperidol were not significant factors.

Other associated problems for patients with a CRE included hemoglobin desaturation and laryngospasm during emergence in the operating room (table 6). Compared with other patients who had general anesthesia, patients who had CREs had more cardiac complications in PACU (hypotension, hypertension, tachycardia and new dysrhythmias). Patients with a CRE had a greater rate of unplanned ICU admission and delay in PACU discharge (solely because of patient complications). A total of 20 patients had an unanticipated ICU admission after a CRE. These 20 patients accounted for 36.4% of all unanticipated admissions to the ICU from the PACU during the 33-month period. In addition, PACU arrival scores[11] (scored 0–10) for patients

Table 5. Anesthetic Management Factors Associated with Critical Respiratory Events

Management	n*	Rate of Critical Respiratory Events	Relative Risk	95% Confidence Interval	Adjusted Relative Odds†	95% Confidence Interval
Premedication						
Sedative	2,611	2.0	1.87	(1.37–2.55)	2.00	(1.49–2.69)
Opioid ± sedative	3,432	2.6	2.51	(1.95–3.23)	1.76	(1.24–2.49)
No premedication§	17,631	1.0	1.00	—	1.00	—
Induction Agent						
Thiopental	18,230	1.6	3.86	(2.5–5.9)	2.46	(1.56–3.89)
Propofol§	5,158	0.4	1.00	—	1.00	—
Sedative						
Any benzodiazepine	13,634	1.5	1.26	(1.02–1.60)	1.28	(0.99–1.64)
Inhalational Agent						
Enflurane	12,682	1.4	1.09	(0.88–1.36)	‡	‡
Isoflurane§	9,765	1.4	1.00	—	‡	‡
Antiemetic						
Droperidol ≥ 0.01 mg · kg	6,089	1.8	1.36	(1.06–1.73)	1.05	(0.76–1.45)
Droperidol < 0.01 mg · kg	5,433	1.1	0.87	(0.64–1.16)	1.29	(0.97–1.71)
No droperidol§	12,120	1.3	1.00	—	1.00	—
Opioid						
Only fentanyl, >1–≤ 2 $\mu g \cdot kg^{-1} \cdot h^{-1}$	8,595	1.1	0.76	(0.58–0.99)	1.07	(0.79–1.43)
Only fentanyl, >2 $\mu g \cdot kg^{-1} \cdot h^{-1}$	3,529	1.3	0.91	(0.65–1.28)	1.87	(1.26–2.79)
Fentanyl, morphine combination	1,689	2.8	1.95	(1.40–2.73)	1.56	(1.06–2.29)
Alternate narcotic choices	1,167	1.3	0.90	(0.53–1.53)	0.98	(0.54–1.77)
Fentanyl, ≤1 $\mu g \cdot kg^{-1} \cdot h^{-1}$ or nil§	8,694	1.4	1.00	—	1.00	—
Ventilation/muscle Relaxant						
Spontaneous—mask	4,620	0.3	0.21	(0.12–0.36)	0.68	(0.34–1.31)
Spontaneous—tracheal intubation	380	1.8	1.26	(0.60–2.67)	2.21	(0.95–5.13)
Controlled with						
Atracurium, ≥0.25 $mg \cdot kg^{-1} \cdot h^{-1}$	1,252	3.4	2.30	(1.61–3.29)	2.17	(1.40–3.34)
Vecuronium, ≥0.04 $mg \cdot kg^{-1} \cdot h^{-1}$	7,844	1.4	0.95	(0.73–1.25)	1.19	(0.87–1.62)
Pancuronium, ≥0.02 $mg \cdot kg^{-1}h^{-1}$	1,399	2.2	1.52	(0.74–2.01)	1.45	(0.91–2.33)
Any combination	1,010	1.8	1.22	(1.02–2.26)	1.28	(0.81–2.00)
Controlled with low-dose§	7,074	1.5	1.00	—	1.00	—
Atracurium, <0.25 $mg \cdot kg^{-1} \cdot h^{-1}$ or Vecuronium, <0.04 $mg \cdot kg^{-1} \cdot h^{-1}$ or Pancuronium, <0.02 $mg \cdot kg^{-1} \cdot h^{-1}$						

* Total may be less than 24,157 patients because of missing data for some variables.

† Adjusted for all anesthetic factors, as well as patient and surgical factors.

‡ Not included in the logistic regression.

§ Reference group.

with a CRE (4.2 ± 1.7) were significantly less than for patients without a CRE (7.1 ± 2.1) ($P < 0.001$). During the period of hospitalization, 3 patients who experienced a CRE (0.9%) and 78 with no CRE (0.3%) died.

Discussion

Respiratory complications remain one of the most important areas of concern regarding major morbidity and increased mortality in the postanesthesia period. This study of a large consecutive group of patients after general anesthesia has identified multiple factors: patient factors (age > 60 yr, male gender, diabetes, and obesity); surgical factors (emergencies and cases > 4 h), and anesthetic choices (premedication, induction with thiopental, fentanyl > 2.0 $\mu g \cdot kg^{-1} \cdot h^{-1}$, fentanyl and morphine combination, and atracurium ≥ 0.25 $mg \cdot kg^{-1} \cdot h^{-1}$) that were associated with specific respiratory complications in the PACU. The low number of deaths in our study (81 in hospital) made it difficult

Table 6. Associated Variables/Outcomes in Patients with Critical Respiratory Events

	n	Rate of Critical Respiratory Events (%)	Relative Risk	99% Confidence Interval
In the cperating room (Associated variables)				
Difficult tracheal intubation (>2 laryngoscopies)	313	2.6	1.61	(0.66–3.92)
Hemoglobin desaturation (<90%) at emergence	65	9.2	6.97	(2.52–19.23)
Laryngospasm at emergence	30	23.3	17.70	(6.87–45.61)
In the post anesthesia care unit (Associated outcomes)				
Tachycardia (>120/min, >15 min)	292	6.5	5.10	(2.80–9.31)
Hypertension (20% greater than preoperatively, >15 min)	503	5.0	3.84	(2.28–6.46)
Hypotension (20% less than preoperatively, >15 min)	597	3.4	2.54	(1.43–4.53)
Dysrhythmia (changed from preoperative or PVC's >5/min)	46	17.4	15.44	(5.90–40.41)
Unplanned intensive care unit admission	55	36.4	41.90	(20.69–84.86)
Delay in post anesthesia care unit discharge (due to patient complication)	656	4.7	4.27	(2.67–6.82)
Agitation	641	2.6	2.00	(1.07–3.72)
Nausea and vomiting (any complaint)	2,315	1.7	1.26	(0.83–1.90)
Excessive pain (nursing care predominantly concerned with pain control)	1,340	0.9	0.65	(0.31–1.37)
Shivering (>15 min)	1,263	1.3	0.94	(0.50–1.78)
In hospital				
Deaths	81	3.7	2.82	(0.70–11.39)

to show a relation between CRE and mortality. However, the risk of other major adverse cardiac outcomes, unanticipated ICU admission, and delay in PACU discharge after a CRE, was significantly increased over other patients admitted to PACU after general anesthesia.

Other studies have also demonstrated the impact of respiratory-related problems in the perioperative period. Respiratory complications in the postoperative period were recorded in a French study of 198,103 anesthetics performed at several hospitals. The overall frequency of major respiratory problems (fatal, life threatening, or producing severe sequelae), 0.02%, was lower than ours (1.3%), but 42% of their complications lead to death or coma within the first 24 h of the operation.[12] Although primarily studies of operating room events, closed claims analyses found that respiratory events were the commonest cause of major injury associated with anesthesia.[13,14] Another study revealed that 0.4% of patients admitted to the PACU required an unanticipated admission to ICU, and as in our study, one third of these cases were due to major respiratory problems.[15]

Studies in this field define respiratory problems in somewhat different ways. A recent study of consecutive patients admitted to PACU (82.3% after general anesthesia) documented common postoperative respiratory problems (6.9% needed ongoing upper-airway support, and in 3.2% hemoglobin saturation was <90% during room-air–breathing at the time of discharge).[3] An earlier report by the same group documented a low incidence of tracheal intubation in the PACU for respiratory difficulty (0.19%),[5] similar to ours (0.09%). In a large study of four hospitals, inpatients who went to the PACU after any anesthetic technique, 2.7% of patients had major respiratory problems (hypoventilation, requirement for reintubation, pulmonary edema, or bronchospasm).[2]

Some studies have focused on predictors for severe respiratory outcomes. One study found severe adverse respiratory outcomes in 0.4% of patients and, as in our study, identified obesity with these respiratory problems.[1] From a retrospective review of records, Beard *et al.* identified 1.9% of patients who suffered adverse respiratory problems in the PACU after general anesthesia.[6] Events were more frequent for older age, male gender, thoracic or abdominal procedures, and use of paralyzing drugs or fentanyl in the operating room or opioids in the PACU. A study of patients who were given general anesthesia identified a positive correlation between decreased level of consciousness and respiratory morbidity on arrival in PACU (2.9%) and recommended routine practices for prevention.[16] Other specific anesthetic factors that have been implicated by case re-

ports or small controlled studies in the etiology of respiratory problems include opioids, sedatives, induction agents, inhalational anesthetics, and nondepolarizing neuromuscular relaxants.

Our study demonstrated that the use of premedication (sedatives with or without opioids) and intraoperative opioids (fentanyl > 2.0 $\mu g \cdot kg^{-1} \cdot h^{-1}$ and fentanyl with morphine) were significant factors in postoperative respiratory problems. Opioids used for preoperative sedation (morphine, meperidine) have a longer duration of action than the newer, short-acting intraoperative agents (fentanyl). Opioid levels at the time of transfer to the PACU are highly dependent on timing of the intraoperative dose. It is noteworthy that more than 20% of the patients with a CRE were given opioid antagonists at the time of their respiratory event in the PACU, implying that in some of these patients a residual opioid effect is an important factor. In addition, the combination of fentanyl or other opioids and midazolam has been shown to place patients at higher risk for hypoxemia and apnea.[17]

Few studies have examined the relation of the induction agent and postoperative respiratory problems. A study in eight volunteers demonstrated an acute depression of the carbon dioxide response curve after both propofol and thiopental but a more prolonged time to recovery of this response after propofol (more than 20 min).[18] However, other studies have shown that immediate recovery after thiopental is slower than that after propofol.[19-21] Although our study did not control for choice of induction agent, logistic regression identified an increased risk of major PACU respiratory problems with thiopental even after accounting for duration and type of surgery and patient illnesses.

No differences in respiratory outcome related to choice of inhalational anesthetic were identified in our study. The inhalational anesthetics depress the response to carbon dioxide and the reactions to hypoxemia.[22-24] They also suppress the activity of the upper-airway muscles predisposing to airway obstruction, even at subanesthetic doses.[25] Because we were unable to measure end-tidal concentrations of the inhalational anesthetics at either the termination of anesthesia or during the early part of the PACU stay, the contribution of inhalational anesthetics to CREs could not be assessed in this fashion.

Residual neuromuscular blockade in the early postoperative period, diagnosed by impaired neuromuscular transmission, has been documented in as many as 25% of patients who received nondepolarizing muscle blockade intraoperatively.[26,27] Furthermore, although ventilation and maximum inspiratory pressure may be adequate, the muscles of airway protection may be nonfunctional because of residual doses of nondepolarizing muscle relaxants.[28] In our study, 59.7% of patients with a CRE required insertion of an oral/nasal airway to relieve obstruction and 8.3% of patients who had a CRE required further antagonism of residual neuromuscular blockade. Although we were unable to determine the degree of neuromuscular blockade at the termination of anesthesia or in PACU, patients who received larger dosages of muscle relaxants (atracurium ≥ 0.25 $mg \cdot kg^{-1} \cdot h^{-1}$) in our study, were shown to be at risk of CREs. This information adds further evidence to the impact of residual paralysis after anesthesia and its associated morbidity.

The strengths of our study include the large number of cases of CREs, for which information was collected prospectively and reviewed independently in a systematic fashion. This methodology enabled us to examine risk factors associated with well-defined CREs, but the etiology of respiratory complications remains complex and multifactorial. There are additional factors, not explained by drug choice or dosage, that may be responsible for respiratory problems in the PACU. Examples of these factors include timing of opioid administration, adequacy of muscle relaxant antagonism, and wakefulness of patients before tracheal extubation and transfer to the PACU. These factors or practice patterns were not measured in our study. Even in our large series, there were insufficient numbers of cases to study each drug or drug combination individually requiring that groupings of drugs and dosages be used. Given the rarity of respiratory events, it is not feasible to study the effect of a single drug in a randomized clinical trial because an extremely large number of patients would need to be studied.[29] Thus, our study of 325 patients with a CRE should be considered a preliminary look at some of the important factors associated with complex respiratory problems. A more complete examination of the effect of some of the individual drugs will require a still larger series of patients.

A CRE is not a benign event; patients who had this ventilatory problem were at an increased risk of cardiac events, prolonged stay in the PACU, and unexpected ICU admissions—factors associated with major morbidity and increased costs to the health care system. We have identified patient and surgical factors that increased risk but are beyond the control of the anesthesiologist. However, even after controlling for these pa-

tient and surgical factors, we have also identified variables related to anesthetic management that play an important role in the etiology of a CRE in the PACU.

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