Respiratory Compromise is Common, Costly and Deadly

Executive Summary

- Respiratory compromise is a critical postoperative complication that dramatically increases the likelihood of adverse outcomes and the cost of patient care.
- Current monitoring strategies for the early identification of postoperative respiratory compromise may be inadequate.
- A comprehensive and continuous patient monitoring strategy encompassing respiratory rate, pulse oximetry and capnography has the potential to reduce the incidence and severity of postoperative respiratory compromise, and improve patient outcomes and reduce the cost of care.

Clinical Overview

Postoperative respiratory compromise represents a significant health care burden in terms of increased morbidity and mortality along with increased length of hospital stay and cost of care. Despite this established clinical and monetary burden, evidence suggests that current patient monitoring strategies are not optimal for the rapid identification of postoperative respiratory compromise. The implementation of a rigorous and comprehensive patient monitoring system has the potential to improve patient outcomes and reduce the cost of care. Given that patient ventilation and oxygenation are separate physiological processes, a number of clinical care guidelines currently recommend monitoring of oxygenation by pulse oximetry and monitoring of ventilatory function with capnography in high-risk patients. (Table 1)

Respiratory compromise may be precipitated by a range of postoperative pulmonary complications (PPCs), the most common of which is often referred to as respiratory insufficiency, arrest and failure (RIAF).1,2 These complications have a complex and multifactorial etiology, including preoperative, intraoperative and postoperative risk factors (see Covidien.com/RespiratoryCompromise for more detail on the pathogenesis of RIAF).1,3

Respiratory failure is defined as inadequate gas exchange by the respiratory system such that arterial oxygen levels cannot be maintained within normal levels.4 Respiratory failure is often related to respiratory obstruction and/or central drive failure.4 In both anesthesia and sleep, there is a loss of muscle tone because of decreased cortical influences and chemoreceptor drive, and changes in mechanoreceptor input. These factors can lead to the loss of airway patency.5 In the case of anesthesia, reductions in airway muscle tone can be further compounded by the direct suppression of neural and muscular activity by the anesthetic agents themselves. Thus, loss of wakefulness is compounded by anesthesia-induced depression of airway muscle tone along with depression of arousal ability leading to a reduced response to asphyxia.5

RIAF tends to be more common in older patients with more comorbidities such as liver disease, congestive heart failure, cancer, COPD and cardiovascular disease.7-10 Additional risk factors for the development of RIAF include obesity.

Table 1. Summary of current patient monitoring guidelines

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>ASA</th>
<th>APSF</th>
<th>ASPMN</th>
<th>Joint Commission</th>
</tr>
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<tbody>
<tr>
<td>Continuous pulse oximetry for patients at risk for respiratory compromise</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Continuous capnography for patients at risk for respiratory compromise</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Continuous monitoring by telemetry may be used</td>
<td>X</td>
<td>X</td>
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</tbody>
</table>

American Society of Anesthesiologists (ASA), Anesthesia Patient Safety Foundation (APSF), American Society for Pain Management Nursing (ASPMN)
and sleep disordered breathing.\textsuperscript{11,12} The administration of opioid analgesics is often associated with respiratory depression. For that reason, the need for naloxone rescue therapy can provide insight into the development of RIAF. Given this risk, the Anesthesia Patient Safety Foundation concluded that “continuous electronic monitoring of oxygenation and ventilation should be available and considered for all patients and would reduce the likelihood of unrecognized clinically significant opioid-induced depression of ventilation in the postoperative period.”\textsuperscript{13}

\section*{Incidence}

Key studies summarizing the incidence and clinical burden of postoperative respiratory compromise are summarized in Table 2 and presented in depth at Covidien.com/RespiratoryCompromise. While the overall incidence of pulmonary complications is influenced by the definition and criteria used for evaluation, evidence to date suggests that general PPCs are relatively common. With respect to respiratory depression and RIAF, studies suggest an incidence of approximately 1.5\% to 7\%.\textsuperscript{2,11,12,14-16} A 2010 database analysis of more than 700,000 elective surgical patients by Linde-Zwirble et al revealed an incidence of respiratory failure of 1.7\%.\textsuperscript{14} Bloom et al identified an incidence of respiratory depression as determined by naloxone rescue of 3.7\% among 894,076 surgical discharges after abdominal surgery.\textsuperscript{15} Additionally, a recent study of Medicare patients by Agarwal et al demonstrated a RIAF incidence of approximately 5\% in 2005, which increased to approximately 7\% in 2009. The authors \textbf{projected RIAF incidence out to 2019 and showed an expected increase of 31.6\% to 1,269,242 cases.\textsuperscript{2} Based on a study by Kelley et al, the incidence of RIAF in septic patients (9.6\%) may be even higher than that seen in the general population.\textsuperscript{9} Across all types of PPCs, including pneumonia, the rate of occurrence is roughly one in eight of all surgical patients.\textsuperscript{14,17,18} In a 1995 registry study of 2,291 patients, Lawrence et al demonstrated that PPCs were almost twice as common as postoperative cardiac complications (9.6\% vs. 5.7\%; p<0.00001).\textsuperscript{17} A survey of Premier database hospital discharges in 2008 revealed more than 160,000 cases of PPCs among 1,233,475 patients (13.1\%). Extrapolation of these data suggested a nationwide annual incidence of more than 1 million PPC cases.\textsuperscript{18} In a 2010 analysis, Linde-Zwirble et al demonstrated an incidence of PPCs of 11.6\% with a projected annual incidence of 583,300 cases per year.\textsuperscript{14} Although respiration rate monitoring is not able to diagnose PPCs such as pneumonia, it may have a role in detecting the resulting deterioration in respiratory function and provide an early alert.

\section*{Clinical Burden}

Evidence to date suggests that postoperative respiratory compromise is a major contributor to the risk of morbidity or mortality following surgery. Key studies investigating the clinical burden of postoperative respiratory compromise are described below (see Table 2 and Covidien.com/RespiratoryCompromise for more detail).

\subsection*{Mortality}

A number of studies have shown that the development of postoperative RIAF is associated with increased mortality.\textsuperscript{19-22} A 2012 database analysis of ~20,000 patients by Gupta et al revealed that patients who developed postoperative respiratory failure had a ~300-fold increase in 30-day mortality (15.66\% vs. 0.05\%; p<0.0001).\textsuperscript{19} Fischer et al demonstrated a 147-fold increase in mortality in abdominal reconstruction patients who experienced postoperative respiratory failure (14.7\% vs. 0.1\%; p<0.001).\textsuperscript{20} In a 2005 study of more than 100,000 patients by Khuri et al, patients with RIAF as demonstrated by failure to wean from mechanical ventilation had 30-day, one-year and five-year mortality rates of 29\%, 56\% and 78\%, respectively, as compared to mortality rates of 2\%, 9\% and 42\% for complication-free patients.\textsuperscript{22} The authors also demonstrated an 87\% reduction in median survival for patients who had experienced general pulmonary complications compared to patients without complications (2.2 years vs. 17.3 years).\textsuperscript{22} In a 2010 analysis by Linde-Zwirble et al, PPCs were associated with 70.3\% of all deaths in patients who had no respiratory resource use before surgery. When the authors extrapolated the findings to the national scale, pulmonary complications were estimated to be associated with 46,200 additional deaths.\textsuperscript{18} In a registry-based analysis of 86,270 surgical patients, Sigl et al demonstrated that patients aged 16-64 years who experienced a postoperative pulmonary complication had a 77-fold increase in the risk of in-hospital mortality, a 2.9-fold increase in the risk of one-year
post-discharge mortality, a 27.8-fold increase in the risk of having a hospital stay >30 days, and a 1.7-fold increase in the risk of readmission within 30 days (all \( p < 0.005 \)).

Cost of care
Not surprisingly, the development of postoperative respiratory compromise significantly increases the cost of care. Studies indicate that depending on the population analyzed, the projected annual cost of postoperative respiratory compromise ranges from $1.05 billion to $23.5 billion, with a projected 2019 cost of RIAF of $37.3 billion.2,15,16,18 In a 2010 statistical brief, Wier et al list RIAF as one of the common conditions associated with rapidly increasing hospital costs, with estimated total costs for 2007 of $7.78 billion attributed to more than 385,000 total hospital stays.24 In the March 2010 Health Grades Patient Safety in American Hospitals Study, the excess costs attributable to postoperative respiratory failure were $1.85 billion.25

Table 2. Summary of Key Studies

<table>
<thead>
<tr>
<th>Reference</th>
<th>PPC</th>
<th>Incidence</th>
<th>Mortality</th>
<th>Additional LOS</th>
<th>Additional Cost</th>
<th>Total Cases A</th>
<th>Total Additional LOS A</th>
<th>Total Cost A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimick et al 200426</td>
<td>All</td>
<td>3.4%</td>
<td></td>
<td>14 days</td>
<td></td>
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<tr>
<td>Khuri et al 200527</td>
<td>All</td>
<td>5.4%</td>
<td>30-day: 22% vs. 2%</td>
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<td></td>
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<td>1 year: 46% vs. 9%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>5 years: 71% vs. 41%</td>
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</tr>
<tr>
<td>Bloom et al 201028</td>
<td>RD</td>
<td>3.7%</td>
<td>8.4% vs. 3.3%</td>
<td>8 days</td>
<td></td>
<td>$18,322</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bloom et al 201028</td>
<td>All</td>
<td>7.2%</td>
<td>6.5% vs. 0.6%</td>
<td>9 days</td>
<td></td>
<td>$27,293</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linde-Zwirble et al 201029</td>
<td>All</td>
<td>13.1%</td>
<td>70.3% of deaths</td>
<td></td>
<td></td>
<td></td>
<td>1,062,000</td>
<td>$11.9 billion</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>associated with PPC</td>
<td></td>
<td></td>
<td></td>
<td>2.9 million floor days</td>
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<td></td>
<td></td>
<td>1.9 million ICU days</td>
<td></td>
</tr>
<tr>
<td>Linde-Zwirble et al 201029</td>
<td>RF</td>
<td>1.7%</td>
<td>1 death/10 cases</td>
<td>1 ICU day/2 cases</td>
<td>$24,000</td>
<td>583,300</td>
<td>867,400 floor days</td>
<td>$3.4 billion</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>584,200 ICU days</td>
<td></td>
</tr>
<tr>
<td>Sigl et al 201023</td>
<td>All</td>
<td>4.9% (≤65 years)</td>
<td>RR: 77 (&lt;65 years)</td>
<td>RR: 28 (&lt;65 years)</td>
<td>$12,547</td>
<td>700,182 (2005)</td>
<td>964,495 (2009)</td>
<td>$17.4 billion</td>
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<tr>
<td></td>
<td></td>
<td>9.3% (≥65 years)</td>
<td>RR: 19 (≥65 years)</td>
<td>RR: 25 (≥65 years)</td>
<td></td>
<td>1,269,242 (2019)</td>
<td></td>
<td>$23.5 billion</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>$37.3 billion</td>
</tr>
<tr>
<td>Agarwal et al 201111</td>
<td>RIAF</td>
<td>2.8%</td>
<td>23.2% vs. 2.9%</td>
<td>8.9 days</td>
<td></td>
<td>$28,876</td>
<td></td>
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<td>964,495 (2009)</td>
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<td></td>
<td></td>
<td></td>
<td>1,269,242 (2019)</td>
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<tr>
<td>Agarwal et al 201111</td>
<td>RIAF</td>
<td>2.8%</td>
<td></td>
<td></td>
<td></td>
<td>$5,745</td>
<td>($2,121-$12,072)</td>
<td></td>
</tr>
<tr>
<td>Agarwal et al 201120</td>
<td>RIAF</td>
<td>4.93% (2005)</td>
<td>7.04% (2009)</td>
<td></td>
<td></td>
<td>$34,952</td>
<td>29,700</td>
<td>$1.05 billion</td>
</tr>
<tr>
<td>Gupta et al 201119</td>
<td>RF</td>
<td>0.4%</td>
<td>15.66% vs. 0.05%</td>
<td>8.0 days</td>
<td></td>
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<tr>
<td>Kelley et al 20127</td>
<td>AllG</td>
<td>2.2%</td>
<td>3.1% vs. 0.1%</td>
<td>7.5 days</td>
<td>14.3 days (ICU)</td>
<td>$25,670</td>
<td>$47,615 (ICU)</td>
<td></td>
</tr>
<tr>
<td>Kelley et al 20128</td>
<td>RIAF</td>
<td>0.91%</td>
<td>34.6% vs. 1.2%</td>
<td>7.4 days</td>
<td>2.9 days (ICU)</td>
<td>$18,208</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fischer et al, 201320</td>
<td>RF</td>
<td>6.0%</td>
<td>14.7% vs. 0.1%</td>
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<td></td>
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</tr>
<tr>
<td>Kelley et al, 201321</td>
<td>RIAF</td>
<td>9.6%</td>
<td>43% vs. 17%</td>
<td>4.11 days</td>
<td></td>
<td>$12,547</td>
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</tr>
</tbody>
</table>

LOS, length of stay; PPC, postoperative pulmonary complication; RD, respiratory depression; RIAF, respiratory insufficiency, arrest and failure; RF, respiratory failure; RR, relative risk; a Estimated national level; b Mortality presented as PPC vs. non-PPC; c Projected annual total across all PPCCs; d Relative risk for length of stay >30 days; e Projected; f Average (range) loss for hospital cost minus Medicare payment; g Elective surgery cases.
Lawrence et al demonstrated that pulmonary complications resulted in a significantly longer length of stay than cardiac complications (22.7 days vs. 10.4 days; p=0.001).17 Dimick et al demonstrated that postoperative respiratory complications were associated with a 14-day longer mean length of stay and an extra $57,689 in total hospital costs (both p<0.001).26 In a 2010 analysis of the Premier Hospital database, Linde-Zwirble et al estimated that on a national scale, composite PPCs were associated with 2.9 million added floor days, 1.9 million added ICU days and $11.9 billion in added costs.18 Hospital readmissions within 30 days are approximately two times more likely in patients with PPCs at discharge, with an average readmission for a respiratory complication lasting approximately five days at a cost of more than $8,000 and an associated mortality rate of 10%.23,27 Extrapolating these results to the national scale, these authors estimated that respiratory complications resulted in more than 74,000 readmissions that were associated with 356,000 additional hospital days, $643 million in additional cost and 7,500 additional deaths.27

Strategies to reduce the clinical impact of postoperative respiratory compromise
Adverse events are often preceded by observable deterioration of patient condition, leading to the conclusion that many in-hospital adverse events may be preventable. In a 2002 study of 118 in-hospital cardiac arrest cases, Hodgetts et al concluded that approximately 62% of the cases were potentially avoidable.28 Respiratory depression and respiratory insufficiency are among the most common precipitating causes of in-hospital resuscitation or cardiac arrest events.29-31 In a 2009 analysis, Fecho et al demonstrated that respiratory depression was the precipitating cause of 61% of non-CPR resuscitation calls.29 Peberdy et al showed that acute respiratory insufficiency was the precipitating cause of 38% of in-hospital cardiac arrest cases.30 Wang et al found that 65% of respiratory arrest cases progressed to cardiopulmonary arrest with 10 minutes.31

Implementation of a comprehensive, continuous patient monitoring strategy
Unfortunately, despite the importance of patient monitoring, current patient monitoring strategies may not be ideal for the rapid identification of postoperative respiratory compromise. A 2009 analysis by Chen et al demonstrated that almost 77% of patient records were missing at least one vital sign immediately preceding an adverse event and that respiratory rate was the least commonly documented vital sign.32 Quach et al demonstrated delayed emergency team activation in 50% of patients with respiratory distress with a median delay of 12 hours.33 In these patients, delayed emergency team activation was associated with a twofold increase in mortality.33 The early recognition of patient deterioration has been identified as the primary determinant of the success of intervention. The implementation of a rigorous patient monitoring system in the postoperative setting has been shown to result in the reduction of rescue calls and a decline in ICU transfers.34 Also, adverse outcomes tend to be more common at night when patient monitoring may be less frequent or less comprehensive.30 Together, the data suggest that improved patient monitoring strategies may enable earlier interventions and improved patient outcomes. Given that patients are at the greatest risk for RIAF in the first 24 hours postoperatively, these patient-monitoring strategies should be employed as soon as possible following surgery.21,35

Respiration rate
Extreme respiration rate is a strong predictor of in-hospital mortality. In a 2004 analysis of 6,303 patients admitted to five hospitals, Buist et al demonstrated that a decrease in respiratory rate <6 respirations/minute was the strongest evaluated predictor of mortality, with a 13.7 fold (95% CI: 2.9-64.0, p<0.001) increase in the risk of mortality.36 In this patient cohort, increased respiratory rate (>30 respirations/minute) was the second strongest predictor of mortality, with an associated odds ratio of 6.1 (95% CI: 3.6-10.6, p<0.001).36 In an analysis of more than 6,000 emergency department patients, Barfod et al found that respiratory abnormalities were the strongest predictor of ICU admission, with an associated odds ratio of 9.1 (95% CI: 3.5-23.8, p<0.0001) for a rate of >35 respirations/minute.37 Unfortunately, respiration rate is often the least well-documented vital sign, potentially because of lack of clinical care staff time, knowledge or equipment constraints.32,38

Continuous pulse oximetry
A 2006 study by Ochroch et al demonstrated that the implementation of continuous pulse oximetry monitoring had beneficial effects on the timing and reasons for ICU transfer, such that there was a significant reduction in the
duration of ICU stay and thus estimated cost of ICU care. In this patient cohort, the estimated cost of ICU stay was approximately $23,000 less in the monitored patients as compared to the unmonitored patients. Gallagher et al demonstrated that 100% of bariatric surgery patients studied (n=15) experienced postoperative hypoxemia (defined as <90% for at least 30 seconds) and concluded that continuous pulse oximetry monitoring with an alarm set for <90% for at least 10 seconds would have captured all of these desaturation events. Taenzer et al demonstrated that the implementation of a patient surveillance system based on pulse oximetry with nursing notification of alarm violation via wireless pager resulted in a reduction of rescue events from 3.4 to 1.2/1,000 discharges along with a reduction in ICU transfers from 5.6 to 2.9/1,000 patient days.

**Capnography**

Several studies have suggested that capnography may provide the earliest indicator of respiratory distress. Oxygen saturation can be maintained even at low respiration rates, and lethal hypercarbia can occur in the presence of normal oxygen saturations. Consequently, the American Society of Anesthesiologists recommends that a comprehensive patient monitoring strategy for deeply sedated patients should include the monitoring of respiration rate along with exhaled CO₂ and apneic events by capnography in addition to the traditional monitoring of heart rate and SpO₂ by pulse oximetry. In a 2007 analysis, Overdyk et al used continuous pulse oximetry and capnography monitoring of 178 patients receiving postoperative patient-controlled opioids to show that the incidence of oxygen desaturation (SpO₂ <90%) was 12%, while the incidence of bradypnea (respiratory rate <10 for at least 3 minutes or <10 for at least 2 minutes) ranged from 41% to 58%. The authors concluded that continuous respiratory monitoring was optimal for the safe administration of patient-controlled opioids and stressed that episodes of respiratory depression could rapidly progress to respiratory failure if undetected. The Anesthesia Patient Safety Foundation has recently encouraged monitoring of patient oxygenation and ventilation in patients receiving patient-controlled analgesia (PCA) or neuraxial opioids in the postoperative setting.

A recent analysis of a national hospital survey concluded that continuous electronic monitoring of PCA patients reduced adverse events, costs and expenses. Specifically, of hospitals that monitored some or all of PCA patients with pulse oximetry or capnography, more than 65% reported a reduction in either overall adverse events or costs and expenses. For hospitals not currently using continuous monitoring, 86.7% indicated they were considering the use of continuous monitoring technology. For this analysis, 95.1% of hospitals were concerned about alarm fatigue and 87.8% of hospitals believed that a reduction in false alarms would increase the use of patient monitoring devices, such as an oximeter or capnograph. Finally, 70.7% of the hospitals surveyed indicated a preference for a single monitor that accurately incorporated key vital signs such as pulse rate, SpO₂, respiratory rate and etCO₂. For a summary of current clinical guidelines and a comparison of available monitoring modalities for the detection of postoperative respiratory compromise, see Covidien.com/RespiratoryCompromise.

**Conclusion**

Postoperative respiratory compromise is a relatively common postsurgical event that is associated with increased morbidity and mortality and increased cost of care. Evidence to date suggests that some type of postoperative pulmonary complication occurs in approximately one in eight surgical patients and that the development of pulmonary complications is associated with more than two-thirds of all postoperative hospital deaths. Unfortunately, current patient monitoring strategies may not be optimal for the early identification of postoperative respiratory compromise. The implementation of a comprehensive patient monitoring strategy encompassing the continuous assessment of respiration rate, pulse oximetry and capnography may enable early identification of postoperative respiratory compromise. Improved patient monitoring in conjunction with the implementation of a medical emergency team or rapid response team (MET/RRT) intervention strategy may help reduce the incidence and severity of subsequent events. Better strategies for preventing and managing postoperative respiratory compromise have the potential to improve patient outcomes and reduce the cost of care.
REFERENCES


