Continuous noninvasive respiratory volume monitoring for the identification of patients at risk for opioid-induced respiratory depression and obstructive breathing patterns

Christopher J. Voscopoulos, MD, Colin Marshall MacNabb, MS, Jenny Freeman, MD, Samuel M. Galvagno, Jr., DO, PhD, Diane Ladd, DNP, *and* **Edward George, MD, PhD,** *Waltham, Massachusetts*

BACKGROUND: Opioid-induced respiratory depression (OIRD) and postoperative apnea (POA) can lead to complications after surgery or traumatic injury. Previously, real-time monitoring of respiratory insufficiency and identification of apneic events have been difficult. A noninvasive respiratory volume monitor (RVM) that reports minute ventilation (MV), tidal volume, and respiratory rate is now available. The RVM was used to report the effect of opioids on respiratory status as well as demonstrate apneic breathing patterns in a hospital postanesthesia care unit.

METHODS: RVM traces were collected from 132 patients. Predicted MV (MV_{PRED}) for each patient was used to calculate and the "percent predicted" MV ($MV_{MEASURED}$ / MV_{PRED} × 100%) before opioid administration. Patients were stratified patients into two categories: "at risk," MV of less than 80% MV_{PRED}, and "not at risk," MV of 80% MV_{PRED} or greater. After opioid dosing, patients with MV of less than 40% MV_{PRED} were categorized as "unsafe." POA was defined as more than five apneic or hypopneic events per hour.

RESULTS: Of the 132 patients, 50 received opioids. Baseline MV was 7.2 ± 0.5 L/min. The MV-based protocol classified 18 of 50 patients as at risk before opioid administration. After the first opioid dose administration, at-risk patients experienced an average MV decrease (36.7% ± 8.5% MV_{PRED}) and 13 of 18 decreased into unsafe; the 32 not at-risk patients experienced a lesser average MV decrease (76.9% ± 6.3% MV_{PRED}). Only 1 of 32 not at-risk patients had a decrease in MV to unsafe. The proposed protocol had a sensitivity of 93% and a specificity of 86%. Of the 132 patients, 26 displayed POA. Of the 26 patients, 12 experienced POA without receiving opioids. Of the 26 patients with POA, 14 also received opioids, and of those, 6 were classified as unsafe.

CONCLUSION: This investigation indicates that at risk and unsafe respiratory patterns occur frequently after procedure. RVM provides continuous noninvasive objective measurements of OIRD and POA. The RVM may prove a useful tool in opioid dosing and in recognition and management of POA and strong potential value in the rapid detection of OIRD and apnea in the contemporary combat casualty environment. (*J Trauma Acute Care Surg*. 2014;77: S208–S215. Copyright © 2014 by Lippincott Williams & Wilkins)

LEVEL OF EVIDENCE: Care management study, level V.

KEY WORDS: Noninvasive respiratory volume monitoring; opioid-induced respiratory; depression; postoperative apnea; identification.

Postoperative pain management frequently includes the use of opioids, which can cause respiratory depression. Obstructive breathing patterns, often unappreciated preoperatively, can be initiated or exacerbated by anesthetics and opioids. Postoperative apnea (POA), unlike other forms of apnea, is often a combination of both obstructive and central apnea. Neither patient-controlled analgesia nor more vigilant bedside monitoring has eliminated POA or opioid-induced respiratory depression (OIRD),[1,2] both of which are associated with significant patient risk.[3–9] Objective quantitative assessment of respiratory status in nonintubated patients could reduce postoperative respiratory complications, decrease health care costs, and improve patient safety.[10] Despite the use of oximetry and capnography, prolonged hypoventilation still occurs, leading to oxygen desaturation and hypercarbia.[11] Supplemental oxygen can mask early signs of hypoventilation, causing a delay in recognition of OIRD.[12]

In many settings, opioids can be overadministered to treat reported pain scores or ensure patient satisfaction. Conversely, to minimize the possibility of inducing OIRD, many providers underadminister analgesics postoperatively for patients on chronic opioid therapy or for seriously injured casualties with acute pain, despite recent studies showing that failure to recognize and treat acute pain may result in increased incidence of chronic pain syndromes and worsen surgical outcomes.[12–21]

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From the Department of Anesthesiology (E.G.), Massachusetts General Hospital, Harvard Medical School, Boston; Department of Anesthesiology, Pain and Perioperative Medicine (C.J.V.), Brigham and Woman's Hospital; Respiratory Motion, Inc. (C.M.M., J.F., D.L.), Waltham, Massachusetts; Department of Anesthesiology (S.M.G.), University of Maryland School of Medicine, Baltimore, Maryland; and School of Nursing, West Virginia University (D.L.), Morgantown, West Virginia.
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Address for reprints: Jenny Freeman, MD, Respiratory Motion, Inc., 411 Waverley Oaks Rd, Building 1, Suite 150, Waltham, MA 02452;
email: jfreeman@respiratorymotion.com.

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Recent studies emphasize the inadequacy of current monitoring. Relying on late signs of respiratory insufficiency increases patients' risk for complications and potentiates more costly interventions. Since hypercarbia and hypoxemia are usually preceded by hypoventilation, adequate monitoring of minute ventilation (MV) could provide an earlier clinical indicator, improving the intervention timetable in patients' favor. A noninvasive respiratory volume monitor (RVM), which provides MV, tidal volume (TV), and respiratory rate (RR) measurements and displays a real-time respiratory volume curve, is now available for clinical use. This study assesses the ability of RVM to adequately monitor respiratory status in the clinical setting and proposes a theoretical framework for a first-order risk stratification based on respiratory status to predict incidences of OIRD and POA in postoperative patients and provide a conceptual infrastructure in which real-time monitoring can be combined with risk stratification to reduce the incidence of respiratory complications.

PATIENTS AND METHODS

Subjects

This study was approved by the Partners Institutional Review Board (Boston, MA). All subjects provided written informed consent before enrollment. Inclusion criteria were English-speaking men and women aged 18 years to 99 years undergoing elective joint replacement surgery. Health history, anthropometrics, and basic demographics were obtained.

Primary Protocol

Impedance-based RVM (ExSpiron, Respiratory Motion, Inc., Waltham MA) collected digital respiratory traces, MV, TV, and RR measurements from 132 patients (age, 68 years; range, 19–87 years; body mass index (BMI), 30.2 kg/m^2; range, 15.4–46.4 kg/m^2). Data collection was initiated preoperatively and continued during surgery and throughout the postanesthesia care unit (PACU) stay, following general (30 patients) or spinal (102 patients) anesthesia administration. The clinical staff members were blinded to the RVM measurements. PadSet electrodes were placed at the sternal notch, xiphoid, and right midaxillary line as previously described.[22] Historically, the use of thoracic impedance measurements to quantitate respiratory volumes were disappointing;[23] however, the RVM system used here has demonstrated strong correlations (mean ± 95% confidence interval [CI], 0.96 ± 0.16) for regular and erratic breathing and clinically relevant accuracy (average error of 9.3%, 9.0%, 1.8% for MV, TV, and RR, respectively) between RVM and spirometric measurements in a broad set of subjects.[15]

"Predicted" MV (MV_{PRED}) was calculated for each patient using standard formulas: body surface area[24] × 4 (men); body surface area × 3.5 (women).[25] MV_{PRED} represents adequate MV during quiet respiration in awake, nonintubated patients. "Percent predicted" was defined as $MV_{MEASURED} / MV_{PRED} \times 100\%$. Individual "preoperative baseline" MV (MV_{PREOP}) measurements were obtained during 2 minutes of uninterrupted breathing before opioid or anesthetics administration.

To create a first-order protocol for patient care based on RVM measurements, we started with the ARDSnet protocol for weaning patients off mechanical ventilation, which defines adequate ventilation associated with successful extubation. Since the ARDSnet protocol uses a cutoff of 40% of the predicted value for normal respiration to indicate inadequate ventilation, unsuitable for extubation (albeit in TV instead of MV), this became the criteria for designating a patient with an MV of less than 40% predicted as "unsafe." For example, in an 80-kg patient with a low normal RR of 8, an MV of 40% MV_{PRED} would translate to 2.6 L/min. If one would not consider such a mechanically ventilated patient to be safe for extubation with sole reliance on spontaneous breathing, we assumed spontaneous breathing below this cutoff to be inadequate (unsafe) and with potential to result in respiratory complications if left untreated.

Using average ventilator settings in the operating room (OR), we defined "adequate ventilation" in anesthetized patient. For the 30 patients receiving general anesthesia, the ventilator MV was a mean ± SD of 79% ± 15% MV_{PRED}, between 47% MV_{PRED} and 103% MV_{PRED}. No patient was managed at an MV of less than 40% MV_{PRED}. Therefore, we designated MV of less than 80% MV_{PRED} in the postoperative period as "at risk." OR ventilator settings also supported the ARDSnet-derived definition of unsafe, since no patients were ventilated at less than 47% MV_{PRED}. The 40% unsafe cutoff was less than the lowest ventilator setting and half of the average OR MV of 80% MV_{PRED}.

Analyzing the Effects of Opioids

All patients received 0.2-mg hydromorphone via patient-controlled analgesia pump. One patient also received two boluses of 25-μg fentanyl. Average RVM measurements were calculated from 30-second segments approximately 30 minutes after PACU arrival, within the 30 minutes before and after opioid administration, and within 30 minutes before discharge. Before opioid administration, patients were classified as at risk ($MV < 80\%\ MV_{PRED}$) or not at risk ($MV \geq 80\%\ MV_{PRED}$), sustained for at least 2 minutes. Following opioid administration, patients were classified as unsafe if their recorded MV was less than 40% MV_{PRED}, sustained for at least 2 minutes.

Analyzing Obstructive Breathing Patterns

A post hoc analysis characterized apneas and hypopneas for each patient. Apneas were defined as episodes with no detected breaths for 10 or more seconds and hypopneas were defined as episodes with TV reduction of more than 50% (from baseline) lasting for 10 or more seconds. A patient was included in the POA cohort if they experienced five or more episodes of apneas or hypopneas per hour during the entire PACU stay. Most patients had an increase in POA after narcotics or during somnolence not temporally associated with opioids. To quantify the worst episodes of repetitive apneas, the maximum number of events per hour in the PACU was calculated.

Statistical Analyses

Multifactor analysis of variance evaluated differences in patient demographics between the different groups. Paired two-tailed *t* tests were used to calculate the effect of opioids on MV (e.g., MV levels before vs. after opioid administration). One-sample *t* tests evaluated whether group average MV levels

were significantly different from predefined cutoff levels (e.g., 80%, 40%). Conventional sensitivity and specificity analyses evaluated the predictive abilities of the proposed classification models.[26] All analyses were performed in Matlab R2012b (Mathworks, Natick, MA).

RESULTS

Continuous RVM traces were recorded and analyzed from 132 patients undergoing elective joint replacement. Thirty patients received general anesthesia, and 102 received regional anesthesia.

Opioid Administration Causes Respiratory Depression

Of the 132 patients, 50 (38%; mean age, 65 years; range, 19–83 years; mean BMI, 29.8 kg/m^2; range, 19.2–46.4 kg/m^2) received one or more opioid doses in the PACU. Baseline MV (MV_{PREOP}) in this 50-patient cohort was 7.2 ± 0.5 L/min (mean ± SEM, 93.1% ± 6.1% MV_{PRED}; Fig. 1*A* and *B*). The average MV for this cohort within 30 minutes after arrival at the PACU was slightly elevated (8.2 ± 0.5 L/min; 106.3% ± 6.3% MV_{PRED}) and remained practically unchanged until after the first opioid dose administration, after which RVM showed a significant decrease in the average MV, from 8.1 L/min to 5.2 L/min (31.4% ± 3.0% decrease, $p < 0.0001$, paired t test). The decrease in MV was driven primarily by a reduction in TV (from 575 mL to 430 mL, 20.9% ± 3.5% decrease). RR had a lesser decrease (from 14.0 breaths per minute to 12.5 breaths per minute, 11.1% ± 3.0% decrease). Both decreases were statistically significant ($p < 0.0001$, paired t test).

Real-Time Prediction of OIRD

To better understand effects of opioids on individuals, patients were categorized as at risk and not at risk based on the MV recorded before initial opioid administration in the PACU. An MV of less than 80% MV_{PRED} (for >2 minutes) was used to categorize patients as at risk, and an MV of 80% MV_{PRED} or greater was used to categorize patients as not at risk. The at-risk patients receiving opioids showed an average MV decrease of 36.7% ± 8.5% of MV_{PRED} (significantly <80% MV_{PRED}, $p < 0.001$, Fig. 1*C*) after opioid administration, whereas the not at-risk group showed a smaller MV decrease of 76.9% ± 6.3% MV_{PRED}, not significantly lower than the 80% MV_{PRED} threshold ($p > 0.2$, Fig. 1*D*).

Based on these observations, a first-order clinical classification scheme was proposed, which estimated each patient's risk of respiratory depression, providing an infrastructure for clinicians to develop treatment protocols and individualized care. The classification was designed to provide maximum sensitivity, with some trade-off of specificity. We hypothesized that at-risk patients would be more likely to develop respiratory depression and become unsafe with standard doses of opioids

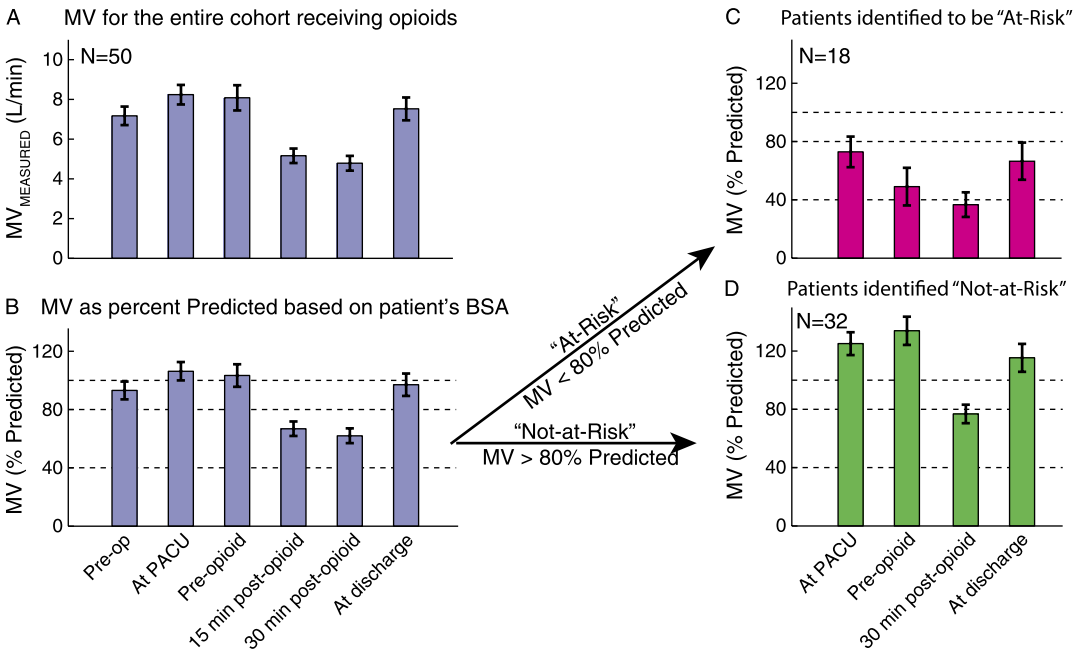

Figure 1. *A*, MV measurements at various time points during the perioperative period. Across the entire patient population, there was a distinct depression in MV within 15 minutes of the administration of the first opioid dose in the PACU. The average MV level across the whole population does not noticeably decrease further in the following 15 minutes and recovers to baseline levels before discharge. *B*, MV across the cohort calculated as percent predicted, based on individual body surface area. The plot demonstrates a similar trend as in *A*; however, by using MV as percent predicted (MV_{PRED}), we are able to normalize the opioid response to account for patient size. *C*, Patients designated at risk for respiratory depression. The *red bars* show the course of 18 (36%) of the 50 patients who received an initial opioid dose when their MV was less than 80% MV_{PRED} and subsequently experienced severe respiratory depression. *D*, Patients designated not at risk for respiratory depression. The *green traces* describe the course of the remaining 32 (64%) of the 50 patients who received an initial dose of narcotics when their MV was greater than 80% MV_{PRED} and subsequently experienced minimal respiratory depression throughout their PACU stay.

and, as a result, should be potentially considered for closer monitoring or a modified opioid dosing regimen. Of the 50 patients receiving opioids, the protocol classified 18 of 50 as at risk (MV < 80% MV_{PRED}) and 13 of these 18 had MV decreases into the unsafe (MV < 40% MV_{PRED}) range after opioid administration. Only 1 of the 32 remaining patients, classified as not at risk (MV ≥ 80% MV_{PRED}) had a decrease in MV to unsafe (Fig. 2*A*). This classification scheme had a success rate (sensitivity) of 93%, with a correct rejection rate (specificity) of 86% and a negative predictive value (NPV) of 97%. The Type II error (false-negative) rate was 7.1% (Fig. 2*A*). Only 1 (2%) of 50 patients with potential respiratory compromise following opioid administration was misclassified.

Systematic post hoc analysis of the natural variability in MV measurements illustrated the differential effects of opioids on patients classified as at risk versus not at risk (Fig. 2*B*). For a patient at risk, MV in the 30 minutes before opioid administration is less than 80% MV_{PRED} more than 50% of the time, and at the time of opioid administration, the 2-minute average MV is less than 80% MV_{PRED} (Fig. 2*B*, *black curve*, left panel). In the 30 minutes after opioid administration, the cumulative distribution of MV shifts such that 50% or more of the time, the patient's MV is unsafe (<40% MV_{PRED}; Fig. 2*B*, *red curve*, left panel). In contrast, the shift in the cumulative distribution of MV in a patient not at risk (MV ≥ 80% MV_{PRED}; Fig. 2*B*, right panel) is much smaller, and the MV is never unsafe (<40%

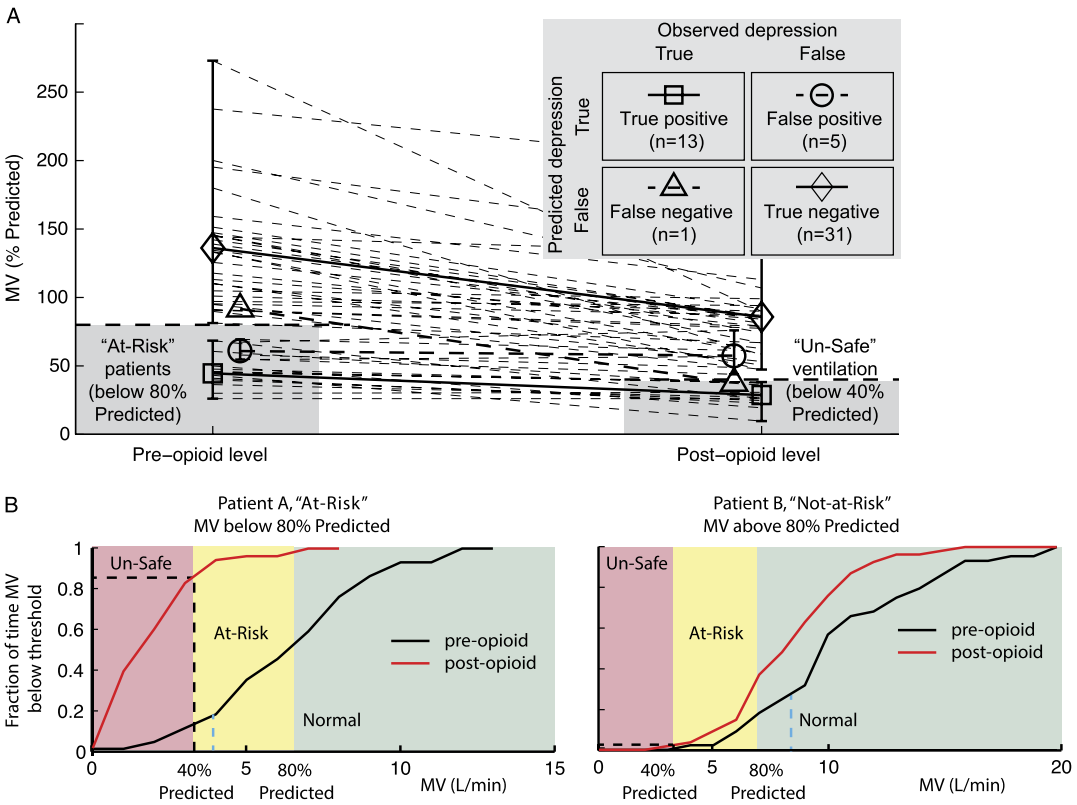

Figure 2. *A*, Classification of protocol performance. Patients were stratified based on their individual percent predicted MV levels before opioid administration with a cutoff level of an MV less than 80% predicted. Eighteen patients were identified as at risk (<80% predicted, *square* and *circle*), and 32 were identified as not at risk (>80% predicted, *diamond* and *triangle*). Of the 18 patients classified at risk, 13 displayed unsafe MV levels (defined as <40% predicted) after opioid administration (*square*), whereas the remaining 5 did not display unsafe MV levels. Of the 32 not at-risk patients, 31 demonstrated not unsafe MV, whereas only in the 32 not at-risk patients MV was considered unsafe, dropping to less than 40% predicted. This protocol yielded a sensitivity of 92.9%, a specificity of 86.1%, with a positive predictive value of 72.2% and an NPV of 96.9%. Importantly, this protocol focuses more on sensitivity than specificity, with only one patient with potential respiratory compromise misclassified (note NPV > 95%). *B*, Individual patient plots of MV levels before and after an opioid dose. *B*1, The distribution of time spent at different MV levels for an at-risk patient. Preopioid MV was measured at 50% predicted (*vertical blue dashed line*). Curves demonstrate the cumulative distribution functions of MV for 30 minutes before (*solid black curve*) and 30 minutes after (*red curve*) administration of 0.2-mg hydromorphone. The curve shifts such that following opioid administration, more than 80% of the time MV is at unsafe levels (<40% predicted [3.1 L], *black dashed line*). *B2*, The distribution of time spent at different MV levels for a not at-risk patient. Preopioid MV was recorded at 105% predicted (*vertical blue dashed line*). Curves demonstrate the cumulative distribution functions of MV for 30 minutes before (*solid black curve*) and 30 minutes after (*red curve*) administration of 0.2-mg hydromorphone. The curve shift is minimal following opioid administration and essentially no time during the 30 minutes following an opioid dose is MV at unsafe low levels (<40% predicted [3.4 L], *black dashed line*). This analysis method can be used as the basis for creating customized opioid protocols, developing discharge criteria and identifying patients requiring additional monitoring once they leave the PACU.

MV_{PRED}) following opioid administration. The outcome of this stratification scheme is summarized in Figure 3.

Real-Time Monitoring of Apneic Breathing

During their PACU stay, 26 (18%) of 132 patients (mean age, 67.5 years; range, 53–86 years; mean BMI, 27.2 kg/m^2; range, 15–38 kg/m^2; 15 males) displayed POA. Only 20% (5 of 26) of these patients had a previous diagnosis of obstructed sleep apnea (OSA), and 80% (21 of 26) did not. In the 26 patients who displayed POA, an average of 35 ± 4.2 apneic events (12.3 ± 1.2 events per hour) was observed during their PACU stay. These apneic events were grouped in distinct periods. Most patients who displayed apnea had significant variability in event frequency during different portions of their PACU stay, with an increase in frequency after opioids or during somnolence not temporally associated with opioids. The average maximum number of apneas for a given hour in the PACU across all patients was 22.2 ± 2.3 events (range, 7–50 events). These events had an average duration of 15.7 ± 0.6 seconds (range, 12–24 seconds) between consecutive breaths. Surprisingly, multifactor analysis of variance found no effect of age, sex, or BMI in differentiating patients with and without POA ($p > 0.05$ for all factors).

Fourteen patients demonstrating POA also received opioids in the PACU, and 6 (43%) of 14 were classified as unsafe (<40% MV_{PRED}) after opioid administration. Only 8 (22%) of 36 patients without POA dropped into the unsafe MV range. Figure 4 shows representative respiratory volume traces from two patients with POA.

DISCUSSION

This study demonstrates that RVM can adequately monitor and quantify respiratory patterns and the effects of opioids in nonintubated postoperative patients. The first-order post hoc classification scheme described here demonstrates high sensitivity and specificity for identifying patients at risk for becoming unsafe following opioid administration based on the proposed 80/40% MV_{PRED} thresholds.

In this study, decreases in TV contributed more to OIRD than decreases in RR (21% vs. 11%), underscoring the importance of monitoring respiratory volumes, not just rates. In this cohort, opioid administration had a greater negative effect on TV compared with RR. Post hoc analysis revealed that nearly 20% of the patients experienced notable episodes of POA and, similar to a recently published study,[27] more than 80% of POA patients did not have a preexisting diagnosis of OSA, underscoring the unique pathophysiology of POA.[28] In patients demonstrating POA, the rate of OIRD was almost double that of those without POA (43% vs. 22%). RVM predicted respiratory depression in all but one of these POA patients. The primary objective indicator of respiratory compromise continues to be pulse oximetry. However, the inaccuracy of oximetry increases with increasing desaturation (accuracy, ±2% with $Sa_{O_2} > 90$; ±5% with Sa_{O_2} of 80–90; and ±12% with $Sa_{O_2} < 80$)[29–31] and with hypovolemia or vascular disease.[11] Sp_{O_2} levels decline only after respiratory decompensation has begun.[11,29] Delivery of supplemental oxygen exacerbates this hysteresis.[9] Standard orders to increase oxygen administration to maintain saturations above a specified level can lead to even later recognition of respiratory compromise.[29] Patients in hypercarbic respiratory failure can have normal or near-normal oxygen saturations when receiving supplemental oxygen,[11,29] belying their true respiratory status. Lynn and Curry[11] discuss the inadequacies of pulse oximetry and the dangers of relying on the 90% Sp_{O_2} threshold, citing the risk of unexpected rapid respiratory decline, which can progress to clinical instability and death.[11]

Some reviews promote the benefits of end-tidal CO_2 ($P_{et}CO_2$) measurement in predicting impending respiratory compromise in advance of pulse oximetry data, but there are clear disadvantages of reliance on $P_{et}CO_2$. $P_{et}CO_2$ generally underestimates Pa_{CO_2} in stable intubated patients. When ventilation-perfusion mismatch occurs, the difference between these measurements grows, and $P_{et}CO_2$ becomes less reliable and more difficult to interpret.[32,33] Breathing pattern changes affect the capnography wave form, making the measurements less accurate in patients with erratic breathing, such as those recovering from anesthesia.[33,34] Oxygen administration can dilute $P_{et}CO_2$ levels, masking changes.[34] Accuracy in nonintubated patients has been questioned because of changes in oxygen flow, potential mouth breathing, and maintenance of

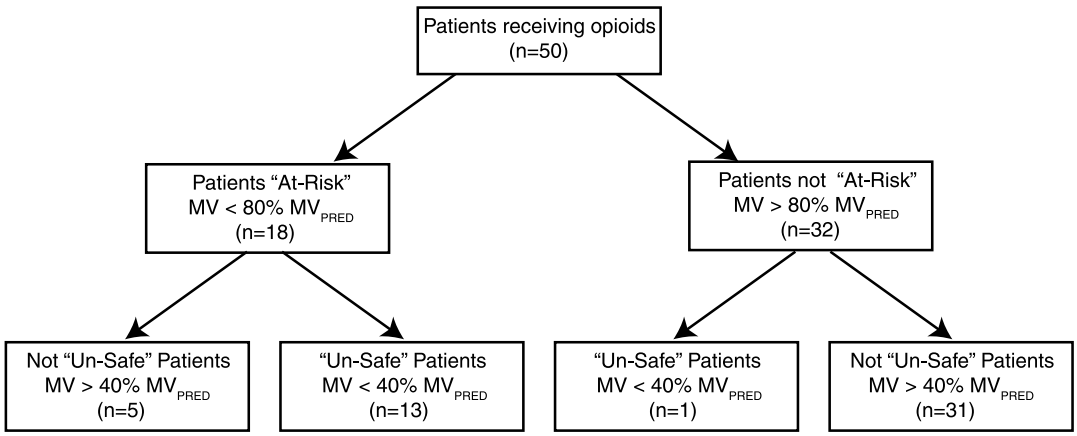

Figure 3. Distribution of the patient cohort receiving opioids into at-risk and unsafe categories. The flowchart summarizes the initial patient classification based on their MV before the first opioid dose (MV < 80% MV_{PRED} vs. MV ≥ 80% MV_{PRED}) and then shows the fraction of patients in each of the two categories that become unsafe (MV < 40% MV_{PRED}).

proper sensor positioning. Additional problems arise when drugs or cardiac output influence pulmonary blood volumes or peripheral perfusion, which limits or negates the ability of pulse oximetry to interpret the arterial tree wave form.[35,36] Controversy exists as to whether there is true utility for capnography beyond validation of endotracheal tube placement.[33]

Continuous MV monitoring provides a new way to assess respiratory status and delivers early warning of OIRD. RVM has potential to provide feedback on the effect of opioids, individualize opioid dosing protocols, and assist with triage decisions. As in standard pulmonary function tests, the ratio of postoperative $MV_{MEASURED}$ to a calculated $MV_{PREDICTED}$ can quantify the level of respiratory depression over a wide range of patients. This study observed that administration of opioids to patients with an MV of less than 80% MV_{PRED} for adequate ventilation may lead to potentially dangerous respiratory

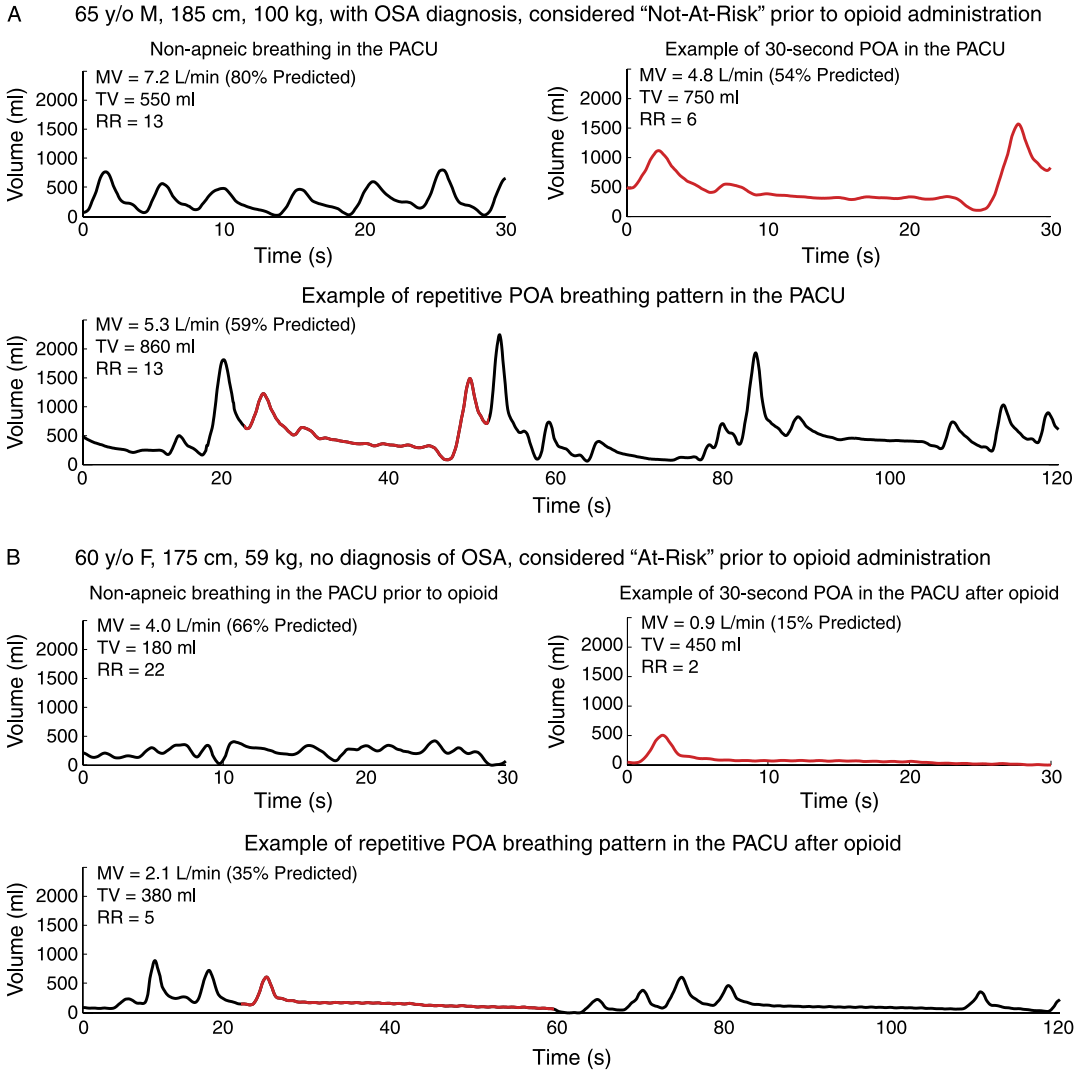

Figure 4. Example of respiratory volume traces from two representative patients who demonstrated POA breathing in the PACU. A, Traces from a patient with preexisting diagnosis of OSA. During periods of quiet, nonapneic breathing (left), MV for this patient dropped to 7.2 L/min, approximately 80% of his predicted MV_{PRED} of 9.0 L/min. The right part of the panel shows POA breathing patterns, likely when the patient fell asleep, showing a reduction in MV to 4.8 L/min during a long apneic pause. Note that the patient's MV never dropped into the unsafe zone of less than 40% MV_{PRED}. The bottom part of the panel shows more than a 2-minute period of this repetitive apneic breathing; the average MV was recorded at 5.4 L/min (59% of MVPRED). B, Traces from a patient without a preexisting diagnosis of OSA. Note that this patient is unlikely to be considered at high-risk for apnea based on her demographics. The left part of the panel shows the respiratory pattern in the 30 minutes before the patient receiving the first dose of opioid in the PACU. She was breathing with a shallow, rapid respiratory pattern and an MV of 4.0 L/min, approximately 66% of her predicted MV_{PRED} of 6.0 L/min, placing her into the at-risk category. The right part of the panel shows that shortly after the administration of a 0.2-mg dose of hydromorphone, POA breathing patterns began, likely triggered by the opioid, with a substantial reduction in MV down to 0.9 L/min during a long apneic pause (15% of MV_{PRED}), placing the patient into the unsafe zone. The bottom part of the panel shows that during a 2-minute period of this repetitive apneic breathing, the average MV in this patient was recorded at 2.1 L/min (35% of MV_{PRED}), still placing the patient in the unsafe zone.

depression (<40% MV_{PRED}). Patient-specific protocols may reduce episodes of respiratory compromise while optimizing pain control. The use of RVM can help guide care providers to use multimodal pain management strategies that have less impact on respiratory drive. This may include the use of opioids such as methadone, tramadol, tapentadol, nonsteriodal anti-inflammatories, anticonvulsants, intravenous acetaminophen, N-methyl-D-aspartate (NMDA) receptor antagonists, or neuraxial or regional anesthesia techniques.[37–40] More aggressive but safe use of opioids in difficult-to-treat patients with significant opioid tolerance due to severity of injury, body habitus, or chronic use may be possible with quantitative RVM measurements of respiratory status.

Furthermore, RVM has the potential to direct and adjust therapeutic interventions and provide an objective real-time assessment of the efficacy of an intervention, such as the use of neuraxial anesthesia to treat rib fractures. RVM may prove effective at the point-of-care for rapidly assessing whether noninvasive ventilation (NIV) is warranted and whether implementation of NIV has positively affected the pretreatment respiratory parameters.[34,36] The current standard of relying solely on blood gas measurements can greatly delay interventions.

Limitations of the study include the following: (1) given its blinded nature, no interventions were undertaken when patients were defined as either at risk or unsafe; (2) no patients in this study had an adverse event in the PACU, so the 80/40% MV_{PRED} thresholds were not fully clinically validated; (3) to execute the study in a relatively controlled environment, it was conducted in a hospital setting and the cohort was limited to elective orthopedic surgery patients and was not representative of all patients after surgery or traumatic injury.

RVM's ability to provide continuous, real-time measurements of the adequacy of ventilation directly, rather than monitoring secondary indicators, can provide information early enough to allow for timely interventions and has the potential to reduce primary intubations, reintubations, the need for and the effect of NIV, the requirement for opioid reversal, and other respiratory complications. Data presented here also support the potential for RVM to assist in creating protocols to help prevent respiratory decompensation by individualizing pain management regimens. Patients at risk can receive lower opioid doses. Patients with apneas or unsafe MV can be assessed, and interventions can be initiated before progression to respiratory compromise. Patients in severe pain with adequate RVM measurements may safely receive additional opioids, potentially decreasing the incidence and severity of posttraumatic stress disorder after traumatic injuries.[41] Since 43% of postoperative patients experience inadequate pain control, RVM could improve both patient safety and satisfaction and reduce complications from inadequate pain control.[42]

The recent availability of RVM permits the collection of real-time respiratory volume data in nonintubated patients in the postoperative setting. This study demonstrated that the RVM device could report episodes of POA as derived from RVM respiratory traces and OIRD reported as low MV measurements. Analysis of the data led to the development of a first-order algorithm, proposing a stratification scheme to identify patients that would be more likely to decrease their MV into an unacceptably low range after opioid administration. The new data provided by the RVM may be useful to individualize care, not only by better defining and quantitating existing respiratory status but also by providing the basis for patient stratification and implementation of patient-specific pain management protocols. Such applications have great potential for preventing episodes of significant respiratory depression, improving patient safety and optimizing analgesia for critically injured casualties.

AUTHORSHIP

C.J.V. helped write and revise the manuscript. C.M.M. helped analyze the data. J.F. helped design the study as well as write and revise the manuscript. S.M.G. helped write the manuscript. D.L. helped write and revise the manuscript. E.G. helped write the manuscript.

DISCLOSURE

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