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ORIGINAL RESEARCH

A risk stratification algorithm using non-invasive respiratory volume monitoring to improve safety when using post-operative opioids in the PACU

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Abstract Late detection of respiratory depression in non-intubated patients compromises patient safety. SpO_2 is a lagging indicator of respiratory depression and $EtCO_2$ has proven to be unreliable in non-intubated patients. A decline in minute ventilation (MV) is the earliest sign of respiratory depression. A non-invasive respiratory volume monitor (RVM) that provides accurate, continuous MV measurements enables clinicians to predict and quantify respiratory compromise. For this observational study, practitioners were blinded to the RVM measurements and pain management followed the usual routine. Patients were stratified by their MV on PACU admission and classified as "At-Risk" or "Not-At-Risk," with progression to "Low MV" status following opioids assessed for each category. The purpose was to determine if stratifying based on MV on PACU arrival could identify patients at higher risk for respiratory depression. Ability to identify in advance patients at higher risk for respiratory depression following standard opioid dosing would drive changes in pain management and improve patient care. RVM and opioid administration data from 150 PACU patients following elective joint-replacement surgery were collected in an observational study. "Predicted" MV (MV_{PRED}) and "Percent Predicted" ($MV_{MEASURED}/MV_{PRED} \times 100$ %) were calculated for each patient using standard formulas. Prior to opioid administration, patients were classified as either "Not-At-Risk" ($MV \geq 80$ % MV_{PRED}) or "At-Risk" ($MV < 80$ % MV_{PRED}). "Low MV" was defined as $MV < 40$ % MV_{PRED}. Post-operative apnea (POA) was defined as $\geq$5 ten-second apneas per hour of PACU stay. We compared the incidences of Low MV following a single opioid dose, POA, and Low MV at discharge for both groups. In the PACU, 74/150 patients received opioids. Within 15 min of opioid administration, 32 % (24/74) developed Low MV. The risk-stratification algorithm identified 22/24 patients (92 % sensitivity). Only 46 % of them had POA, and the majority had Low MV without POA. At discharge, 29/150 patients had Low MV and those receiving opioids were 50 % more likely to display Low MV (23 vs. 16 %). The RVM can identify patients at-risk for opioid-induced respiratory depression and/or experiencing POA. Monitoring of MV can guide opioid-dosing regimens and may increase patient safety across the continuum of care.

Keywords Respiratory monitoring · Patient safety · Risk-stratification · Minute ventilation · Opioids

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1 Introduction

Opioids are commonly used to treat moderate to severe post-operative pain [1] and although multimodal perioperative analgesia has been advocated for some time [2], narcotic analgesia remains the mainstay of post-operative pain therapy in the United States [3–8]. As a result, opioid induced respiratory depression (OIRD) is a well-recognized complication in the post-operative period. Unfortunately, neither

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patient-controlled analgesia (PCA) nor careful bedside monitoring with current technologies have sufficiently reduced complications due to OIRD. Opioids given in the PACU for post-operative pain have unpredictable effects due to the confluence of patient specific opioid sensitivity, intraoperative opioids, sedating drugs and residual anesthetic agents [9, 10]. Stratifying and triaging patients based on risk of developing OIRD prior to opioid administration could enhance safety by allowing clinicians to individualize pain management and could aid in selecting the monitoring strategy and determining the best location for follow-up care.

In a survey of closed anesthesia malpractice claims associated with respiratory depression, Lee et al. [11] found that 88 % of respiratory depression occurred within 24 h of surgery and 13 % within 2 h of arriving on the general hospital floor (GHF). In the closed claims study, respiratory rate (RR) and SpO2 were being monitored continuously 57 % and 32 % of the time, respectively. Importantly, 97 % of the claims were judged to be likely preventable with better monitoring. Surprisingly, 63 % of these events occurred in patients under 50 years and 55 % of patients had ASA status 1 or 2 [11]. In the associated editorial, Daniel Sessler noted that most severe adverse outcomes do not result in malpractice claims, despite occurring at a "concerning rate" [12]. He also noted that only 1/4 of patients had documented or likely undiagnosed obstructive sleep apnea (OSA), which is often considered a major risk-factor. In fact, post-operative opioids were found to be a greater contributor to these adverse events than OSA. This is particularly important for "healthy" patients, considered low-risk, in whom, despite routine SpO_2 monitoring, late detection of respiratory depression continues to cause serious complications. To address this issue, a recent Joint Commission Sentinel Event Alert suggested that clinical staff should not rely solely on SpO_2, especially for patients on supplemental oxygen [13].

Current practice for monitoring post-operative, non-intubated patients uses surrogate indicators of respiratory adequacy, generally SpO_2 or RR alone [14, 15] and, uncommonly, end-tidal CO_2 ($EtCO_2$) [16–20]. Continuous measurement of minute ventilation (MV), which provides the earliest signs of respiratory insufficiency [21] has not been previously available, but a bioimpedance-based respiratory volume monitor (RVM) has recently been developed which provides continuous tidal volume (TV), MV, RR measurements and real-time respiratory traces for non-intubated patients [22–25]. While apneic episodes have traditionally been difficult to detect and evaluate outside of a sleep laboratory, the RVM is capable of detecting and discerning abnormal respiratory patterns including apnea and hypopnea [24]. The RVM used here has been shown to accurately and consistently report MV, TV, and RR in non-intubated volunteers and surgical patients with clinically relevant accuracy (average error <10 % for MV and TV and <2 % for RR) between the RVM and spirometric measurements [22] or mechanical ventilator values [25]. In addition, the RVM was shown to be capable of discerning the much smaller respiratory volumes associated with obstructed breaths [22], versus hypoventilation [23].

The current study was designed to detect and quantify OIRD and post-operative apnea (POA) in post-operative patients. We hypothesized that quantitative respiratory volume measurements could be used, as previously suggested [23], to identify patients at risk for OIRD. Furthermore, we wanted to evaluate patients with POA, and assess the adequacy of ventilation at the time of proposed discharge in an attempt to risk-stratify patients headed to the GHF. Using quantitative RVM assessments, a first-order algorithm was developed for projected use in directing opioid dosing and patient discharge. The implementation of such an algorithm could potentially improve outcomes, enhance patient safety, and improve efficiency of care.

2 Methods

2.1 Primary protocol

The study was conducted at the Massachusetts General Hospital and was approved by the Partners Institutional Review Board (Boston, MA). Inclusion criteria were English-speaking men and women aged 18–99 years undergoing elective joint-replacement surgery. Exclusion criteria were pregnancy or lactation. Health history and basic demographic data were obtained. Anesthesia and post-operative pain management were determined by the clinical anesthesiologist and were not part of this research protocol. Times, dosages, routes of medications, doses and delivery methods of supplemental O_2, and vital signs (BP, HR, RR, and O_2 saturation) were recorded throughout the study. A bioimpedance-based RVM (ExSpiron, Respiratory Motion, Inc., Waltham, MA) was used to monitor the patients and collect digital respiratory traces throughout the study. Electrode PadSets were placed in the recommended positions: sternal notch, xiphoid, and right mid-axillary line at the level of the xiphoid, as previously described.

All monitoring and clinical data were collected pre-operatively, during surgery, and throughout the entirety of the post-anesthesia care unit (PACU) stay. In the patients undergoing surgery under general anesthesia, continuous data from the ventilator (Apollo, Draeger Medical Inc., Telford, PA) were also collected. Perioperative patient care was done according to standard practice by clinical staff who were blinded to the RVM measurements [23]. Post-operatively, patients received a standard opioid regimen

and were typically managed on hydromorphone PCA with a 0.2 mg demand dose, 10 min lockout interval, no basal rate, and a 1 h limit of 1.5 mg.

The RVM continuously recorded "Measured" MV ($MV_{MEASURED}$). "Predicted" MV (MV_{PRED}) was calculated for each patient using standard formulas: Body surface area (BSA) × 4 for men, BSA × 3.5 for women [26, 27]. MV_{PRED} is considered to represent expected minute ventilation under baseline conditions of quiet respiration in the awake, non-intubated patient. "Percent Predicted" was defined as $MV_{MEASURED}/MV_{PRED} \times 100$ %. The ventilation management chosen by the clinical anesthesiologists suggests that, with protocols geared towards providing adequate ventilation to an anesthetized patient, which take into consideration the thermal and metabolic influences of the orthopedic operating room environment, and which are geared toward minimizing potential damage to lung tissue via the use of low tidal volume and plateau pressure based techniques that diminish trans-pleural pressures, a MV of 80 % predicted was considered adequate in the setting of continuous one-to-one monitoring by an anesthesiologist.

2.2 Respiratory depression risk assessment criteria

Three criteria were used to evaluate each patient's respiratory status: (1) sustained "Low MV" ($MV < 40$ % MV_{PRED}) within 15 min of opioid administration, (2) repeated episodes of post-operative apnea (POA) in the PACU and (3) persistently "Low MV" immediately prior to PACU discharge.

Following a previously developed protocol [23], patients receiving PCA opioids were risk-stratified before and after first PCA opioid dose in the PACU: 0.2 mg hydromorphone in 71 patients, 25 mcg fentanyl in 2 patients and 2 mg morphine in one patient. Patients who had sustained $MV < 80$ % MV_{PRED} for more than 2 min prior to the opioid dose were considered "At-Risk" and patients who sustained $MV < 40$ % MV_{PRED} for at least 2 min within the 15 min following the opioid dose were considered to have "Low MV". Previous work suggests that maintained MV below 40 % MV_{PRED} for at least 2 min can be considered to be "Unsafe [23]." The cutoff was based on the ARDSnet recommendations for weaning patients off mechanical ventilation. The ARDSnet defines adequate ventilation to be at least 40 % of the predicted value for normal respiration (albeit in TV instead of MV). Patients unable to maintain 40 % of the predicted value indicate inadequate ventilation and are considered unsuitable for extubation, hence this became the criteria for defining $MV < 40$ % predicted as "Low MV [28]." Note that, in patients receiving a second opioid dose within the 15 min following the first dose, only the MV measurements before the second dose were used.

Apnea was defined as no detected breaths for greater than 10 s and hypopnea defined as a greater than 50 % reduction in TV from baseline for more than 10 s. Patients who displayed, on average, more than five apneic/hypopneic events per hour over the entire PACU stay were considered to have POA.

To evaluate respiratory status at the time of PACU discharge, the last 30 min of each patient's PACU stay were analyzed, and patients who had spent more than 10 of these 30 min (>33 %) with a $MV < 40$ % MV_{PRED} were identified. These patients were also designated to have "Low MV" with the potential to remain in the PACU or transfer to a setting with continued respiratory monitoring. This designation was based on physiologic principles for the purposes of this analysis and not outcomes data. Given the commonly observed transient fluctuations in MV in non-ventilated patients, singular Low MV measurements were not considered aberrant. However, a consistent display of MV measurements <40 % MV_{PRED} comprising more than 1/3 of the last half hour of PACU stay was considered excessive and used as a first-order definition of a "Low MV" state at discharge. This definition provided a method that could be easily translated into a clinical protocol. A more precise cutoff would likely be derived by integrating or compounding the MV measurements during the same period, but would not be easily available to the clinician at the bedside. Upon examining each of the patient traces at discharge from the PACU, we noted that this definition of "Low MV" included both patients with consistently Low MV as well as those who had substantive Low MV episodes interspersed with episodes of higher MV associated with stimulation, but did not include patients with transient MV dips.

2.3 Analyses

Multi-factor analysis of variance (MFANOVA) was used to evaluate differences in patient demographics between different groups. Paired two-tailed *t* tests were used to calculate the effect of opioids on MV. Fisher Exact Test was used to compare the likelihood of patients demonstrating "Low MV" between groups. Conventional sensitivity and specificity analyses were used to evaluate the predictive abilities of the proposed classification models [29]. All analyses were performed in Matlab R2012b (MathWorks, Natick, MA) and $p < 0.05$ was considered significant.

3 Results

We obtained written informed consent from 170 patients undergoing elective orthopedic total joint replacement. 20 patients were excluded due to incomplete data or

withdrawal from the study. In the remaining cohort of 150 patients (age 66 ± 9.6 years; BMI: 30.2 ± 5.5 kg/m^2), 34 underwent surgery under general anesthesia and 116 under spinal anesthesia.

Since continuous monitoring of respiratory volumes in the non-intubated patients in this study was not available by other means, a direct assessment of the accuracy of RVM measurements in the PACU was not possible. Instead, our analyses focused on three factors which have predictable effects on respiratory volumes and could be used to assess the adequacy of the RVM measurements: (1) respiratory trace and corresponding MV measurements around the times of opioid administration (2) episodes of POA and the corresponding MV measurements, and (3) prolonged episodes of Low MV prior to discharge.

3.1 Real-time prediction of opioid-induced respiratory depression: "the 80/40 protocol"

PCA opioids (typically 0.2 mg hydromorphone) in the PACU were administered to 74 of the 150 patients (49 %, age 65 ± 10.6 years, mean BMI: 29.7 ± 5.4 kg/m^2, 26 women). Of these 74 patients, 2 received 25 mcg fentanyl and 1 received 2 mg morphine PRN as a first opioid dose in the PACU, the remaining 71 patients received the 0.2 mg hydromorphone as a first PACU opioid dose. We used a previously developed risk-stratification protocol [23], summarized in Fig. 1, to stratify patients into two categories: "At-Risk" and "Not-at-Risk" based on the measured RVM MV before opioid administration. Similarly, the protocol classified patients as "Low MV" and "Not-Low MV" based on the MV after the opioid dose.

Prior to opioid administration:

- If a patient had sustained MV below 80 % MV_{PRED} for at least 2 min, the patient was classified as "At-Risk".
- If a patient had no episodes of sustained MV below 80 % MV_{PRED} for at least 2 min, the patient was classified as "Not-at-Risk".

Following opioid administration:

- If a patient had sustained (more than 2 min) MV below 40 % MV_{PRED}, the patient was classified as "Low MV".
- If a patient had no episodes of sustained MV below 40 % MV_{PRED}, the patient was classified as "Not-Low MV".

During the 15 min following the first opioid dose in the PACU, 24 of the 74 patients (32 %) had a sustained MV less than 40 % MV_{PRED} and were classified as "Low MV". 22 of the 24 patients who developed "Low MV" had been previously classified as "At-Risk", indicating that "Low MV" was usually preceded by "At-Risk" classification. In this cohort, the stratification protocol had a sensitivity of 92 %, specificity of 80 %, positive predictive value of 69 % and a negative predictive value of 95 % for determining if patients would develop "Low MV" after opioid administration based on the prior measured MV values. This protocol identified all but two of the patients who developed "Low MV" after opioid administration.

Figure 2 shows RVM trends (MV, TV, and RR), as well as several respiratory trace "snapshots" from a representative patient upon PACU arrival, pre opioid administration, and post opioid administration.

3.2 Real-time monitoring of apneic breathing in the PACU

Thirty-two of the 150 patients (21 %; age: 66 ± 9.1 years; BMI: 27.9 ± 4.5 kg/m^2, 11 women) had POA in the PACU. Twenty-six of the 32 patients (81 %) did not have a previous diagnosis of OSA, a finding consistent with previous work [30]. Further analysis revealed no systematic differences in age, sex, height, or weight between the group with and without POA ($p > 0.05$, MFANOVA). Patients with POA had a slightly lower (but significantly different) BMI than the non-POA patients (27.9 ± 0.8 vs. 30.9 ± 0.5 kg/m^2, $p < 0.01$). Twenty-one of the 32 POA patients (66 %) received opioids and 11 of the 21 (52 %) had further reductions in MV and developed "Low MV".

3.3 Persistent respiratory depression prior to discharge from the PACU

To identify patients who would be potentially susceptible to respiratory compromise after discharge from the PACU to a lower acuity environment, we analyzed the MV recordings during the last 30 min prior to discharge. Patients were considered to have "Low MV" if they spent more than 10 of the last 30 min in the PACU with MV < 40 % MV_{PRED}.

In the current study, 76 patients received no opioids or other sedatives in the PACU and therefore had no discrete events that could cause or exacerbate respiratory compromise. Twelve of the 76 patients (16 %) without PACU opioids were found to have "Low MV" at discharge, and only 3 of the 12 had POA.

Further analysis of the average MV measurements in the 30 min prior to discharge in patients without PACU opioids revealed that patients with POA who had "Low MV" had MVs that were not significantly different from patients without POA who had "Low MV" (2.8 ± 0.8 vs. 3.6 ± 0.8 L/min, 51 % MV_{PRED} vs. 58 % MV_{PRED}, $p > 0.05$ respectively, Fig. 3, inset). In fact, a comparison of the average MV at discharge among all 4 patient sub-groups (with and without opioids and with and without POA) revealed no

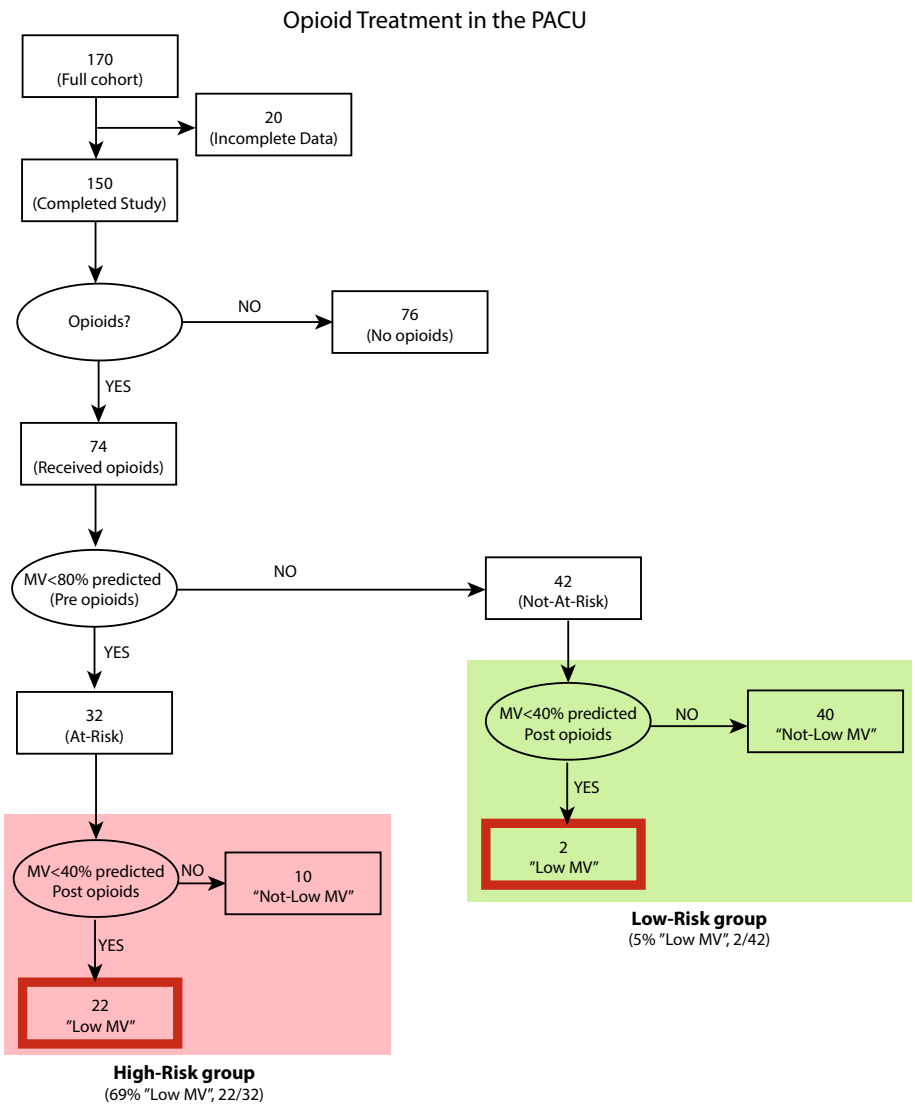

Fig. 1 Opioid treatment in the post-anesthesia care unit (PACU). Post-hoc analysis of the patients who received opioids in the PACU (74 patients, 49 %) reveals that patients who receive opioids when minute ventilation (MV) is greater than 80 % of predicted MV (MV_{PRED}) remain "Not-Low MV" 95 % of the time whereas patients who receive opioids with MV < 80 % MV_{PRED} become "Low MV" 69 % of the time. 32 patients were identified as "At-Risk" and 42 were identified as "Not-At-Risk". 22 of the 32 patients classified "At-Risk" displayed "Unsafe" MV levels after opioid administration, whereas the remaining 10 did not. 40 of 42 "Not-At-Risk" patients demonstrated "Not-Low MV" MV, whereas only two of the 42 "Not-At-Risk" patients were considered "Low MV". This protocol yielded a sensitivity of 91.6 %, a specificity of 80.0 %, with a positive predictive value (PPV) of 68.8 % and a negative predictive value (NPV) of 95.2 %. Importantly, this protocol focuses more on sensitivity than specificity, with only two patients with potential respiratory compromise misclassified (note the NPV > 95 %). This suggests that, if a patient with an MV < 80 % MV_{PRED} requires opioids for pain management; they could be switched to a "low dose protocol". This would likely reduce the number of "At-Risk" patients that then develop "Low MV" after opioids, both in the PACU and later on the floor

significant difference among patients who had "Low MV". In contrast, in all 4 sub-groups the MV for the "Low MV" patients was systematically and significantly lower than for the patients who were "Not-Low MV" (Fig. 3, inset).

A summary of the "Low MV" patients among the 8 categories studied here is presented in Fig. 4. Within 15 min of opioid administration, 32 % of patients (24 out of 74) developed "Low MV". This fraction was significantly higher in the group with POA than in the group without POA (52 vs. 25 %, $p < 0.05$). At discharge, 19 % of all patients (29 out of 150) demonstrated "Low MV". Once again, in the POA group this fraction was significantly higher than in the group without POA (38 vs. 14 %, $p < 0.01$). At discharge, in the group that received opioids, 23 % of patients demonstrated "Low MV" versus 16 % in the group without opioids ($p > 0.3$).

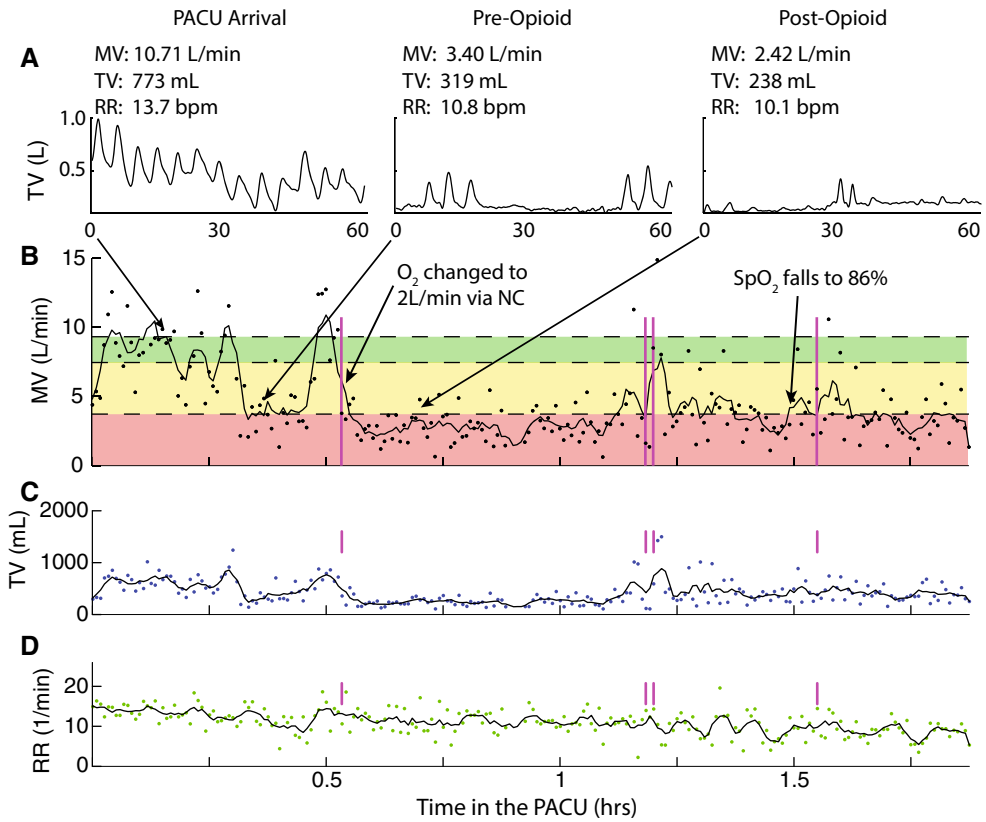

Fig. 2 Example case of the recorded course of a patient in the post-anesthesia care unit (PACU). Note that care providers were blinded to the respiratory volume monitor (RVM) data. Three minute ventilation (MV) zones are depicted: MV > 80 % of MV_{PRED} (*green*); MV 80 % to 40 % of MV_{PRED} (*yellow*); MV < 40 % of MV_{PRED} (*red*). **a** 53 y/o male (185 cm, 109 kg, BMI of 31.7 kg/m^2) arrived in the PACU with adequate MV ranging between 9 and 11 L/min (85–110 % predicted) (*left panel*). Shortly thereafter he transitioned to a persistent POA breathing pattern (*middle panel*) and after the first dose of hydromorphone patient-controlled analgesia (PCA) demonstrates severe respiratory depression (*right panel*). **b** Continuous MV trend displays the respiratory course of this patient as associated with features of his care. During the first ½ h in the PACU, patient's MV is in the *green zone* (≥80 % MV_{PRED}), indicating adequate MV. The period that follows clearly demonstrates the effects of POA, with the MV trend dropping to just over 40 % MV_{PRED} ("At-Risk"). This appears to be primarily due to a decrease in the volume of the "rescue" breaths and not associated specifically with a change in the apneic pauses between breaths. As the nurse wakes the patient to assess his pain score (peak in MV prior to first dose of PCA opioids), the MV transiently increases, but rapidly drops below 40 % MV_{PRED} ("Low MV") following opioid administration. The patient remains in the "Low MV" range for nearly 2 h, showing transient increases in MV only around times when the patient is stimulated while vital signs are being obtained (pain score recorded as 0 out of 10 just prior to PCA opioid administration), likely corresponding to episodes in the awake state when the patient pushed the PCA button. Without the benefit of seeing the RVM data, the patient is discharged from the PACU with "Low MV" instead of being considered for remaining in PACU, transfer to step-down, or additional monitoring on the floor. It is important to note that SpO_2 remained at or above 95 % on 2L nasal cannula except during a single transient decrease to 86 %, as noted in the figure. As this desaturation was not associated with any intervention or change in oxygen delivery, it was likely considered to be an artifact. **c** Tidal volume (TV) trends capture some of the respiratory dynamics shown in **b**, but not as clearly as the MV trends. **d** Respiratory rate (RR) trends have the least event-specific information of all 3 trends. RR remains between 8 and 20 breaths/min for the duration of the PACU stay, providing no indication of this patient's post-operative apnea (POA) and respiratory insufficiency

4 Discussion

Opioid induced respiratory depression occurs in both teaching centers [31–36] and community hospitals [37] and continues to be a significant patient safety risk. The stratification algorithm presented here demonstrates clinically-relevant sensitivity and selectivity (92 and 80 %, respectively) at determining whether patients will have Low MV or adequate MV after opioids in the PACU. The RVM was also able to detect and quantify sustained periods of POA and has potential to markedly increase safety for patients in the post-operative period by more appropriate pain management, better decision making regarding when to discharge, where to send the patient and whether to maintain continuous respiratory volume monitoring on the general floor. Current clinical practice for non-intubated patients relies heavily on surrogate and indirect indicators of respiratory status (e.g. SpO_2, $EtCO_2$, and observation), which, because they are late indicators of an impending respiratory event, continue to put susceptible patients at risk for

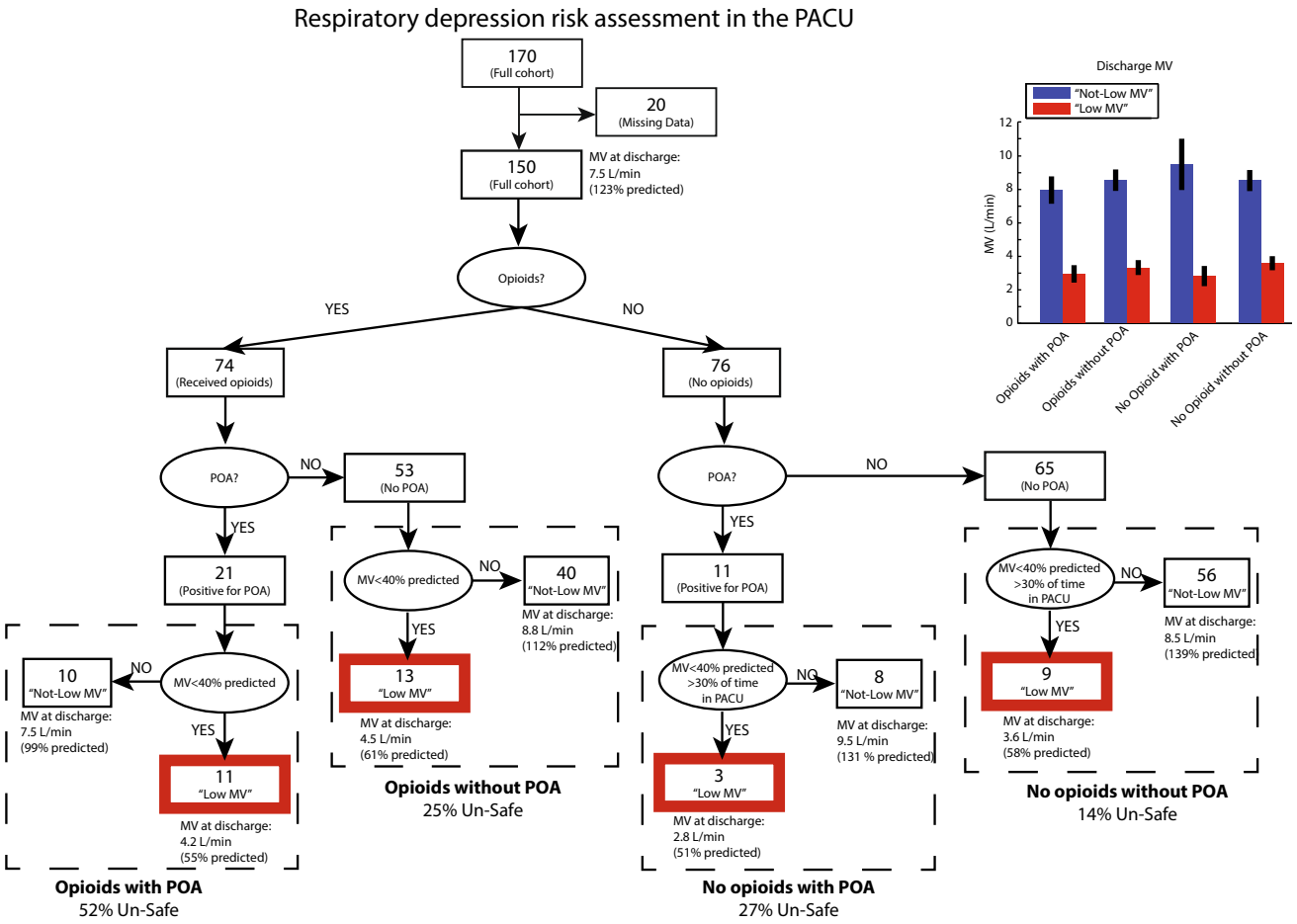

Fig. 3 Patient classification based on the three criteria investigated in this study. Not surprisingly, patients who (a) display post-operative apnea (POA) and (b) receive opioids are 3.7 times more likely to develop "Low MV" in the post-anesthesia care unit than those who have neither POA nor opioids. Interestingly, a simple protocol based on continuous monitoring of minute ventilation (MV) accurately predicted all but 2 of the patients who manifest "Low MV"

serious complications. Missing from clinicians' armamentarium has been the ability to monitor minute ventilation, and to observe traces of respiratory patterns.

The purpose of this observational study was to build on previous work by collecting RVM measurements from a broad group of patients in the PACU who were undergoing standard care in order to track response to opioids, and to further understand how to use RVM data to develop treatment algorithms for individualized patient care. We show that stratifying patients based on the quantitative RVM MV measurements as being "At-Risk" or as having "Low MV" could help individualize care. In this setting, RVM measurements could help define opioid sensitivity, assist with defining opioid dosing, and promote the consideration of other forms of pain management or non-pharmacologic interventions.

While this manuscript suggests one plausible stratification scheme, more work is needed to identify exact MV cutoffs, which may vary by patient cohort. This study used a previously developed protocol based on the cutoffs of 80 % MV_{PRED} and 40 % MV_{PRED} to risk-stratify patients. The resulting classification yielded higher sensitivity (92 %) than specificity (80 %) and higher negative predictive value (95 %) than positive predictive value (68 %). The specificity and positive predictive values presented here suggest that this protocol may not be fraught with false alarms, avoiding the significant problem of alarm fatigue associated with other monitoring technologies [38]. Based on this work, protocols with patient-specific PCA settings or PRN opioid dosing guided by RVM MV data acquired in the PACU may now be developed to reduce respiratory compromise while optimizing pain control and patient satisfaction across the continuum of care. In addition, identifying patients at risk for respiratory depression in the PACU may have substantial impact on patient safety on the hospital floor, or after discharge from day-surgery.

In contrast, the closed claims analysis highlights that utilizing general patient characteristics such as OSA or

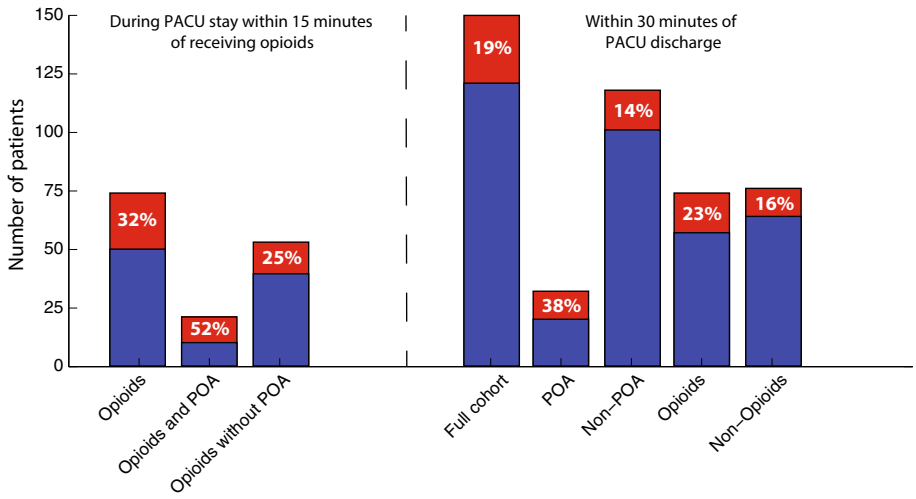

Fig. 4 Summary of the patients identified to be potentially "Unsafe" split into corresponding categories. Within 15 min of opioid administration, 32 % of patients (24 out of 74) developed "Low MV". This fraction was higher (52 %, 11 out of 21) in the group with post-operative apnea (POA) than in the group without POA (25 %, 13 out of 53, $p < 0.05$). At discharge, 19 % of all patients (29 out of 150) demonstrated "Low MV". Once again, in the POA group this fraction was higher (38 %, 12 out of 32) than the group without POA (14 %, 17 out of 118, $p < 0.01$). In the group receiving opioids, 23 % of patients (17 out of 74) demonstrated "Low MV", whereas in the group without opioids this fraction was only 16 % (12 out of 76)

ASA classification appears insufficient to create useful protocols to risk-stratify patients [11]. While OSA is prevalent, and both central and obstructive apneic episodes occur commonly after surgery, not every patient with OSA diagnosis or POA is at-risk. Instead, assessment of the variability and duration of apneic and hypopneic episodes and the size of recovery breaths in the PACU, which are directly related to the adequacy of ventilation, can be best accomplished by continuous quantitative MV measurements. RVM traces detect apneic episodes in the PACU, but more importantly, the RVM quantifies the reduction in MV caused by POA and provides a way to quantify the impact of a previous OSA diagnosis in postoperative patients, with or without central apnea related to anesthesia and analgesia.

In this study, traditional risk factors for OSA (age, gender and BMI) were not predictive of POA. Our results suggest that pre-operative identification of patients "At-Risk" for POA may be challenging, especially given the fact that, in this study, patients with lower BMI rather than higher BMI had an increased incidence of POA. This latter finding has important clinical relevance, since it contradicts the general concept that higher BMI increases risk for respiratory depression, and BMI is frequently used as a predictor of post-operative respiratory complications in this context. Our results suggest that instead of monitoring just high BMI patients, the level of risk may be distributed throughout the spectrum of patient body habitus. Perhaps all patients should be monitored with an RVM postoperatively. This is in line with the 2011 American Society of Anesthesiologists' guidelines requiring monitoring of not just oxygenation, but also ventilation [39], and the quantitative metrics of MV and TV provided by the RVM may provide the best way to meet this directive.

This study has several limitations: the sample size is small, there is some degree of homogeneity of the study population (elective joint replacement surgery patients), it lacks demonstration of negative outcomes in the "Low MV" patients and, given the blinded nature of the study, it does not allow for understanding of how healthcare providers would use the continuous MV data in clinical practice. We also did not attempt to associate "Low MV" measurements with oxygen desaturation, respiratory complications or interventions. Until more work is done, the MV values indicative of poor respiratory outcomes will remain inexact. Nonetheless, given an understanding of respiratory physiology, it is clear that thresholds exist for Low MV below which a patient would be considered to be "Unsafe". The 40 % "Low MV" threshold suggested here is generally associated with MV in the 2–3 L/min range, which most anesthesiologists would consider to be suboptimal.

Building on this study, implementation of the RVM system in the PACU could have immediate impact on risk stratification and individualized care protocols. Data collected in the higher acuity (and better staffed) PACU setting could be leveraged to select patients "At-Risk," while the infrastructure is being built for more ubiquitous monitoring throughout the hospital. This strategy could provide both near-term and long-term solutions to reduce post-operative respiratory complications and markedly improve patient safety. In addition, patients who are found to be at

low-risk for OIRD and POA could more quickly meet discharge criteria and thereby improve PACU efficiency and throughput.

The "80/40 Protocol" described here provides a starting point towards the development of specific perioperative protocols to direct opioid dosing, implementation of multimodal therapy, consideration of non-pharmacological interventions, and decisions regarding timing of PACU discharge and level of follow-up care. Randomized trials are being conducted to explore the impact of implementation of RVM based protocols on patient safety.

Funding The study was supported by Respiratory Motion, Inc.

Compliance with ethical standards

This paper describes an observational study conducted on human subjects. This study was approved by the Partners Human Research Committee (#2011P002898) prior to subject enrolment. All subjects provided written informed consent before entering into the study.

Conflict of interest Christopher Voscopoulos reports that he is an investor in Respiratory Motion, Inc. (<0.5 %). Kimberly Theos reports no conflict of interest. H.A. Tillmann Hein reports that he is an investor in Respiratory Motion, Inc. (<0.5 %). Edward George reports no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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