

Evaluation of respiratory volume monitoring (RVM) to detect respiratory compromise in advance of pulse oximetry and help minimize false desaturation alarms

Samuel M. Galvagno, Jr, DO, PhD, Peggy G. Duke, MD,
Daniel S. Eversole, PhD, and Edward E. George, MD, PhD, Waltham, Massachusetts

BACKGROUND:	Monitoring respiratory function is important. By continuously monitoring respiratory volumes, respiratory depression could be identified before hypoxemia and drive earlier intervention. Here, we evaluate the temporal relationship of respiratory volume monitoring (providing real-time minute ventilation [MV], tidal volume, and respiratory rate in nonintubated patients) to hypoxic episodes and its potential to help classify true vs false desaturations (related to patient movement/probe dislodgement).
METHODS:	Respiratory volume monitoring data, oxygen saturation (SpO ₂), oxygen supplementation, and opioid use were analyzed in 259 patients following orthopedic surgery. Detection of “low MV” (<40% of predicted MV) in advance of low SpO ₂ (<90%) was used to classify true and false desaturations. Patients were also stratified based on opioid use and development of low MV. Patient's length of stay (LOS) and number of SpO ₂ alarms were compared across groups (± opioids; ± low MV).
RESULTS:	The electronic health records reported 113 SpO ₂ alarms; 105 (93%) not preceded by low MV and considered false. Low MV preceded the eight true desaturations by 12.8 ± 2.8 minutes. One hundred ninety-eight patients (76%) of 259 experienced one or more low MV events. Patients with low MV had significantly longer postanesthesia care unit (PACU) LOS than those maintaining “adequate MV”: 2.8 ± 0.1 hours vs. 2.4 ± 0.1 hours (<i>p</i> < 0.001). Patients receiving opioids had increased likelihood of low MV (69% vs. 80%; <i>p</i> < 0.05) and had significantly longer PACU LOS than those without opioids (2.9 ± 0.1 hours vs. 2.3 ± 0.1 hours; <i>p</i> < 0.001). In the opioid group, PACU LOS was 75% longer in patients developing low MV versus maintaining adequate MV (3.0 ± 0.1 hours vs. 1.7 ± 0.2 hours; <i>p</i> < 0.001).
CONCLUSION:	Respiratory volume monitoring can provide advanced warning of impending oxygen desaturation and potentially reduce the number of false SpO ₂ alarms. Opioid administration increased low MV events correlating with increased LOS. Respiratory volume monitoring can help clinicians individualize patient care, decrease false alarms, adjust opioid dosing, and increase PACU throughput. Similar benefits may translate to the general care floor and prehospital and posthospital environments. (<i>J Trauma Acute Care Surg.</i> 2016;81: S162–S170. Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.)
LEVEL OF EVIDENCE:	Diagnostic study, level II.
KEY WORDS:	Respiratory monitor; respiratory insufficiency; respiratory failure; pulse oximetry; respiratory volume monitor.

Surveillance of respiratory status is a critical component of patient care in any clinical setting. Unfortunately, current clinical practice relies on secondary indicators of respiratory status, usually oxygen saturation (SpO₂) measured by pulse oximetry, in lieu of monitoring ventilation. Early identification of respiratory insufficiency using real-time respiratory volume monitoring has the potential to allow clinicians to alter

treatments in time to prevent more serious complications. A noninvasive monitor that rapidly and accurately measures ventilation would have great use in virtually all patient care environments, from the battlefield or other sites of traumatic injury, through transport, throughout the hospital in both critical care and general ward locations, and after discharge into the patients' home.

Until recently, the ability to monitor ventilation in nonintubated patients has remained elusive. A Food and Drug Administration–approved noninvasive bioimpedance–based respiratory volume monitor (RVM; ExSpirom, Respiratory Motion, Inc, Waltham, MA) has recently become available and provides real-time respiratory data with continuous trends of minute ventilation (MV), tidal volume (TV), and respiratory rate (RR) in nonintubated patients. Clinical studies have demonstrated strong correlation (mean, 0.96; 95% confidence interval, 0.93–0.99 for regular and erratic breathing) and clinically relevant accuracy (average error accuracy of 9.3% for MV, 9.0% for TV, and 1.8% for RR) between the RVM and spirometric measurements.¹ Respiratory volume monitor and ventilator volume measurements during mechanical ventilation or spontaneous breathing demonstrated average MV and TV accuracy of more than 90% and RR accuracy greater than 95%.²

Submitted: December 21, 2015, Revised: April 22, 2016, Accepted: April 26, 2016,
Published online: June 1, 2016.

From the Department of Anesthesiology (S.M.G.), University of Maryland School of Medicine, Baltimore, Maryland; Department of Anesthesiology (P.G.D.), Emory University School of Medicine, Atlanta, Georgia; Respiratory Motion, Inc. (D.S.E.), Waltham, Massachusetts; and Post Anesthesia Care Units (E.E.G.), Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts.

Portions of this work were presented at the Society of Critical Care Medicine (SCCM), Phoenix, Arizona, January 18, 2015; at the International Anesthesia Research Society, Honolulu, Hawaii, May 2015; and as an oral presentation at the Military Health Services Research Symposium (MHSRS), Ft. Lauderdale, Florida, August 19, 2015 by Dr. Galvagno.

Address for reprints: Daniel S. Eversole, PhD, Research Scientist, Respiratory Motion, Inc, 411 Waverley Oaks Rd, Suite 150, Waltham, MA 02452; email: daniel.eversole@respiratorymotion.com.

DOI: 10.1097/TA.0000000000001152

Inadequate ventilation is frequently a precipitating event leading to respiratory depression or arrest and has proven difficult to detect using pulse oximetry. Since capnography has not proven as useful in nonintubated patients as once hoped, clinicians generally rely on pulse oximetry, despite its well-documented limitations³⁻⁵ continues to be a first-line monitor. More recently, studies have illustrated the inadequacies of inferring a patient's respiratory status via monitoring of hypoxemia to the extent that in patients receiving supplemental oxygen, basing care on selected SpO₂ thresholds (<90% to <92%) can be fatal owing to delay in the diagnosis of significant hypoventilation, hypercarbia, and impending respiratory failure.⁶⁻¹⁰

Furthermore, false alarms, a well-recognized problem with pulse oximetry, lead to alarm desensitization and fatigue. Clinicians, plagued by an excessive number of alarms, of which approximately 90% are false,^{4,11-13} have responded by disabling, decreasing volume, changing settings, or ignoring alarms altogether. Alarm safety is a Joint Commission national patient safety issue, and in 2015, the Commission mandated that improvements be made to ensure that alarms on medical equipment are heard and responded to on time.¹⁴

Epstein et al.¹⁵ reported approximately 11% of postanesthesia care unit (PACU) patients experienced at least one hypoxemic episode (SpO₂ alarm sustained for ≥ 2 minutes) and approximately 41% of these hypoxemic episodes were unresolved after 3 minutes. They also found that 69% of hypoxemic episodes occurred more than 30 minutes after PACU arrival, a time with less ongoing attention and potentially less availability of advanced care providers. To address this, Epstein et al. suggested reconsidering staff allocation, a costly change that might not improve patient safety. Instead, an editorial by Weissman and Freeman¹⁶ proposed that earlier detection of respiratory compromise by RVM could provide additional time to address a patient's deteriorating condition. In addition to earlier warning, the RVM's truncal electrode placement provides stable measurements and decreases the likelihood of sensor dislodgement or susceptibility to extremity motion and can lead to fewer false alarm distractions and facilitate workflow.

In this study, we hypothesized that the RVM would detect respiratory depression significantly earlier than pulse oximetry, help clinicians identify SpO₂ alarms that are artifacts (i.e., false alarms) triggered by patient motion or probe dislocation, and reveal when serious respiratory compromise is masked by the administration of supplemental oxygen.

METHODS

Subjects

This study was conducted at Massachusetts General Hospital (MGH) and approved by The Partners Institutional Review Board (Boston, MA). Written informed consent was obtained from all patients before enrollment. Inclusion criteria were English-speaking men and women aged 18 to 99 years undergoing elective joint replacement surgery.

Primary Protocol

A noninvasive, impedance-based respiratory volume monitor (ExSpirom, Respiratory Motion, Inc.) was used to continuously and quantitatively measure real-time MV, TV, and RR.

Thoracic PadSet electrodes were placed in the recommended positions (sternal notch, xiphoid, and right midaxillary line at the level of the xiphoid), as previously described.¹ Medical history, anthropometrics, and basic demographics were obtained. In this observational study, clinicians were blinded to the RVM measurements and perioperative patient care followed standard practice, i.e., no changes were made to pain management protocols, PACU care, or interventions based on RVM measurements.

Respiratory volume monitor data collection was started preoperatively, continued during surgery (using either general or spinal anesthesia), and terminated upon discharge from the PACU. SpO₂ values, measured as part of the routine PACU care, were collected by the bedside monitor and oximetry system in clinical use (B40 GE patient monitor, GE Healthcare, Milwaukee, WI; LNCS Actx adult adhesive sensor; Masimo Corp, Irvine, CA). Time-stamped SpO₂ values, routinely recorded at 60-second intervals, were obtained from the Massachusetts General Hospital electronic health records (EHRs). From the PACU nursing records, we retrieved the following events, with approximate times noted: PACU admission and discharge, supplemental oxygen (mode and flow rate), clinician-administered opioids (dose), and any clinician recorded desaturation events. Patients with postoperative pain were typically managed on patient-controlled analgesia (PCA) pumps using either hydromorphone, 0.2 mg/mL, or morphine, 1 mg/mL. Dosing timestamps were obtained from the PCA log. The total opioid dose was calculated in morphine milligram equivalents (MME)/kg for each patient using the following conversion ratios: 1 mg morphine = 1 MME; 0.13 mg hydromorphone = 1 MME; 10 μ g fentanyl = 1 MME.¹⁷

Each patient's predicted MV (MV_{PRED}), representing the expected MV during quiet respiration in the awake, nonintubated patient, was calculated based on BSA and patient's sex.¹⁸ Measured MV (MV_{MEASURED}) was converted to percent predicted MV (MV_{MEASURED}/MV_{PRED} \times 100%). Low MV was defined as MV less than 40% MV_{PRED} sustained for a period of 1 minute or longer. The criteria chosen for low MV less than 40% MV_{PRED} was originally based on The Acute Respiratory Distress Syndrome Network (ARDSnet) protocol¹⁹ for weaning patients off mechanical ventilation, which suggests that adequate ventilation associated with successful extubation is greater than 40% of the predicted value for normal respiratory volumes, and MV less than 40% MV_{PRED} was subsequently used to define inadequate ventilation to risk-stratify patients in the PACU.²⁰ Any measured low MV within a 10-minute period following the first low MV alarm was considered part of the same event.

Correlating Minute Ventilation With Pulse Oximetry Data

Timestamps for both RVM measurements (MV, TV, and RR) and SpO₂ values recorded in the EHR were aligned to facilitate the classification of pulse oximeter alarms. The pulse oximeter alarm (low SpO₂) in the PACU was set at SpO₂ less than 90% as per standard hospital protocol. All terms and their abbreviations are summarized in Table 1. Consistent with Epstein et al., a low SpO₂ recorded for 1 minute was considered to be a "transient alarm," and low SpO₂ sustained for a period of 2 minutes or longer (i.e., a minimum of two consecutive 1-minute data points) was considered a "hypoxemic episode".¹⁵ We further stratified hypoxemic episodes into "true desaturation"

TABLE 1. Definition of Terms and Their Abbreviations

Term	Abbreviation	Definition	Calculation	Ref
Measured minute volume	MV _{MEASURED}	The real-time MV reported by the RVM		
Predicted minute volume	MV _{PRED}	Expected MV under baseline conditions of quiet respiration in the awake nonintubated patients	Male: $BSA \times 4$ Female: $BSA \times 3.5$	(18)
Percent predicted minute volume	% MV _{PRED}	In percentage, the degree of deviation MV _{MEASURED} is from the MV _{PRED}	$(MV_{MEASURED}/MV_{PRED} \times 100)$	(1)
Adequate minute volume	Adequate MV	$MV \geq 40\% MV_{PRED}$		
Low minute volume	Low MV	$MV < 40\% MV_{PRED}$ sustained for a period of 1 minute or longer		
Low minute volume event	Low MV event	Low MV within a 10-minute period following the first low MV alarm		
Pulse oximeter alarm	Low SpO ₂	SpO ₂ < 90%		(15)
Transient alarm		SpO ₂ < 90% recorded for only 1 minute		
Hypoxemic episode		SpO ₂ < 90% sustained for a period of 2 minutes or longer		
True desaturation		Low SpO ₂ associated with a preceding low MV event		
False desaturation		Low SpO ₂ coinciding with adequate MV and patient movement		
False alarm		Either a transient alarm or false desaturation		
True alarm		A true desaturation		

if the hypoxemic episode was associated with a preceding low MV and “false desaturation” when the hypoxemic episode coincided with patient movement and/or pulse oximeter probe malposition. Both transient alarms and false desaturations were considered to be “false alarms”. A true desaturation was considered to be a “true alarm”. In patients undergoing elective surgery, the etiology of true desaturation in the PACU commonly requires a patient to first experience low MV, typically resulting from opioid-induced respiratory depression, residual neural muscular blockade, or uncompensated and recurring apnea. It is important to note that in patients with underlying conditions such as chronic obstructive pulmonary disease (COPD) and congestive heart failure, true desaturation may present after tachypnea and low perfusion rates. In this study, we are limited to stating a hypoxemic episode is a true desaturation only when associated with a preceding low MV; nursing records in many cases do not discern the cause for the recorded hypoxemic episode.

Statistical Analysis

Multifactor analysis of variance was used to evaluate differences in patients' demographics between different groups. Unpaired two-sided *t*-tests were used to compare length of stay (LOS) across groups and the Fisher exact test was used to investigate the occurrence of low MV with opioid administration and administration of supplemental oxygen. All analyses were performed in MATLAB R2012b (Mathworks, Natick, MA), with a *p* < 0.05 considered significant. All values in the manuscript are reported as mean ± standard error of the mean (SEM), unless otherwise noted.

RESULTS

Data were obtained from 273 patients. Fourteen patients were excluded owing to missing data (SpO₂, RVM) or withdrawal of consent. Of the remaining 259 patients (140 females; mean age, 67 years; range, 28–91 years; mean body mass index

(BMI), 29.8 kg/m²; range, 19.0–49.1 kg/m²) included in the analysis, 82 patients (32% of cohort) had general anesthesia and 177 (68%) had spinal anesthesia. Patients were monitored for a mean of 2.7 ± 0.1 hours in the PACU.

Identification of True Desaturation by Monitoring Low MV

The MV trends were aligned with recorded SpO₂ values to analyze the following: (1) the MV preceding and during a low SpO₂ alarm, to help differentiate true desaturation and false desaturation events, and (2) severity and timing of a low MV event related to a low SpO₂ alarm.

Figure 1 provides an example of a 70-year-old female patient with BMI, 36.7 kg/m²; MV_{PRED}, 7.2 L/min, who experienced a true desaturation event. Over much of her 183-minute PACU stay, the MV_{MEASURED} was less than 80% MV_{PRED}, stabilizing at or below 40% MV_{PRED} for the last 50 minutes of the PACU stay. It was during this period when readings from the pulse oximeter, which remained at 100% before this point, drifted to levels below 90%. The patient experienced 10 recurring low MV events commencing at 149 minutes before the true desaturation, with the most closely preceding low MV event occurring 12.6 minutes before the true desaturation.

Figure 2 provides an example of a 63-year-old female patient with BMI, 29.1 kg/m²; and MV_{PRED}, 7.0 L/min, with multiple false desaturation events. This patient was admitted to the PACU with an MV_{MEASURED} greater than 150%. Over the course of her 121-minute PACU stay, she experienced four transient alarms (1-minute low SpO₂) and one hypoxemic episode. Concurrent with all low SpO₂ alarms (both hypoxemic episodes and transient alarms), the patient experienced large increases in MV, coinciding with movement and/or exertion.

We analyzed all low SpO₂ alarms (i.e., transient alarms and hypoxemic episodes) recorded across the entire patient population to evaluate the relationship of low MV to desaturation and to determine the number and proportion of true desaturations

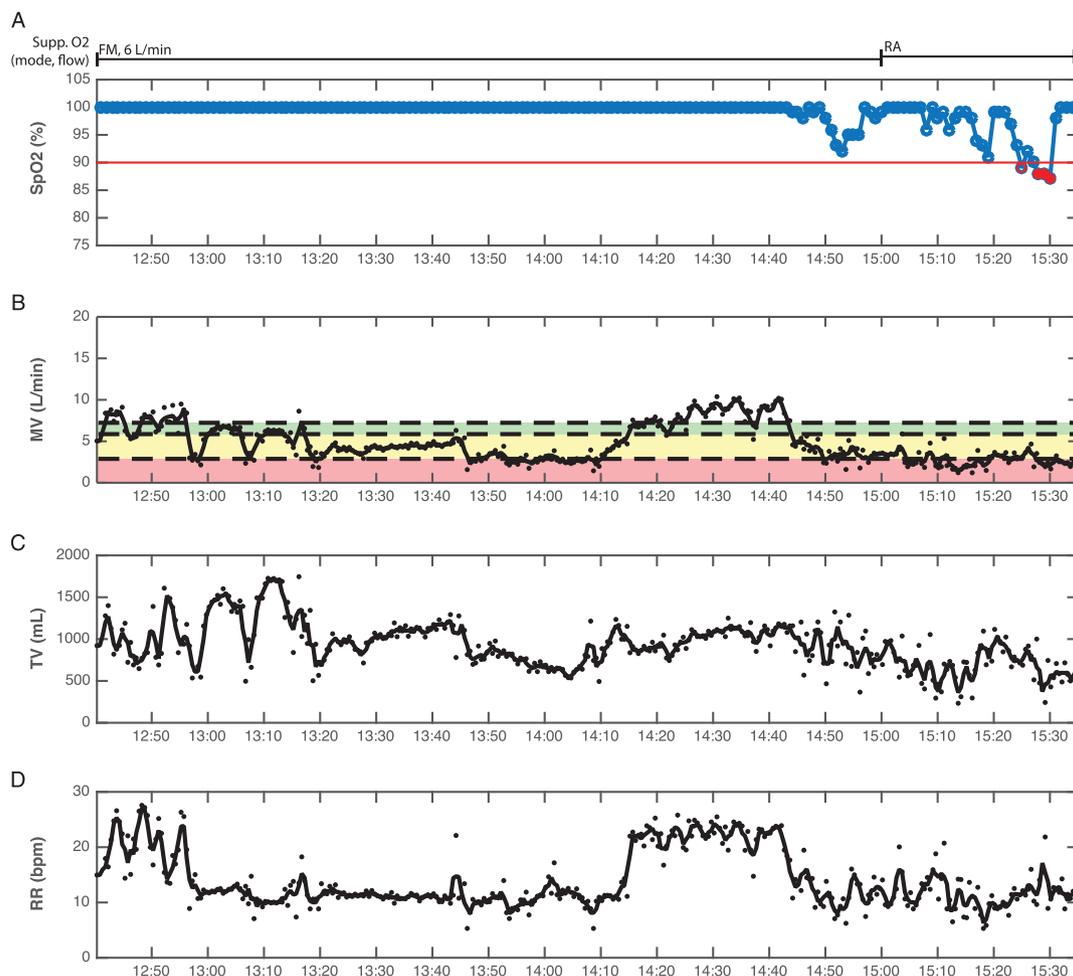


Figure 1. Patient with true desaturation event. A 70-year-old female patient (BMI, 36.7 kg/m²; MV_{PRED}, 7.2 L/min) with a 25-pack-year smoking history and previous diagnosis of COPD, type 2 diabetes, and heart disease presented for right total hip replacement surgery. After surgery under general anesthesia, the patient was monitored in the PACU for 183 minutes with pulse oximetry and RVM. Here, we present recorded SpO₂ values (A) aligned with the RVM trends of MV (B), TV (C), and RR (D). SpO₂ values (open blue circles) were recorded in the EHR at 1-minute intervals. One-minute transient alarms and false desaturation are indicated as red circles and true desaturations are indicated as filled red circles. In the PACU, the patient experienced a single 1-minute transient alarm in addition to a single hypoxemic episode, lasting 3 minutes. The patient was initially placed on supplemental oxygen by facemask (6 L/min) and transitioned to room air during phase 3 of the PACU. A morphine PCA pump was implemented, but no doses were administered. The patient experienced 10 recurring low MV events commencing 149 minutes before the true desaturation with the most closely preceding low MV event occurring 12.6 minutes before the true desaturation. SpO₂ values remained steady, indicating the pulse oximeter was well seated on the patient's finger. Note that low MV was more associated with a decrease in TV than RR.

(i.e., hypoxemic episodes preceded by low MV events). Given the multiple measurements and clinical interventions that occurred, we created a plot to facilitate visualization of key temporal and dimensional features. Low MV events and clinical markers (EHR recorded low SpO₂ alarm, supplemental O₂, and opioids) for each patient were temporally overlaid on a one-dimensional axis representing each patient's PACU LOS, as shown in Figure 3.

We found that all 113 low SpO₂ alarms were concentrated in 46 of the 259 patients (18% of the cohort). Of the 113 low SpO₂ alarms, 87 (77%) were transient alarms (1-minute low SpO₂), and 26 (23%) met the criteria for a hypoxemic episode (i.e., ≥ 2 minutes). Of these hypoxemic episodes, 65% was 2 minutes, 27% was 3 minutes, 4% was 4 minutes, and 4%

was more than 5 minutes long. All recorded hypoxemic episodes were separated by at least 3 minutes and had no missing data. Hypoxemic episodes occurred in 18 patients; 12 of these 18 patients had one or more accompanying transient alarms. Note that 74% of all low SpO₂ alarms occurred more than 30 minutes after admission to the PACU, which agrees with the 68.8% reported by Epstein et al.¹⁵ None of the patients in the study were reintubated.

SpO₂ Is a Late Indicator of Respiratory Depression

Correlation of hypoxemic episodes with RVM measurements shows that only 8 of 113 (7%) low SpO₂ alarms were true desaturations (identified in seven patients—four females; mean age, 69 years; range, 58–83 years; BMI, 27.2 kg/m²; range,

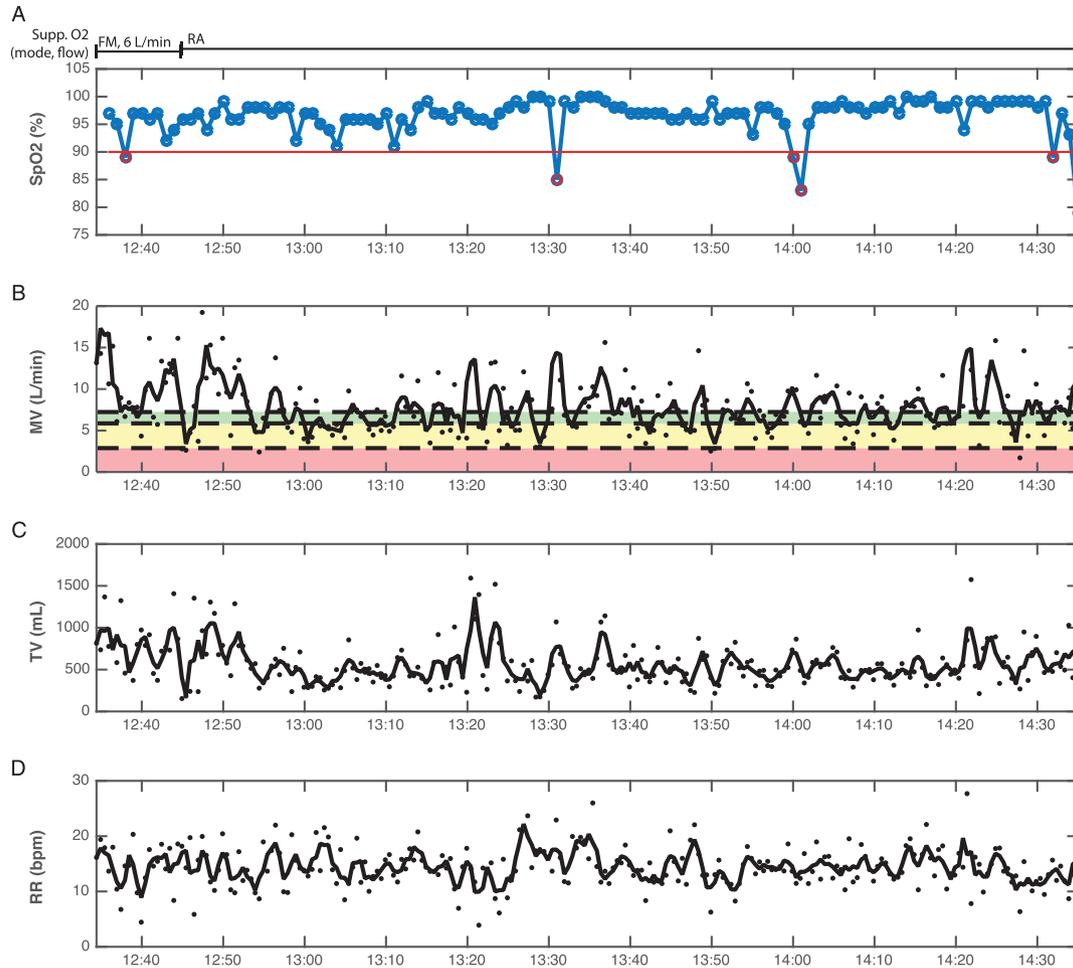


Figure 2. Patient with multiple false alarms. A 63-year-old female patient (BMI, 29.1 kg/m²; MV_{PRED}, 7.0 L/min) with a 4.5-pack-year smoking history and no diagnosed respiratory issues presented for right total knee arthroplasty/replacement. After surgery under spinal anesthesia, the patient was monitored in the PACU for 121 minutes with pulse oximetry and RVM. Here, we present recorded SpO₂ values (A) aligned with the RVM trends of MV (B), TV (C), and RR (D). SpO₂ values (open blue circles) were recorded in the EHR at 1-minute intervals. One-minute transient alarms and false desaturation are indicated as red circles. In the PACU, the patient experienced four 1-minute transient alarms in addition to a single hypoxemic episode, lasting 2 minutes. The patient was initially placed on supplemental oxygen by facemask (6 L/min) and within 15 minutes of PACU arrival transitioned to room air. A femoral nerve block for postoperative pain control was administered postoperatively. As the block wore off, nursing records indicated pain scores greater than four of 10 and a hydromorphone PCA pump was implemented, from which one dose was administered. Admitted to the PACU with a MV_{MEASURED} greater than 150% MV_{PRED}, the patient maintained a MV_{MEASURED} centered approximately 100% MV_{PRED} throughout her PACU stay. Concurrent with each low SpO₂ alarm, the patient experienced large increases in MV. Contrasting with the SpO₂ signal reported in the true desaturation patient, here SpO₂ values fluctuate continuously, considered to be from the pulse oximeter not being well seated on the patient's finger. Fluctuations in both MV and SpO₂ indicate excessive patient movement.

21.9–36.7 kg/m²; six of seven received spinal anesthesia). True desaturations were 2.5 ± 0.3 minutes in length and the low MV event most immediately preceding a true desaturation occurred at a mean of 12.8 ± 2.8 minutes earlier. Importantly, these true desaturations generally followed repeated low MV events. Patients with true desaturation had a mean of 4.9 ± 0.9 low MV events commencing 71.4 ± 16.5 minutes before a true desaturation. Multifactor analysis of variance found no statistically significant difference in the demographics of the patients with true desaturation (i.e., true alarms) vs false alarms (*p* > 0.2 for height, weight, age, BMI, sex, and all cross-effects). The remaining 18 of 26 hypoxemic episodes coincided with excessive

patient motion and adequate MV, that is, MV greater than 40% MV_{PRED}.

Stratification of Patients by Occurrence of Low MV

Of the 259 patients, 198 (76%) experienced at least one low MV event (2.3 ± 0.1 low MV events per hour), with the remaining 61 patients (24%) maintaining adequate MV throughout their PACU stay. The LOS in the PACU for patients experiencing low MV was significantly longer than those who maintained adequate MV (2.8 ± 0.1 hours vs. 2.4 ± 0.1 hours, respectively (*p* < 0.001)). Of the 259 patients, 202 (78%) were on supplemental oxygen for most of their PACU stay, and 137

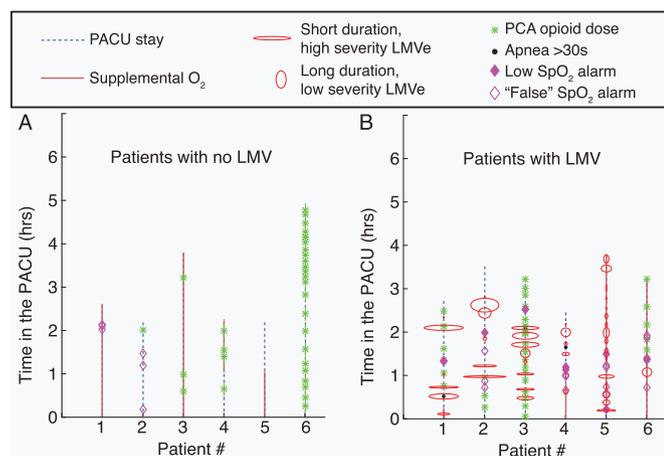


Figure 3. Visualization of the respiratory status of patients in the PACU. Each patient is visualized along an individual line, parallel to the y -axis (Fig. 1). The *dashed blue line* represents each patient's timeline in the PACU, with arrival at the PACU aligned with the x -axis. Supplemental O_2 is displayed as a *solid red line* overlaid on top of the *dashed blue*, spanning the regions where supplemental O_2 was delivered. Along each patient axis, we display low MV events with red ellipses. The length of each ellipse (along the y -axis) denotes the temporal duration of a low MV event, whereas the width of each ellipse corresponds to the severity of each event with wider ellipses corresponding to more severe (i.e., lower MV) low MV event. In addition, PCA opioid doses are visualized as *green asterisks*, apneic pauses longer than 30 seconds as *black dots*, and low SpO_2 alarms as *purple diamonds*. False SpO_2 alarms (i.e., 1-minute transient alarms and false desaturations) are displayed with *hollow symbols* and true desaturations displayed with *solid symbols*.

(68%) of those 202 patients experienced at least one low MV event without a low SpO_2 alarm recorded in the EHR. In contrast, of the remaining 57 (22%) patients who were maintained on room air during their PACU stay, 28 (49%) experienced at least one low MV event without a low SpO_2 alarm recorded in the EHR ($p < 0.05$).

The percent of time each patient maintained MV less than 40% MV_{PRED} was further analyzed during the first and last 30 minutes in the PACU (Fig. 4). Arrows indicate the percentage of patients with MV below 40% of MV_{PRED} for at least 10 minutes (one third of each 30-minute segment), indicating increased opioid sensitivity or other cause of respiratory depression and potentially a threat to patients' safety. In the first 30 minutes in the PACU, approximately 18% of patients experienced low MV for at least one third of the time. This percentage remained at approximately 21% in the 30 minutes before discharge from the PACU, which could suggest that these patients may require RVM or other monitoring as they are transferred to the floor.

In 35 (18%) of the 198 patients with at least one low MV event, there were 75 recorded low SpO_2 alarms in the EHR of which only one was noted in the PACU nursing records. Of the recorded 75 low SpO_2 alarms, 58 were 1-minute transient alarms, 9 were false desaturations, and 8 were true desaturations.

In 11 (18%) of the 61 patients without a preceding low MV event, there were 38 recorded low SpO_2 alarms in the EHR of which 29 were 1-minute transient alarms and 9 were false desaturations.

Opioids Increase Likelihood of Respiratory Depression; Low MV Increases LOS

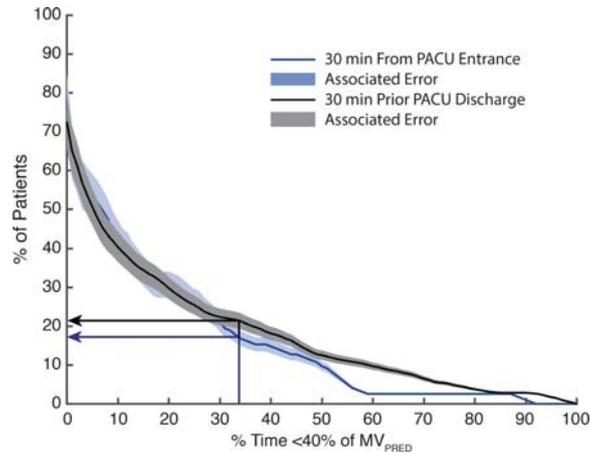
Patients were further stratified according to administration of opioids. One hundred sixty-six (64%) of 259 patients received opioids. Patients on opioids had an increased likelihood of low MV (69% vs 80%; $p < 0.05$). Furthermore, patients receiving opioids in the PACU had significantly longer LOS than those who did not receive opioids (2.9 ± 0.1 hours vs. 2.3 ± 0.1 hours; $p < 0.001$). In the opioid group, the LOS in the PACU increased substantially with low MV. One hundred thirty-three (80%) of 166 patients on opioids with low MV spent 75% longer in the PACU than the 33 (20%) patients on opioids without low MV (3.0 ± 0.1 hour vs. 1.7 ± 0.2 hours; $p < 0.001$).

DISCUSSION

Our results affirm that approximately 93% of SpO_2 alarms recorded in the EHR were likely false.¹⁵ Respiratory volume monitoring detected respiratory depression in advance of all true desaturations by 12.8 ± 2.8 minutes from immediately preceding low MV events. Repeated low MV alarms began a mean of 71.4 ± 16.5 minutes before each true desaturation, which, if acted on, might have eliminated the true desaturations. The lag between inadequate ventilation and the onset of hypoxemia as measured by the pulse oximeter is a critical period. The results from this study demonstrate that RVM provides advanced warning of respiratory depression compared to oximetry, uniquely enabling providers to prevent desaturation rather than treat it.

A significantly larger fraction of the patients on supplemental O_2 had low MV without a low SpO_2 alarm (68% vs 49%; $p < 0.05$), supporting evolving knowledge that supplemental oxygen masks respiratory depression until late in the event. SpO_2 desaturation alarms based on preset thresholds, typically less than 92 to less than 90%^{3,5-10} have led to late detection of respiratory depression and death.²¹⁻²⁴ Our results support previous work showing that pulse oximetry best detects periods of hypoventilation when a patient is breathing room air.²⁵ It has been suggested, and recently reinforced, that all patients on oxygen should have additional monitoring of their ventilation status.^{26,27} While the data reported here clearly support this view, it should not be overlooked that approximately 49% of patients on room air also demonstrated periods of low MV, suggesting that pulse oximetry alone may also not be sufficient to monitor respiratory status of postoperative patients who may have compromised ventilation from opioids or residual neuromuscular blockade.

Respiratory volume monitoring in conjunction with, or in advance of, pulse oximetry has the potential to increase patient safety by providing earlier detection of deteriorating respiratory status and reducing the number of false alarms. Protocols based on RVM data could help mitigate effects of alarm fatigue. Responding to all alarms does not address the underlying



	No Pt [%]	LMV in PACU [#/hr]	Recorded SpO ₂ Alarms				Opioids			
			Transient (1-min)	Hypoxemic events (≥2min)		No. Pt [%]	Dosage	Frequency	PACU LOS	
				False	True	RN Records	[μg/kg/hr]	[Doses/hr]	[hr]	
With Low MV:	198 [76%]	2.3 ± 0.1	58	10	7	1	133 [67%]	40 ± 3	2.0 ± 0.1	2.8 ± 0.1
No Low MV:	61 [24%]	0	29	9	0	1	33 [53%]	33 ± 4	2.3 ± 0.2	2.4 ± 0.1
Total:	259 [100%]	1.8 ± 0.1	87	19	7	2	166 [64%]	39 ± 2	2.1 ± 0.1	2.7 ± 0.1

Figure 4. Stratification of patient cohort by occurrence of low MV. The plot above shows the percent of patients in which the RVM measured MV levels below the 40% MV_{PRED} threshold. Respiratory volume monitoring data for the entire patient cohort was segmented into two important 30-minute periods: the 30 minutes starting at PACU arrival and the 30 minutes before discharge from PACU. In the table, patients were stratified based on the occurrence of low MV. In each group, we determined the number of SpO₂ alarms recorded in the EHR and PACU nurse records, the number of patients receiving opioids, the average dosage and frequency of opioid administration, and the PACU LOS.

problem and drains clinical resources and time. Continuous quantitative ventilation measurements at the bedside allow for the tailoring of opioid dosing regimens for each individual patient. Such a patient-centered approach may enhance detection of increased opioid sensitivity, allow for changes to opioid management based on each patient's response, help inform rational use of expensive nonopioids, reduce PACU LOS, enable triage of patients to an appropriate setting post-PACU, and help determine the most appropriate monitoring strategy. Similar findings regarding the clinical relevance of the RVM have been reported in other care settings, like the ICU²⁸ and endoscopy/procedural sedation.^{29,30}

Postanesthesia care unit LOS significantly increased in patients with low MV events (2.8 ± 0.1 hours Vs. 2.4 ± 0.1 hours; $p < 0.05$) and opioid use increased the likelihood of a low MV event in the PACU. Our data show that patients receiving opioids who also experience low MV events spent nearly 75% more time in the PACU versus patients receiving opioids who did not experience low MV events (3.0 ± 0.1 hours vs. 1.7 ± 0.2 hours; $p < 0.001$). These findings suggest that instead of using a uniform opioid dosing regimen, clinicians could individualize opioid dosing or better select patients for expensive multimodal analgesic regimens based on real-time RVM data.

This study has limitations. First, given the sample size, the current study did not stratify specific patient populations based on the following: (1) significant respiratory disease, e.g., COPD and congestive heart failure; (2) obstructive sleep apnea; (3) decreased respiratory reserve, e.g., pregnant women, elderly, ultramorbidly obese, children; (4) increased physiologic reserve, e.g., athletes; and (5) general versus spinal anesthesia. Second, events recorded in the EHR correlated poorly with PACU nursing records. The SpO₂ recordings represent snapshots rather than averages of SpO₂ values. Combined with the 15-minute resolution in the nursing records, the clinical indicators used to resolve hypoxemic events remain unclear. These limitations bring into question the reliability of using nursing notes and EHR records, as currently configured, to provide meaningful patient respiratory status for retrospective analysis. When reviewing for quality issues, trying to reconstruct event time-tables and actions taken can be very difficult, if not impossible. Not uncommonly, the chart does not provide evidence or reasons for the patient needing to be urgently or emergently reintubated or having had a cardiopulmonary arrest. Third, in this observational study, clinicians were blinded to the RVM measurements while pulse oximetry was used as part of routine care. Staff, unaware of low MV, could neither assess nor address

the clinical condition of hypoventilation based on RVM data. The number of low MV events per patient is likely artificially inflated from what would be seen when the RVM technology is used to drive clinical assessment and action. Finally, the study was limited to existing PACU monitoring technologies. Comparison of ventilation with EtCO₂ monitoring was not done because EtCO₂ monitoring was not used in the PACU in the study institution. Previous work has well-documented accuracy of the RVM measurements in both intubated and non-intubated patients obviating the need to include spirometry. Additionally, adding spirometry could complicate the study and enhance the Hawthorne effect.

Measurement of MV using the RVM provides the earliest signal of respiratory insufficiency and, with truncal electrode placement, does not suffer from false alarms due to patient movement or probe dislodgement. There are several ways that the results presented here could be translated into clinical practice. One would be to monitor patient ventilation status continuously with RVM and obtain pulse oximetry readings only intermittently on a set schedule or when the MV decreases below a given threshold. This approach may be particularly relevant to patient monitoring in a moving vehicle or during patient transport, where exogenous movement often renders oximetry monitoring suboptimal. Another would be to create an algorithm incorporating both continuous RVM and pulse oximetry data to define alarm parameters. Both of these methods have potential to provide a decrease in false alarms and improve patient safety. Additional studies would need to be designed and conducted to evaluate the clinical efficacy of such methods.

Respiratory volume monitoring technology is not limited to brick-and-mortar hospital settings. Accurate, robust, and portable technologies for use in transport vehicles or mobile clinics, often found in disaster-struck regions or military conflict zones is important. Continuous RVM monitoring of patients in these settings could drive better management decisions regarding treatments and triaging. Having been validated in the more controlled PACU environment allows ready expansion into other settings.

In summary, the RVM is a clinical tool that facilitates earlier identification of true respiratory depression. Delivery of only meaningful alarm breaches is particularly important in less intensely monitored and staffed clinical environments. Our data suggest that RVM monitoring, in conjunction with SpO₂ monitoring, could detect respiratory depression earlier, reduce the number of false alarms, and help hospitals meet The Joint Commission National Patient Safety Goal mandates to deal effectively with alarms. Using the RVM for monitoring nonintubated patients has great potential to improve patient safety, yields greater efficiency, and provides a method for respiratory assessment across the continuum of care.

AUTHORSHIP

S.M.G., P.G.D., and D.S.E. helped analyze the data, write the manuscript, and revise the manuscript. E.G. helped write and revise the manuscript.

DISCLOSURE

Samuel Galvagno and Edward George declare no conflicts of interest. Peggy G. Duke was a part-time consultant to Respiratory Motion, Inc at

the time this article was completed. Daniel S. Eversole was employed by Respiratory Motion, Inc at the time this article was completed. This study was supported by Respiratory Motion, Inc.

REFERENCES

1. Voscopoulos C, Braynov J, Ladd D, Lalli M, Panasyuk A, Freeman J. Special article: evaluation of a novel noninvasive respiration monitor providing continuous measurement of minute ventilation in ambulatory subjects in a variety of clinical scenarios. *Anesth Analg*. 2013;117(1):91–100.
2. Voscopoulos CJ, MacNabb CM, Braynov J, Qin L, Freeman J, Mullen GJ, Ladd D, George E. The evaluation of a non-invasive respiratory volume monitor in surgical patients undergoing elective surgery with general anesthesia. *J Clin Monit Comput*. 2015;29(2):223–230.
3. Jubran A. Pulse oximetry. *Crit Care*. 2015;19(1):272.
4. Shah A, Shelley KH. Is pulse oximetry an essential tool or just another distraction? The role of the pulse oximeter in modern anesthesia care. *J Clin Monit Comput*. 2013;27(3):235–242.
5. Ralston AC, Webb RK, Runciman WB. Potential errors in pulse oximetry. I. Pulse oximeter evaluation. *Anaesthesia*. 1991;46(3):202–206.
6. MacLeod DB, Cortinez LI, Keifer JC, Cameron D, Wright DR, White WD, Moretti EW, Radulescu LR, Somma J. The desaturation response time of finger pulse oximeters during mild hypothermia. *Anaesthesia*. 2005; 60(1):65–71.
7. Young D, Jewkes C, Spittal M, Blogg C, Weissman J, Gradwell D. Response time of pulse oximeters assessed using acute decompression. *Anesth Analg*. 1992;74(2):189–195.
8. Ghai A, Hooda S, Wadhwa R. Lag period with different pulse oximeters leading to variation in reperfusion times. *Acta Anaesthesiol Scand*. 2008; 52(3):447–448.
9. Anand GW, Heuss LT. Feasibility of breath monitoring in patients undergoing elective colonoscopy under propofol sedation: a single-center pilot study. *World J Gastrointest Endosc*. 2014;6(3):82–87.
10. Curry J, Jungquist CR. A critical assessment of monitoring practices, patient deterioration, and alarm fatigue on inpatient wards: a review. *Patient Saf Surg*. 2014;8(1):29.
11. Drew BJ, Harris P, Zègre-Hemsey JK, Mammone T, Schindler D, Salas-Boni R, Bai Y, Tinoco A, Ding Q, Hu X. Insights into the problem of alarm fatigue with physiologic monitor devices: a comprehensive observational study of consecutive intensive care unit patients. *PLoS One*. 2014; 9(10):e110274.
12. Wong M, Mabuyi A, Gonzalez B. First National Survey of Patient-Controlled Analgesia Practices. 2014.
13. Sendelbach S, Funk M. Alarm fatigue: a patient safety concern. *AACN Adv Crit Care*. 2013;24(4):378–386.
14. The Joint Commission. Hospital National Patient Safety Goals. 2015. Available at: http://www.jointcommission.org/assets/1/6/2015_HAP_NPSG_ER.pdf. Accessed December 1, 2015.
15. Epstein RH, Dexter F, Lopez MG, Ehrenfeld JM. Anesthesiologist staffing considerations consequent to the temporal distribution of hypoxicemic episodes in the postanesthesia care unit. *Anesth Analg*. 2014;119(6): 1322–1333.
16. Weissman C, Freeman J. Operational realities in the postanesthesia care unit: staffing and monitoring for safe postoperative care. *Anesth Analg*. 2014; 119(6):1249–1250.
17. Dahan A, Niesters M, Olofsen E, Smith T, Overdyk F. Opioids. In: Barash PG, Cullen BF, Stoelting RK, Cahalan M, Stock MC, Ortega R, editors. *Handbook of Clinical Anesthesia*. 7th Edition. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:501–522.
18. Du Bois D, Du Bois EF. A formula to estimate the approximate surface area if height and weight be known. 1916. *Nutrition*. 1989;5(5):303–311.
19. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med*. 2000; 342(18):1301–1308.
20. Voscopoulos CJ, MacNabb CM, Freeman J, Galvagno SM Jr, Ladd D, George E. Continuous noninvasive respiratory volume monitoring for the identification of patients at risk for opioid-induced respiratory depression and obstructive breathing patterns. *J Trauma Acute Care Surg*. 2014;77(3 Suppl 2): S208–S215.

21. Lynn LA, Curry JP. Patterns of unexpected in-hospital deaths: a root cause analysis. *Patient Saf Surg*. 2011;5(1):3.
22. Chan PS, Jain R, Nallmothu BK, Berg RA, Sasson C. Rapid response teams: a systematic review and meta-analysis. *Arch Intern Med*. 2010;170(1):18–26.
23. Lee LA, Caplan RA, Stephens LS, Posner KL, Terman GW, Voepel-Lewis T, Domino KB. Postoperative opioid-induced respiratory depression: a closed claims analysis. *Anesthesiology*. 2015;122(3):659–665.
24. Winters BD, Weaver SJ, Pfoh ER, Yang T, Pham JC, Dy SM. Rapid-response systems as a patient safety strategy: a systematic review. *Ann Intern Med*. 2013;158(5 Pt 2):417–425.
25. Fu ES, Downs JB, Schweiger JW, Miguel RV, Smith RA. Supplemental oxygen impairs detection of hypoventilation by pulse oximetry. *Chest*. 2004;126(5):1552–1558.
26. Stoelting RK. Continuous postoperative electronic monitoring and the will to require it. *Anesth Analg*. 2015;121(3):579–581.
27. Centers for Medicare & Medicaid Services. Requirements for hospital medication administration, particularly intravenous (IV) medications and post-operative care of patients receiving IV opioids. 2014.
28. Galvagno SM, Brayanov J, Corneille MG, Voscopoulos CJ, Sordo S, Ladd D, et al. Non-invasive respiratory volume monitoring in patients with traumatic thoracic injuries. *Trauma*. 2014;17(3):219–223.
29. Holley K, MacNabb CM, Georgiadis P, Minasyan H, Shukla A, Mathews D. Monitoring minute ventilation versus respiratory rate to measure the adequacy of ventilation in patients undergoing upper endoscopic procedures. *J Clin Monit Comput*. 2016;30(1):33–39.
30. Ebert TJ, Middleton AH, Makhija N. Ventilation monitoring during moderate sedation in GI patients. *J Clin Monit Comput*. 2015;1–5.