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Original Contribution

Improving patient safety during procedural sedation via respiratory volume monitoring: A randomized controlled trial☆

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ABSTRACT

Study objective: Assess the utility of a respiratory volume monitor (RVM) to reduce the incidence of low minute ventilation events in procedural sedation.
Design: Randomized control trial
Setting: Endoscopy suite
Patients: Seventy-three total patients (ASA Physical Status 1–3) undergoing upper endoscopies were analyzed.
Intervention: Patients were randomized into two groups using a computer generated randomization table: Control ($n = 41$): anesthesia provider was unable to see the screen of the RVM; RVM ($n = 32$): anesthesia provider had access to RVM data to assist with management of the case.
Measurements: Minute ventilation (MV), tidal volume, and respiratory rate were continuously recorded by the RVM. MV is presented as percent of Baseline MV ($MV_{Baseline}$), defined during a 30s period of quiet breathing prior to sedation. We defined Low MV as MV < 40% $MV_{Baseline}$, and calculated the percentage of procedure spent with Low MV. Patients in the RVM group were stratified based on whether the anesthesiologist rated the RVM as "not useful", "somewhat useful", or "very useful" during the case.
Main results: Control patients experienced twice as much Low MV compared to RVM patients (15.3 ± 2.8% vs. 7.1 ± 1.4%, $P = 0.020$). The "not useful" (13.7 ± 3.8%) group showed no improvement over the Control group ($p = 0.81$). However, both the "very useful" (4.7 ± 1.4%) and "somewhat useful" (4.9 ± 1.7%) groups showed significant improvement over the "not useful" group ($p < 0.05$).
Conclusions: Patients in the Control group spent more than double the amount of time with Low MV compared to the RVM group. This difference became more pronounced when the anesthesiologist found the RVM useful for managing care, lending credibility to the usage of minute ventilation monitoring in procedural sedation.

1. Introduction

In the fast-paced procedural sedation environment, patients are at risk for respiratory depression due to decreased respiratory drive and loss of muscle tone in the upper airway muscles [1–5]. ASA guidelines state that ventilation should be continuously monitoring during sedation [6], but current respiratory monitors have been insufficient at quantitatively measuring respiratory status. While pulse oximetry is commonly used, it provides a late indication of respiratory depression, especially with the administration of supplemental oxygen [7,8]. Capnography has unfortunately proven to be unreliable in non-intubated patients because of issues of patient non-compliance, patient movement artifacts, and difficulty of interpreting the CO_2 waveforms [9–13]. Monitoring respiratory status in upper endoscopies can be especially difficult because oral instrumentation further compromises capnography cannula positioning. Airway obstruction can be exacerbated by the endoscope, and repositioning to address questionable airway obstruction or respiratory depression can be difficult without interfering with the procedure underway.

A recently developed non-invasive respiratory volume monitor (RVM) (ExSpiron, Respiratory Motion, Inc., Waltham, MA) provides continuous measurements of minute ventilation (MV), tidal volume (TV), and respiratory rate (RR). The RVM has better than 90% accuracy for MV and TV and 98% accuracy for RR in both intubated and non-intubated patients [14,15]. During procedural sedation, the RVM detects

☆ **Disclosures**: Respiratory Motion provided the respiratory volume monitors for this study.

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the decrease in MV and also identifies increases following airway maneuvers such as chin lifts and jaw thrusts [16,17].

In this randomized control trial, continuous respiratory metrics were collected in upper endoscopy patients and the incidence of respiratory depression was quantified. We randomized whether the anesthesiologist managing the case had access to continuous RVM metrics and examined the consequent effects on the patients' respiratory status. We hypothesized that the use of the RVM by the anesthesiologist would result in a decrease in the incidence of respiratory depression in patients under procedural sedation.

2. Materials and methods

2.1. Patients

This parallel-group randomized control trial was approved by the Fletcher Allen Healthcare (renamed University of Vermont Medical Center) Institutional Review Board, and all patients provided written informed consent prior to enrollment. The study was registered at ClinicalTrials.gov (NCT02310230) and followed the CONSORT guidelines [18]. Inclusion criteria included patients scheduled to undergo upper gastrointestinal endoscopy with anesthesiologist-administered sedation, age >21. Exclusion criteria included history of thoracotomy, history of chronic obstructive pulmonary disease, body mass index (BMI) >43. Patients scheduled for a screening upper endoscopy without associated procedures were also excluded, as the duration is usually quite short. Patients were randomly assigned into one of two groups by a computer generated randomization table. In the Control group, the anesthesia provider was unable to see the screen of the RVM. In the RVM group, the anesthesia provider had access to RVM metrics (MV, TV, and RR) displayed on the screen to assist with management of the case.

2.2. Instrumentation

Continuous respiratory metrics were collected via a bio-impedance RVM (ExSpiron, Respiratory Motion, Inc., Waltham, MA) with an attached electrode PadSet spanning the thoracic region. The electrodes were placed in the recommend positions at the sternal notch, xiphoid, and mid-axillary line at the level of the xiphoid. For patients in the Control group, routine monitoring and care were used (oxygen saturation monitoring, blood pressure, heart rate, capnography), and the anesthesia and care team were blinded to RVM measurements. For RVM group patients, RVM metrics of MV, TV, and RR were available in addition to standard monitoring.

2.3. Study procedure

Following patient consent, the PadSet was placed and attached to the monitor. MV, TV, and RR data were continuously acquired from pre-procedure holding until the subject was eligible for discharge from the post-procedure recovery area. Before sedation and once the subject was positioned for their procedure, a thirty-second baseline representative of quiet, normal breathing was taken by the RVM. The average MV from this period was defined as 100% $MV_{Baseline}$. Patients were sedated by anesthesia staff with propofol infusions and boluses, with or without other agents (ketamine, fentanyl, and midazolam). A research assistant recorded the timing and doses of sedating agents throughout the procedure, as well as any airway maneuvers (i.e., chin lift, jaw thrust) and subject positioning changes performed by the care team. For patients in the RVM group, the anesthesia provider was instructed on how to interpret the displayed respiratory trace, MV, TV, and RR and was encouraged to use the RVM to direct care. In the RVM group, the anesthesia provider used a Likert-like scale to assign a rating at the end of the case based on how useful they found the RVM for management of their patient's anesthesia and airway. The rating was on a scale from 1 ("not-useful") through 5 ("very-useful").

2.4. Data analysis

We assessed the respiratory status of patients as $\%MV_{Baseline}$, and defined MV < 40% $MV_{Baseline}$ as Low MV (i.e., potentially unsafe respiratory depression), mirroring the ARDSnet definition of insufficient ventilation for extubation [19]. We calculated the percentage of each patient's case that was spent with Low MV. Total intra-operative propofol was normalized by patient body weight and procedure length. Two-sided *t*-tests were performed to compare procedure times, propofol administered, number of airway maneuvers, mean % $MV_{Baseline}$ throughout the procedure, and percent of procedure with Low MV across Control and RVM groups.

To examine the effects of varying anesthesiologist engagement with the RVM, we further subdivided the RVM group by survey score (1–2: "Not Useful", 3–4: "Somewhat Useful", 5: "Very Useful"). One-way ANOVAs were performed to compare the percentage of procedure with Low MV, procedure time, medication administered, and average airway maneuvers among these subgroups.

Preliminary data indicated patients under standard of care spent approximately 15% of the procedure time below 40% of their $MV_{Baseline}$, with a standard deviation of 10%. We estimated at least 28 patients were needed in each group to detect if the Control group spent half this amount of time with low MV (i.e., 7.5%) [20].

All data are presented as mean ± SEM unless otherwise indicated. All analyses were performed in Matlab 2014b (MathWorks, Natick, MA). Results were considered statistically significant at $P < 0.05$.

3. Results

One-hundred patients (50 Control/50 RVM) were recruited for this study between September 22, 2014 and May 9, 2016. Twenty-seven patients (9 Control/18 RVM) were excluded. Therefore, a total of 73 patients (41 Control/32 RVM) were analyzed (Table 1). Patients were excluded for the following reasons: anesthetics administered prior to baseline MV measurement (4 Control/8 RVM), technical issues (3/3), sedation administered by gastroenterologist (1/0), intubation or general anesthesia (1/4), incorrect monitor setup (0/2), and case cancellation (0/1).

Patients underwent endoscopic ultrasound (EUS, 45 patients), endoscopic retrograde cholangiopancreatography (ERCP, 22 patients), or a hybrid procedure (EUS + ERCP, 6 patients).

3.1. Control vs. RVM group comparison

Patients in Control group (41 patients) and RVM group (32 patients) had similar anthropometrics, procedure lengths, and were administered similar amounts of intra-operative propofol (Table 1).

Respiratory data from representative patients in the Control and RVM groups are displayed in Figs. 1 and 2, respectively. The patient in the Control group (Fig. 1) received 527 mg of propofol and 47 mg of ketamine and spent 20.9% of the procedure under 40% $MV_{Baseline}$. The patient experienced an extended period of time after 11:20 following the final dose of propofol and ketamine. The patient in the RVM group (Fig. 2) received 527 mg of propofol and 10 mg of ketamine and spent 3.8% of the procedure under 40% $MV_{Baseline}$. The anesthesia provider ceased boluses of propofol and ketamine after the patient drops below 40% $MV_{Baseline}$ for as at 10:09 which allowed the patient to recover.

Control group patients spent more than twice the amount of procedure time with Low MV compared to the RVM group (15.3 ± 2.8% vs. 7.1 ± 1.4%, $p = 0.020$, Fig. 3A). The percent of procedure time with Low MV ranged from 0 to 68.8% for the Control group compared to 0–30.8% for the entire RVM group. Furthermore, more Control group patients spent extended periods of time at a Low MV. Specifically, 8/41

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