The Relationship between Minute Ventilation and End Tidal CO$_2$ in Intubated and Spontaneously Breathing Patients

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**Introduction:** End Tidal CO$_2$ (EtCO$_2$) monitoring is the standard of care in intubated patients for both confirming ET-tube placement and monitoring adequacy of ventilation. In contrast, capnography in spontaneously breathing patients can be unreliable in certain settings. A novel, non-invasive Respiratory Volume Monitor (RVM) that can provide accurate measurements of minute ventilation (MV), tidal volume (TV) and respiratory rate (RR) in non-intubated patients is available. Here we study the relationship between EtCO$_2$ and MV in intubated patients under general anesthesia (GA) and in awake, spontaneously breathing patients.

**Methods:** Continuous RVM data (ExSpiron, Respiratory Motion, Inc., Waltham, MA) and ventilator delivered MV and EtCO$_2$ data (Drager Apollo, Andover, MA) from 54 patients (age: 65.2 ± 12.1 yrs, BMI: 31.2 ± 6.3 kg/m$^2$, 31 females) undergoing elective orthopedic surgery with GA was collected. In a separate cohort, continuous RVM and capnography data (Capnostream 20, Smart CapnoLine Plus Oral/Nasal, Filterline Set, Covidien, Mansfield, MA) were collected from 25 volunteers (age: 47.5 ± 10.8 yrs, BMI: 28.9 ± 8.6 kg/m$^2$, 5 females). Hospital patients were managed on the ventilator according to standard care. Volunteers were coached to breathe at varying RRs for 33 min. A Deming regression was used to quantify the relationship (sensitivity) between EtCO$_2$ & MV for each patient. The slopes of the regression were presented as angles from the x-axis. EtCO$_2$ sensitivity and mean values were compared across cohorts using un-paired t-tests.

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**Results:** In a given patient, a plot of EtCO$_2$ measurements against corresponding MV measurements produced a negatively correlated distribution: as MV increases, EtCO$_2$ generally decreases. The sensitivity of EtCO$_2$ to changes in MV, illustrated by the slope of the correlation between EtCO$_2$ and MV in Fig 1, was significantly higher in GA patients than in awake, spontaneously breathing patients (-81 ± 9.6° vs -20 ± 18.7°, p<0.001, Figure 2A). A steep slope (angle close to -90°) indicates high sensitivity, i.e. a small change in MV in GA patients leads to a large change in EtCO$_2$. A flatter line (angle close to 0°) indicates low sensitivity, i.e. a small change in MV would not change EtCO$_2$ much in awake individuals. Measured EtCO$_2$ values were systematically higher in intubated & anesthetized patients than in awake patients monitored by either an oral/nasal or in-line sensor (36.4 ± 4.4 vs. 31.1 ± 4.3 vs. 31.4 ± 3.9 mmHg, respectively, p<0.001 for both, Fig 2B).

**Conclusions:** Even though the cohorts and instrumentation in this study were not exactly matched, some basic conclusions can be drawn. While EtCO$_2$ may be a sound indicator of ventilatory adequacy in patients under GA, its sensitivity to changes in MV is greatly reduced in awake, spontaneously breathing patients. This difference in sensitivity may reduce the utility of EtCO$_2$ in non-intubated patients. Furthermore, the use of a sampling nasal cannula with oral/nasal scoop may introduce additional challenges in EtCO$_2$ monitoring, as it likely captures a mixture of expired and ambient air, thus systematically biasing the reported EtCO$_2$ values. In many volunteers, we were unable to induce significant hypercapnia despite coached hypoventilation over a period of several minutes due to inherent subject respiratory drive. To continue to examine this relationship, follow-up studies of RVM MV vs. EtCO2 during procedural sedation and intra- and post-operatively are in various stages of execution and planning.
Figure 1. (A) Example correlations between MV and EtCO2 in anesthetized and awake patients.

Each data point corresponds to a single 30-sec measurement pair (MV and EtCO2) and the line and confidence ellipse show the best-fit (Deming regression) +/- 1 SD to the data. A patient under general anesthesia (blue) undergoes large changes in EtCO2 (95% CI from 32 to 52 mmHg) resulting from relatively small changes in MV (95% CI from 4.5 to 8.3 L/min). In contrast, a spontaneously breathing patient with an inline EtCO2 sensor (purple) can modulate his EtCO2 much less (27 to 37 mmHg) in response to a much greater change in MV (4.4 to 30.2 L/min). In the same patient a sampling nasal cannula (green) captures similar variation in EtCO2 (17 to 27 mmHg) corresponding to an even larger changes in MV (2.7 to 37.8 L/min). Note that the EtCO2 measurements from the nasal sampling cannula with oral/nasal scoop are systematically lower than with the snorkel and in-line sensor, suggesting that the cannula is unable to capture all of the expired air and instead captures mixed expired and room air.

(B) Summary of the sensitivity of EtCO2 to changes in MV. Each box-plot shows the median slope of the correlation between EtCO2 and MV (red line), the box extends from the 25th to 75th percentile, the whiskers extend to the most extreme non-outlier data points, and statistical outliers are plotted individually with red “plus” signs. Left box: sensitivity in patients under general anesthesia: -81°
±9.6° (mean ± SD). Right box: sensitivity in awake, spontaneously breathing patients: -20° ±18.7°.

(C) Average EtCO\textsubscript{2} values across patient cohorts. The measured EtCO\textsubscript{2} values were systematically higher in intubated and anesthetized patients (right box) that in awake patients monitored by either a sampling nasal cannula (middle box) or in-line sensor (left box), 36.4 ± 4.4 mmHg vs. 31.1 ± 4.3 mmHg vs. 31.4 ± 3.9 mmHg, respectively, all values given as mean ± SD.* p<0.001