

# Is a change in end-tidal carbon dioxide concentration associated with hypotension during periods of general anesthesia with stable mechanical ventilation? Analysis of a large cohort.

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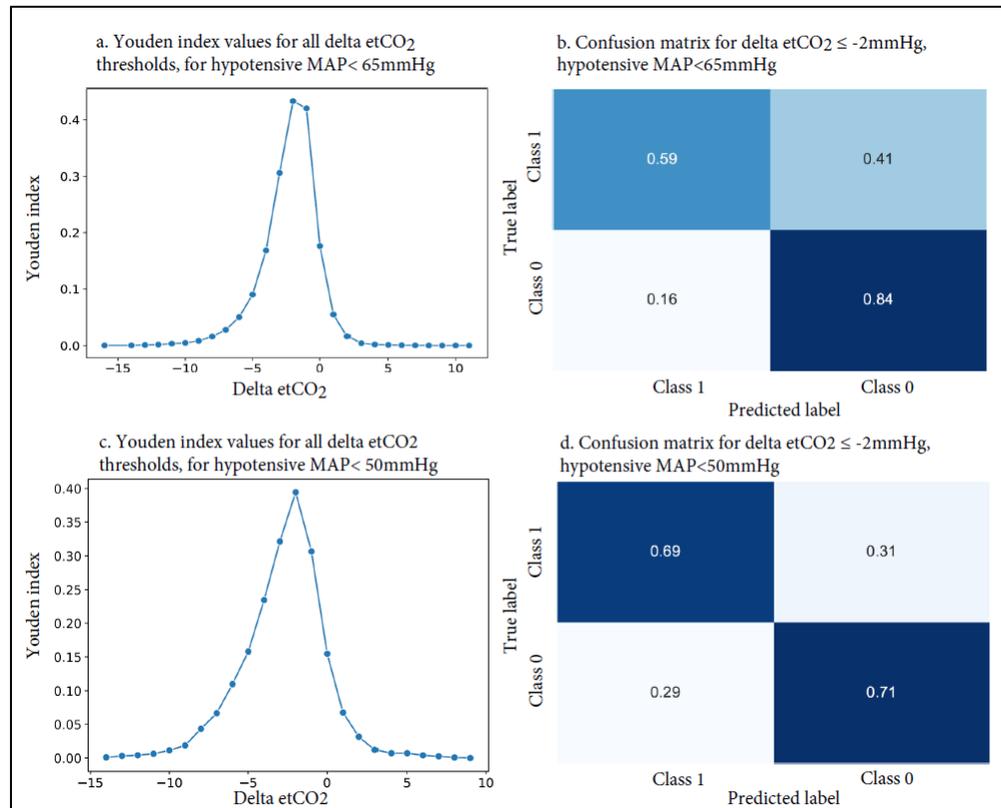
**Introduction:** Detection of intraoperative hypotension relies on measuring non-invasive blood pressure (NIBP) or invasive arterial blood pressure. However, significant decreases in end-tidal carbon dioxide concentration (etCO<sub>2</sub>) can also indicate decreased cardiac output [1]. During most general anesthetics, NIBP is sampled infrequently, typically every 5 minutes as per the Canadian Anesthesiologists' Society guidelines [2], while etCO<sub>2</sub> is monitored on a breath-by-breath basis, i.e. every 3-9 sec. This mismatch in sampling frequencies suggests an opportunity to anticipate acute hypotensive events using capnography before the next NIBP measurement becomes available. The aim of this study is to determine if acute decreases in etCO<sub>2</sub> predict hypotension in patients undergoing general anesthesia during otherwise stable mechanical ventilation.

**Methods:** With Research Ethics Board approval (H20-01248) and waiver of patient consent, we conducted a retrospective study of patients undergoing general anesthesia for non-cardiac surgery at any of eight hospitals within the Fraser Health Authority between Jan'14 and Jun'20. NIBP artifacts were removed [3], and cases without etCO<sub>2</sub> data or < 75% case coverage for mean arterial pressure (MAP) were excluded. Periods of stable mechanical ventilation were identified as episodes with average variability in positive end-expiratory pressure < 5% and in minute ventilation < 2.5%. Our primary outcome was the occurrence of significant intraoperative hypotension with MAP < 65 mmHg and MAP decrease of ≥ 20 mmHg from a baseline measurement 10-min prior to the hypotensive observation. For each hypotensive episode, the change in etCO<sub>2</sub> was calculated as the difference between etCO<sub>2</sub> reading at the time of the hypotensive event and 10-min prior to the event. Magnitude of etCO<sub>2</sub> change was examined as an individual cut-off value, and analyzed for its predictive value. The area under the receiver operating characteristic curve (AUROC) was obtained, with the Youden index identifying the optimal threshold. The analysis was repeated using a hypotension definition of MAP < 50 mmHg.

**Results:** Data from 66,683 procedures were available for analysis, of which 39,581 had at least one episode of intraoperative hypotension with a MAP < 65 mmHg. Data from 63,343 hypotensive episodes with stable ventilation from 12,951 procedures were used in our model; of these 7,456 were labeled as significant (i.e. MAP decrease ≥ 20 mmHg). A maximum Youden index of 0.43 was observed for a decrease of 2 mmHg (Figure 1a & b). The model's AUROC was 0.776 (95% CI 0.77 to 0.782). Using the definition of MAP < 50 mmHg, hypotension was observed in 7,903 procedures from which only 1,331 hypotensive episodes with stable ventilation could be used; of these 980 were labeled as significant. Here, the optimal change in etCO<sub>2</sub> was also ≤ -2 mmHg (Figure 1c & d). This model's AUROC was 0.747 (95% CI of 0.727 to 0.767). Interestingly, acute etCO<sub>2</sub> change of ≤ -5 mmHg did not indicate hypotension (Fig 1a & c).

**Conclusion:** These data suggest that acute changes in etCO<sub>2</sub> were not a reliable predictor for intraoperative hypotensive events, yet more sophisticated analysis approaches should be explored before ruling out this potentially useful clinical warning sign. Data show that an etCO<sub>2</sub> decrease ≤ -2 mmHg had a true positive rate of 59%, and false negative rate of 41% for predicting hypotensive MAP < 65mmHg, implying that hypotensive cases could not be accurately predicted from etCO<sub>2</sub> drops.

**References:** 1. JAMA 1987 Jan 23-30;257(4):512-5. 2. Can J Anaesth. 2018 Jan;65(1):76-104. 3. Anesthesiology. 2017 Jan;126(1):47-65.



**Figure 1:** Youden indices for all delta etCO<sub>2</sub> thresholds and confusion matrices for etCO<sub>2</sub> ≤ -2 mmHg for hypotension defined as MAP < 65 mmHg (a & b) and MAP < 50 mmHg (c & d).