Published in final edited form as:

Pediatr Crit Care Med. 2016 December ; 17(12): 1180–1181. doi:10.1097/PCC.0000000000000962.

Eyes Wide Shut: Improving Physiologic Monitoring During Mechanical Ventilation

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Keywords

physiologic monitoring; capnography; respiratory failure

Effective management of mechanical ventilation achieves adequate gas exchange while limiting adverse impact upon patients. To achieve this goal, it is necessary to monitor appropriate physiologic targets that enable robust bedside decision making. Specific approaches to monitoring should yield data with accuracy, precision and fidelity across the range of physiologic decompensation likely to be encountered; moreover, monitoring – itself – should add minimal morbidity and risk to the patient. Of note, several clinical scenarios call for precise and timely knowledge of arterial $p\text{CO}_2$ (PaCO_2) (e.g. permissive hypercapnia, traumatic brain injury [and other situations with intracranial hypertension], complex acid/base scenarios, as well as challenges in weaning/separation from ventilatory support). Options to acquire this information are compromised by either risk/morbidity (invasive arterial access) or lack of sufficient accuracy/precision (transcutaneous, central venous, capillary, or end-tidal monitoring). Moreover, blood sampling may exacerbate anemia and/or lead to bloodstream infection. As such, development of means for non-invasive, continuous monitoring of PaCO_2 would be impactful.

In this issue of the *Journal*, Baudin and colleagues (1) report pilot evaluation of a novel mathematical model designed to estimate PaCO_2 from volumetric capnography data. The model was developed using multivariable linear regression from variables selected by expert opinion and was refined using data from 65 children at a single center. The approach to this goal was sound, well considered and robustly performed. The power analysis was similarly appropriate. The best model employed the following inputs: end tidal $p\text{CO}_2$, mean airway pressure (P_{AW}), FiO_2 , and 'the capnographic index' (KPIv , e.g. the ratio of S3 and S2 slopes of the volumetric capnography curve). There is plausible physiologic basis for this formula, given the inclusion of two components of the oxygenation (or saturation) index (OI, which reports lung injury severity)(2,3) and KPIv (which reports ventilation-perfusion inhomogeneity and the functional impact of small airway obstruction)(4–6). It is notable that

FiO₂ (but not measures of patient oxygenation, e.g. SpO₂ or PaO₂), was required in the model - perhaps because oxygenation targets for FiO₂ (and P_{AW}) selection at this single center were uniform. It is also notable that physiologic dead space (V_d/V_t) was not required as a separate term in the model; in fact, the authors demonstrate only a slight bias (to the model) imposed by V_d/V_t: a 2 mmHg difference in accuracy as V_d/V_t rose from 0.15 to 0.55. This term may prove more important in cohorts with greater prevalence of increased dead space (severe asthma, decompensated restrictive lung disease, bronchiolitis obliterans, etc.).

A few additional issues should be mentioned. In evaluating external validity of predictive models, study cohort composition is highly relevant; valid study of predictive models require separate cohorts for model derivation (training cohort) and model evaluation (validation cohort). Of the 65 children in the 'training cohort' for the model: 38 (58.5%) had PaO₂/FiO₂ < 300 mmHg; 25 (38.5%) had PARDS(7), of whom 5 (7.6%) were severe (OI 16); 3 (1.5%) had status asthmaticus. Although the numbers are small, the demographics mirror that for a general PICU(8); however, forthcoming multicenter validation of the model in a larger cohort will be essential prior to clinical deployment. Moreover, in considering additional requirements for clinical deployment, the range of values for PaCO₂ in the Bland-Altman plots (Figure 3) are nominally within tolerated clinical values; a model predicting PaCO₂ from ET-CO₂ is only useful if able to predict abnormal, actionable values (e.g. PaCO₂ < 35 and > 65). While 8 subjects did have PaCO₂ 35 mmHg, none had PaCO₂ > 65 mmHg; it will be necessary to demonstrate model fidelity over a broader range of actionable PaCO₂ values in the validation phase. As an additional (though minor) concern, this approach to PaCO₂ estimation cannot be used in the presence of significant airleak (either at the ETT or in the setting of a bronchopulmonary fistula).

Overall, this paper presages a significant advance in monitoring intubated children with respiratory failure and this contribution has the potential to meaningfully impact clinical care. As noted by the authors, in addition to the 'modest' goal of mitigating need for arterial blood sampling, accurate continuous noninvasive estimation of PaCO₂ would enhance development and adoption of sophisticated decision support systems for- and closed-loop approaches to- mechanical ventilation. Both advances (now on our horizon) would meaningfully improve efficient and safe care of children with severe respiratory failure.

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