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Carbon Dioxide Elimination and Oxygen Consumption in Mechanically Ventilated Children

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BACKGROUND: Accurate measurement of carbon dioxide elimination ($\dot{V}_{CO_2}$) and oxygen consumption ($\dot{V}_{O_2}$) at the bedside may help titrate nutritional and respiratory support in mechanically ventilated patients. Continuous $\dot{V}_{CO_2}$ monitoring is now available with many ventilators. However, because normative data are sparsely available in the literature, we aimed to describe the range of $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ values observed in mechanically ventilated children. We also aimed to examine the characteristics of $\dot{V}_{CO_2}$ values that are associated with standard steady state (5-min period when $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ variability are < 10%). METHODS: Mechanically ventilated patients who underwent indirect calorimetry testing were eligible for inclusion, and subjects who achieved standard steady state were included. Normalized $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ values (mL/kg/min) were modeled against subject height, and correlation coefficients were computed to quantify the goodness of fit. A steady-state definition using only $\dot{V}_{CO_2}$ was developed ($\dot{V}_{CO_2}$ variability of < 5% for a 5-min period) and tested against standard steady state using sensitivity and specificity. RESULTS: Steady-state data from 87 indirect calorimetry tests (in 70 subjects) were included. For age groups < 0.5, 0.5–8, and > 8 y, the mean $\dot{V}_{CO_2}$ values were 7.6, 5.8, and 3.5 mL/kg/min. Normalized $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ values were inversely related to subject height and age. The relationships between normalized gas exchange values and height were demonstrated by the models: $\dot{V}_{CO_2} = 115 \times (\text{height in cm})^{-0.71}$ (R = 0.61, *P* < .001) and $\dot{V}_{O_2} = 130 \times (\text{height in cm})^{-0.72}$ (R = 0.61, *P* < .001). Steady-state $\dot{V}_{CO_2}$ predicted standard steady state (sensitivity of 0.84, specificity of 1.0, *P* < .01). CONCLUSIONS: $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ measurements correlated with subject height and age. Smaller and younger subjects produced larger amounts of CO_2 and consumed more O_2 per unit of body weight. The use of a 5-min period when $\dot{V}_{CO_2}$ varied by < 5% predicted standard steady state. Our observations may facilitate greater utility of $\dot{V}_{CO_2}$ at the bedside in the pediatric ICU and thereby extend the benefits of metabolic monitoring to a larger group of patients. *Key words: carbon dioxide elimination; oxygen consumption; mechanical ventilation; children; pediatric; $\dot{V}_{CO_2}$; volumetric capnography; steady state.* [Respir Care 2015;0(0):1–•. © 2015 Daedalus Enterprises]

Introduction

The integration of CO_2 and flow measurements yields carbon dioxide elimination ($\dot{V}_{CO_2}$) measurements that can be a useful metric to detect changes in alveolar ventilation, pulmonary perfusion, CO_2 production, and ventilation optimization.[1-5] Similarly, volumetric oxygen consumption

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($\dot{V}_{O_2}$) can be extrapolated using oxygen and flow to detect the volume of oxygen consumed by the body in a given time period. The combination of $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ is used to calculate energy expenditure and plays an important role in assessing and optimizing nutrition, particularly during critical illness.[1]

Bedside measurements of $\dot{V}_{CO_2}$ and/or $\dot{V}_{O_2}$ in mechanically ventilated patients can be obtained using a stand-alone bedside monitor, a device integrated into the ventilator, or an indirect calorimeter.[6,7] The ability to detect abnormally high or low values could enhance bedside decision support. Hence, reference ranges for these gas exchange measurements are desirable in the critically ill population but are currently not available. We describe observed gas exchange data (both $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$) in a cohort of critically ill, mechanically ventilated subjects admitted to the pediatric ICU (PICU).

To ensure that the values for $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ measured at the respiratory interface reflect cellular CO_2 production and O_2 utilization by the body, a period of steady state must be identified.[8-10] Recently, $\dot{V}_{CO_2}$ was shown to have an expanding role at the bedside and may be sufficient to predict energy expenditure in the majority of mechanically ventilated children.[11] However, methods by which a steady-state interval can be computed on stand-alone $\dot{V}_{CO_2}$ monitors to ensure data quality have not been demonstrated in the literature and are needed. The current standard definition of a steady-state period requires 5 consecutive min during which $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ vary by $\leq 10\%$.[9] Because many devices incorporate $\dot{V}_{CO_2}$ measurements independently of $\dot{V}_{O_2}$ (such as those incorporated into ventilators), a steady-state definition for $\dot{V}_{CO_2}$ is required when interpreting bedside measurements. Recently, $\dot{V}_{CO_2}$ values were shown to provide useful metabolic data and reasonable estimates of energy expenditure in mechanically ventilated children,[11] and methods to determine steady-state conditions with $\dot{V}_{CO_2}$ are desirable. Therefore, we sought to identify a definition for steady state that includes parameters measured by stand-alone $\dot{V}_{CO_2}$ monitors or ventilators and that is in agreement with steady-state $\dot{V}_{CO_2}$ values using the standard definition. This would allow reliable interpretation of the $\dot{V}_{CO_2}$ values at the bedside.

Methods

Gas exchange measurements in mechanically ventilated subjects who underwent indirect calorimetry testing were analyzed from an existing repository of indirect calorimetry data. The study was approved by the institutional review board, and need for informed consent was waived. The methods for gas exchange measurement and data collection were described previously.[10] In brief, the Vmax Encore (CareFusion, San Diego, California) was used to measure minute-to-minute $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ for ∼30 min in each subject using non-dispersive infrared, galvanic cell, and mass flow sensors. Following calibration according to manufacturer specifications, connections were made on the inspiratory and expiratory limbs of the ventilator to measure inspired gas concentrations, expired gas concentrations, and exhaled gas flow. The calculation of $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ was computed using dedicated software that employed the Haldane transformation.

In addition to indirect calorimetry data, subject demographics, endotracheal tube leak, diagnosis, and ICU stay at the time of indirect calorimetry were collected. Subjects were classified into general categories (medical or surgical) and then by specific disease process (respiratory, neurologic, neuromuscular, cardiac, neurosurgical, or other).

QUICK LOOK

Current knowledge

The measurement of carbon dioxide production ($\dot{V}_{CO_2}$) and oxygen consumption ($\dot{V}_{O_2}$) with instruments integral to a ventilator or with an independent device can provide data regarding nutritional requirements and ventilatory efficiency. The presence of leaks in pediatric patients complicates these measurements and can introduce important errors. Establishment of a steady state in this population can be difficult.

What this paper contributes to our knowledge

$\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ measurements correlated with subject height and age. Smaller and younger subjects produced larger amounts of CO_2 and consumed more O_2 per unit of body weight. The use of a 5-min period when $\dot{V}_{CO_2}$ varied by $< 5\%$ predicted a standard steady state.

Description of Gas Exchange Measurement

Subjects who were not able to achieve steady state by the standard definition were excluded from the analysis. Data were analyzed using SPSS 21.0 (IBM, Armonk, New York) and Prism 5.04 (GraphPad Software, San Diego, California). Gas exchange values ($\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$) were normalized to weight (mL/kg/min). Continuous values are expressed as median (interquartile range) if not normally distributed and as mean (95% confidence intervals) if normally distributed. Categorical variables are shown as number (percentage). Normalized gas exchange values (mL/kg/min) were plotted against the subjects' heights, and non-linear regression models were applied. The correlation coefficients were computed for each model to assess the goodness of fit. Analysis of variance was computed for the best performing regression, with a significance

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level set to P = .05. Additionally, $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ values were summarized according to 3 distinct age groups (< 0.5 y, 0.5 to 8 y, and > 8 y). The differences in $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ across age groups were assessed using one-way analysis of variance with Dunnett's multiple-comparison post-test (< 0.5 y group used as referent).

Steady-State $\dot{V}_{CO_2}$ Comparison

Minute-to-minute $\dot{V}_{CO_2}$ data were used to assess the agreement of various definitions for steady state. A total of 6 different definitions for steady state were tested based on the variation of $\dot{V}_{CO_2}$ or of both $\dot{V}_{CO_2}$ and minute ventilation over a 5-min interval for coefficient of variation (SD/mean) at 3 distinct thresholds (5%, 7.5%, and 10%). We compared the new definitions of steady state with the standard steady-state definition of a 5-min window during which $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ vary by < 10%.[9] A custom software macro was built to compute the steady-state definitions using Excel 14.0.6129.5000 (Microsoft, Redmond, Washington). Sensitivity, specificity, and the Fisher exact test were used to quantify the performance of the various $\dot{V}_{CO_2}$-based steady-state definitions and to identify the one with the highest specificity.

Results

A total of 120 indirect calorimetry tests were completed in 92 mechanically ventilated subjects (with 28 repeat tests performed) during the eligibility period. A total of 33 (27.5%) tests, which were conducted in 22 subjects, failed to exhibit steady state. Steady-state measurements were achieved in 87 (72.5%) tests, which were conducted in 70 subjects, and were included in the analysis. The cohort included 35/70 males (50.0%) with median (interquartile range) age, height, weight, and F_{IO_2} of 2.4 (0.68–13.9) y, 79.0 (57.5–118.2) cm, 12.6 (6.5–30.0) kg, and 0.4 (0.3–0.4), respectively. The median ICU stay at which point measurements were recorded was 46 (19–132) d. The median endotracheal tube leak was 4% (0–9%). A breakdown of subject diagnoses is provided in Table 1.

Table 1. Subject Diagnoses

Diagnosis	n
Medical	
Respiratory	20
Neurologic	7
Cardiac	4
Neuromuscular	3
Other	6
Surgical	
Cardiac	14
Respiratory	5
Neurosurgical	4
Neuromuscular	2
Other	5

The cohort consisted of 70 subjects: 40 subjects with a medical diagnosis and 30 subjects with a surgical diagnosis.

Description of Gas Exchange

The mean $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ were 5.4 (95% CI 0.5) and 5.9 (95% CI 0.6) mL/kg/min for the entire cohort. A statistically significant relationship between normalized gas exchange and height was observed with power regression models: $\dot{V}_{CO_2} = 115 \times (\text{height in cm})^{-0.71}$ (P < .001) (Fig. 1A) and $\dot{V}_{O_2} = 130 \times (\text{height in cm})^{-0.72}$ (P < .001) (Fig. 1B). The correlation coefficients were both 0.61 for $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$. Table 2 shows gas exchange over distinct age groups. There were 14, 44, and 27 subjects in the age groups < 0.5 y, 0.5 to < 8 y, and ≥ 8 y, respectively. There were statistically significant differences in $\dot{V}_{CO_2}$ among age groups: < 0.5 y compared with 0.5 to < 8 y (P < .05) and ≥ 8 y (P < .05). For $\dot{V}_{O_2}$, differences were noted between the < 0.5 y group and ≥ 8 y group (P < .05).

Steady-State $\dot{V}_{CO_2}$ Comparison

Minute-to-minute data from 47 subjects were utilized to compare the performance of the 6 steady-state definitions. The sensitivity, specificity, and Fisher exact test results are shown in Table 3. In this cohort, the modified steady-state definition, using a 5-min window for $\dot{V}_{CO_2}$ values (with a coefficient of variation < 5%), predicted true steady-state conditions (obtained by the standard definition) with a sensitivity of 0.84 and a specificity of 1.0 (P < .01).

Discussion

Based on observations of our current cohort, gas exchange values significantly correlated with subject height and were also related to subject age. Both $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ were produced at larger quantities per unit of body weight in younger subjects. Furthermore, the relationship between $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ values (normalized to weight) and height could be described with a simple regression model. Furthermore, if height is not immediately available, one can obtain a reasonable estimate of expected values for $\dot{V}_{CO_2}$ based on age groups. These findings provide a range of gas exchange values seen in a heterogeneous cohort and will aide in the interpretation of gas exchange values observed in the PICU. With the advent of stand-alone and ventilator-incorporated $\dot{V}_{CO_2}$ monitors, a steady-state criterion to help assess reliable measurements is necessary. Standard steady-state conditions for indirect calorimetry testing in our cohort were predicted by a new definition (5-min pe-

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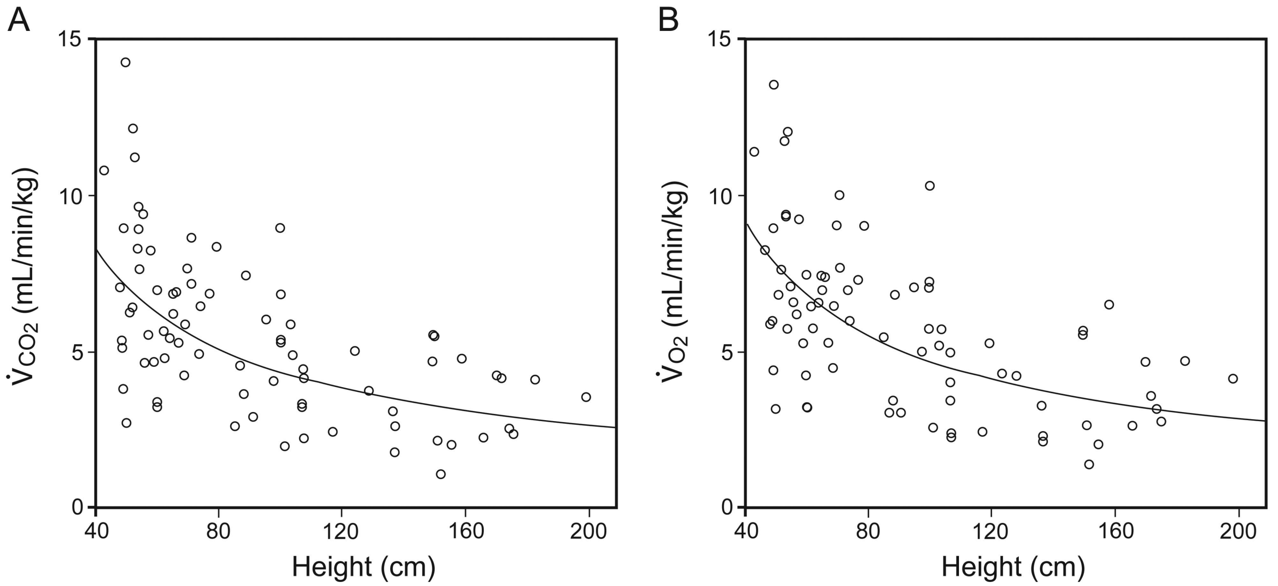

Fig. 1. Normalized gas exchange versus height. Power regression models are depicted and demonstrate the relationship between normalized gas exchange (mL/kg/min) and subject height. A: Power regression model for CO_2 elimination ($\dot{V}_{CO_2}$) = 115 × (height in cm)$^{-0.71}$ ($P < .001$). B: Power regression model for oxygen consumption ($\dot{V}_{O_2}$) = 130 × (height in cm)$^{-0.72}$ ($P < .001$).

Table 2. Normalized Gas Exchange Values Across 3 Age Groups

Age	$\dot{V}_{CO_2}$ (mL/kg/min)	$\dot{V}_{O_2}$ (mL/kg/min)
< 0.5 y (*n* = 16)	7.6 (6.0–9.2)*	8.0 (6.5–9.5)*
0.5 to < 8 y (*n* = 44)	5.8 (5.2–6.4)*	6.5 (5.6–7.4)
≥ 8 y (*n* = 27)	3.5 (3.0–4.0)	3.8 (3.3–4.3)

Values are expressed as mean (95% CI).
* Statistically significant differences in gas exchange values were observed between the denoted age group and the referent group (≥ 8 y).
$\dot{V}_{CO_2}$ = carbon dioxide elimination
$\dot{V}_{O_2}$ = oxygen consumption

Table 3. Performance of New Steady-State Definitions Compared With the Standard Definition

	Sensitivity	Specificity	*P*
$\dot{V}_{CO_2}$ coefficient of variation < 5%	0.84	1.00	< .01
$\dot{V}_{CO_2}$ and $\dot{V}_E$ coefficient of variation < 5%	0.82	1.00	< .05
$\dot{V}_{CO_2}$ coefficient of variation < 7.5%	0.98	0.67	< .01
$\dot{V}_{CO_2}$ and $\dot{V}_E$ coefficient of variation < 7.5%	0.95	0.67	< .05

The standard steady-state definition was used for comparison (carbon dioxide elimination [$\dot{V}_{CO_2}$] and minute ventilation [$\dot{V}_E$] coefficient of variation < 10% for 5 consecutive min). Results for $\dot{V}_{CO_2}$ coefficient of variation < 10% and $\dot{V}_{CO_2}$ and $\dot{V}_E$ coefficient of variation < 10% failed to discriminate between those subjects who achieved steady state and those who did not. Sensitivity, specificity, and the Fisher exact test could not be computed and are therefore omitted.

riod for $\dot{V}_{CO_2}$ with a coefficient of variation < 5%) with high specificity and sensitivity.

Subject-to-subject differences may reflect variations in metabolic rate that could be attributed to level of activity, temperature, or stimulation at the time of the test. A comparative data set (as presented in this study) may enhance the ability to discern whether values for $\dot{V}_{CO_2}$ and/or $\dot{V}_{O_2}$ at the bedside are abnormally high or low. For example, if a 10-y-old patient is observed to have a $\dot{V}_{CO_2}$ of 10.5 mL/kg/min (which corresponds to 3 times the expected value), careful assessment on the part of the clinician is likely indicated. Increases in $\dot{V}_{CO_2}$ can be attributed to changes in clinical status (increased metabolism and increased CO_2 production or changes in ventilation status). In contrast, decreases in $\dot{V}_{CO_2}$ may indicate worsening pulmonary or cardiac performance, decreased consciousness, or inappropriate decreases in ventilator support. Institutional criteria may be developed to target those patients with abnormally high or low $\dot{V}_{CO_2}$ for indirect calorimetry or other intensive assessment and monitoring.

In the present cohort, 27.5% of the tests did not achieve steady state. The recording of specific ventilator data and monitored parameters to determine those at risk for not achieving steady state was beyond the scope of our study, and therefore, we cannot say for certain why individual subjects failed to achieve steady state. However, it has

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been shown in adults that routine ICU care, ICU stay, disease state, and sedation can have a significant effect on absolute $\dot{V}_{O_2}$ and energy expenditure levels, as well as minute-to-minute variation.[12] In children, the levels of sedation and activity and the severity of disease are also associated with achievement of steady state.[13,14] More specifically, increased variation in breathing frequency, ventilator circuit leak, and inspiratory time and higher peak inspiratory levels are associated with an inability to achieve steady state in critically ill, mechanically ventilated children and may result from changes in metabolism.[10]

The steady-state definition of 5 consecutive min of $\dot{V}_{CO_2}$ data with a coefficient of variation $< 5\%$ has not previously been compared with the standard method, which uses a coefficient of variation $< 10\%$ for both $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$.[9] The ability to accurately predict steady-state conditions using $\dot{V}_{CO_2}$ alone may be useful when interpreting data from bedside CO_2 monitors. Although the other definitions for steady-state $\dot{V}_{CO_2}$ that were examined in our present study exhibited high sensitivities, the values for specificity were unacceptably low. In Table 3, it is clear that the definition incorporating minute ventilation in addition to $\dot{V}_{CO_2}$ variability is quite acceptable, with a sensitivity and specificity of 0.82 and 1.00, respectively. The incorporation of minute ventilation variability into the steady-state definition does have the theoretical advantage of making the criteria more stringent and hence more accurate in a larger cohort. $\dot{V}_{O_2}$ values contribute to the variations in metabolic state of critically ill patients; however, our study indicates that this contribution is relatively small during steady state and is likely closely related to variation in $\dot{V}_{CO_2}$.

Values for gas exchange were strongly related to subject height and age. Lindahl et al[15,16] demonstrated that a nonlinear relationship between subject size and gas exchange exists in healthy anesthetized children, but included only children less than ~25 kg in weight. The present cohort of mechanically ventilated children included a wider range of subject height and age and therefore may better reflect subjects admitted to the PICU. Our results confirm those of Lindahl et al,[15,16] as they demonstrate that shorter and younger children have increased metabolism, as reflected by $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ when indexed by size or weight, compared with older children.

Previous investigators reported values for $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ for mechanically ventilated children in their PICU. Framson et al[17] described a heterogeneous cohort of mechanically ventilated children in whom the mean $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ were 4.3 and 5.2 mL/kg/min, respectively, with a mean age of 5.2 y and a mean height of 102 cm. In a survey of 100 mechanically ventilated children, White et al[18] reported a mean $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ of 5.3 and 6.3 mL/kg/min, respectively, for a cohort with a mean age of 4.5 y and a mean height of ~97 cm. Furthermore, in a slightly younger population with a mean age of 4.2 y, Martinez et al[19] reported a mean $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ of 4.8 and 6.1 mL/kg/min, respectively, for a cohort of mechanically ventilated children recently admitted to the PICU. These findings suggest that the values from our study are largely in agreement with values reported elsewhere. However, none of the aforementioned studies reported data normalized to subject size. Our models should be tested in other data sets.

There are important limitations to this study that must be carefully considered. First, the results reflect findings from a single institution and represent a heterogeneous collection of subject sizes and disease states. However, the population does reflect a patient population that is likely to be encountered in the PICU. Second, we used a single device to make gas exchange measurements. Reports suggest that gas exchange data do not necessarily agree among approved devices, with various factors contributing to the disagreement.[20] We chose to utilize a single device to ensure that device-device agreement was not a confounding factor in our study. However, device agreement and individual accuracy are important considerations, and extrapolation of the present findings to devices other than that tested must be done with caution. Furthermore, the device used in this investigation was shown in an in vitro simulation of child metabolism to be accurate and reliable.[21] Third, the time points of data collection were not standardized among the cohort, and accordingly, subjects may have been in different phases of their disease. Because the median duration of ICU stay at which indirect calorimetry measurements were taken was 46 d, our results reflect subjects in a non-acute phase of their disease. However, because the hypermetabolic response noted in critically ill adult patients is not apparent in pediatric critically ill children, differences in stay at the time of indirect calorimetry should not have a significant effect on gas exchange values.[17] Indeed, it has been shown that critically ill, mechanically ventilated children do not tend to exhibit predictable changes in gas exchange as a function of time or disease phase in the ICU.[17] It is possible that certain diseases may exhibit different findings for gas exchange values compared with other diseases, but the number of patients required to demonstrate these differences was prohibitively large. Because it was the aim of this study to describe gas exchange values for the cohort that could yield a single tool for clinicians, we decided not to pursue further analyses based on subcategorized diseases.

Future studies should investigate the feasibility of incorporating steady-state $\dot{V}_{CO_2}$ methods into available ventilators and CO_2 monitors to ensure the quality and reliability of minute-to-minute $\dot{V}_{CO_2}$ data available at the bedside. Software applications that include steady-state criteria thresholds, detection of outliers, and trend views will allow clinical decision making based on these data.

Devices should also include onboard calculation of gas exchange normalized to body weight (mL/kg/min). With the increasing availability of bedside gas exchange monitors and monitors incorporated into ventilators, our observations will help with interpretation of the continuous data and allow them to be incorporated into clinical decision making.

Conclusions

In a cohort of mechanically ventilated children, we observed a large range of $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ measurements. Gas exchange values were strongly related to height and age; smaller and younger patients tended to produce larger amounts of CO_2 per unit of body weight. A new steady-state definition of a 5-min period for $\dot{V}_{CO_2}$ with a coefficient of variation $< 5\%$ was in reasonable agreement with the standard definition and may be used to determine the validity of continuous $\dot{V}_{CO_2}$ measurements at the bedside. Our observations may facilitate greater utility of $\dot{V}_{CO_2}$ at the bedside in the PICU and thereby extend the benefits of metabolic monitoring to a larger group of patients when indirect calorimetry is not available.

REFERENCES

1. Mehta NM, Compher C. ASPEN Clinical Guidelines: nutrition support of the critically ill child. JPEN J Parenter Enteral Nutr 2009; 33(3):260-276.
2. Romero PV, Lucangelo U, Lopez Aguilar J, Fernandez R, Blanch L. Physiologically based indices of volumetric capnography in patients receiving mechanical ventilation. Eur Respir J. 1997;10(6):1309-1315.
3. Russell GB, Graybeal JM. Reliability of the arterial to end-tidal carbon dioxide gradient in mechanically ventilated patients with multisystem trauma. J Trauma 1994;36(3):317-322.
4. Brandi LS, Bertolini R, Santini L, Cavani S. Effects of ventilator resetting on indirect calorimetry measurement in the critically ill surgical patient. Crit Care Med 1999;27(3):531-539.
5. Sullivan KJ, Kissoon N, Goodwin SR. End-tidal carbon dioxide monitoring in pediatric emergencies. Pediatr Emerg Care 2005;21(5): 327-332; quiz 333-325.
6. Stuart-Andrews CR, Peyton P, Robinson GJ, Terry D, O'Connor B, Van der Herten C, Lithgow B. In vivo validation of the M-COVX metabolic monitor in patients under anaesthesia. Anaesth Intensive Care 2007;35(3):398-405.
7. Mehta NM, Bechard LJ, Dolan M, Ariagno K, Jiang H, Duggan C. Energy imbalance and the risk of overfeeding in critically ill children. Pediatr Crit Care Med 2011;12(4):398-405.
8. Petros S, Engelmann L. Validity of an abbreviated indirect calorimetry protocol for measurement of resting energy expenditure in mechanically ventilated and spontaneously breathing critically ill patients. Intensive Care Med 2001;27(7):1164-1168.
9. McClave SA, Spain DA, Skolnick JL, Lowen CC, Kieber MJ, Wickerham PS, et al. Achievement of steady state optimizes results when performing indirect calorimetry. JPEN J Parenter Enteral Nutr 2003;27(1):16-20.
10. Smallwood CD, Mehta NM. Accuracy of abbreviated indirect calorimetry protocols for energy expenditure measurement in critically ill children. JPEN J Parenter Enteral Nutr 2012;36(6):693-699.
11. Mehta NM, Smallwood CD, Joosten KF, Hulst JM, Tasker RC, Duggan CP. Accuracy of a simplified equation for energy expenditure based on bedside volumetric carbon dioxide elimination measurement—a two-center study. Clin Nutr 2014 [Epub ahead of print] doi: 10.1016/j.clnu.2014.02.008.
12. Walsh TS. Recent advances in gas exchange measurement in intensive care patients. Br J Anaesth 2003;91(1):120-131.
13. Joosten KF, Verhoeven JJ, Hop WC, Hazelzet JA. Indirect calorimetry in mechanically ventilated infants and children: accuracy of total daily energy expenditure with 2 hour measurements. Clin Nutr 1999; 18(3):149-152.
14. White MS, Shepherd RW, McEniery JA. Energy expenditure measurements in ventilated critically ill children: within- and between-day variability. JPEN J Parenter Enteral Nutr 1999;23(5):300-304.
15. Lindahl SG, Offord KP, Johannesson GP, Meyer DM, Hatch DJ. Carbon dioxide elimination in anaesthetized children. Can J Anaesth. 1989;36(2):113-119.
16. Lindahl SG. Oxygen consumption and carbon dioxide elimination in infants and children during anaesthesia and surgery. Br J Anaesth. 1989;62(1):70-76.
17. Framson CM, LeLeiko NS, Dallal GE, Roubenoff R, Snelling LK, Dwyer JT. Energy expenditure in critically ill children. Pediatr Crit Care Med 2007;8(3):264-267.
18. White MS, Shepherd RW, McEniery JA. Energy expenditure in 100 ventilated, critically ill children: improving the accuracy of predictive equations. Crit Care Med 2000;28(7):2307-2312.
19. Vazquez Martinez JL, Martinez-Romillo PD, Diez Sebastian J, Ruza Tarrio F. Predicted versus measured energy expenditure by continuous, online indirect calorimetry in ventilated, critically ill children during the early postinjury period. Pediatr Crit Care Med 2004;5(1): 19-27.
20. Smallwood CD, Mehta NM. Gas exchange measurement during pediatric mechanical ventilation–agreement between gas sampling at the airway and the ventilator exhaust. Clin Nutr 2013;32(6):988-992.
21. Wines KN, Rzepecki AK, Andrews AL, Dechert RE. Validation of the V_{max} metabolic cart in a simulated pediatric model. JPEN J Parenter Enteral Nutr 2014 [Epub ahead of print] doi: 10.1177/0148607114527619.