End-Tidal and Arterial Carbon Dioxide Measurements Correlate Across All Levels of Physiologic Dead Space

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BACKGROUND: End-tidal carbon dioxide (P_{ETCO_2}) is a surrogate, noninvasive measurement of arterial carbon dioxide (P_{aCO_2}), but the clinical applicability of P_{ETCO_2} in the intensive care unit remains unclear. Available research on the relationship between P_{ETCO_2} and P_{aCO_2} has not taken a detailed assessment of physiologic dead space into consideration. We hypothesized that P_{ETCO_2} would reliably predict P_{aCO_2} across all levels of physiologic dead space, provided that the expected P_{ETCO_2}-P_{aCO_2} difference is considered. METHODS: Fifty-six mechanically ventilated pediatric patients (0–17 y old, mean weight 19.5 ± 24.5 kg) were monitored with volumetric capnography. For every arterial blood gas measurement during routine care, we measured P_{ETCO_2} and calculated the ratio of dead space to tidal volume (V_D/V_T). We assessed the P_{ETCO_2}-P_{aCO_2} relationship with Pearson's correlation coefficient, in 4 V_D/V_T ranges. RESULTS: V_D/V_T was ≤ 0.40 for 125 measurements (25%), 0.41–0.55 for 160 measurements (32%), 0.56–0.70 for 154 measurements (31%), and > 0.7 for 54 measurements (11%). The correlation coefficients between P_{ETCO_2} and P_{aCO_2} were 0.95 (mean difference 0.3 ± 2.1 mm Hg) for V_D/V_T ≤ 0.40, 0.88 (mean difference 5.9 ± 4.3 mm Hg) for V_D/V_T 0.41–0.55, 0.86 (mean difference 13.6 ± 5.2 mm Hg) for V_D/V_T 0.56–0.70, and 0.78 (mean difference 17.8 ± 6.7 mm Hg) for V_D/V_T > 0.7. CONCLUSIONS: There were strong correlations between P_{ETCO_2} and P_{aCO_2} in all the V_D/V_T ranges. The P_{ETCO_2}-P_{aCO_2} difference increased predictably with increasing V_D/V_T. *Key words: capnography; artificial respiration; blood gas analysis; pediatric; infant; mechanical ventilation; carbon dioxide*. [Respir Care 2010;55(3):288–293. © 2010 Daedalus Enterprises]

Introduction

Capnography is a useful monitoring tool during mechanical ventilation and is the standard of care for confirming endotracheal tube placement[1-5] and monitoring in the operating room setting.[6-8] Capnography is also useful for monitoring the integrity of the ventilator circuit for early detection of mishaps such as inadvertent extubation.[9-11]

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There is less agreement about the utility of continuous capnography for ventilated intensive care unit (ICU) patients.[12] Advocates of capnography believe that end-tidal

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carbon dioxide (P_{ETCO_2}) may be used as a surrogate for arterial carbon dioxide (P_{aCO_2}), which would provide a quick and noninvasive assessment of the adequacy of ventilation. Critics of capnography reference multiple studies that conclude that P_{ETCO_2} and P_{aCO_2} do not reliably correlate in some clinical situations.[13-19] However, many of these clinical situations involve patients with substantially elevated physiologic dead space. The analyses used in those studies differed markedly and failed to consider physiologic dead space and/or its effect on the relationship (ie, expected gradient) between P_{aCO_2} and P_{ETCO_2} as dead space increases.

Physiologic dead-space ventilation is the sum of anatomical dead space from the conducting airways and alveolar dead space from disease processes and/or therapies. The difference between P_{ETCO_2} and P_{aCO_2} is directly proportional to the degree of physiologic dead space.[20-22] Although the alveolar CO_2 concentration is typically slightly greater than that of arterial blood, P_{ETCO_2} is normally 2–5 mm Hg lower than P_{aCO_2},[23] due to mixing of CO_2-containing alveolar gas with exhaled gas devoid of carbon dioxide from the anatomical dead space. In a patient with lung disease the addition of alveolar dead space further dilutes P_{ETCO_2} relative to P_{aCO_2}. The normal ratio of physiologic dead space to tidal volume (V_D/V_T) is 0.20–0.35.[24] The V_D/V_T in adult patients with acute lung injury is generally 0.40–0.55, and in patients with acute respiratory distress syndrome a substantially elevated V_D/V_T is associated with higher mortality.[25]

The objective of this physiology-based study was to evaluate the relationship between P_{ETCO_2} and P_{aCO_2} across a wide range of V_D/V_T values. We hypothesized that P_{ETCO_2} reliably predicts P_{aCO_2} across all levels of physiologic dead space, as long as the increased P_{ETCO_2}-P_{aCO_2} difference predicted by a high physiologic dead space is considered. Despite the fact that multiple earlier studies have compared P_{ETCO_2} and P_{aCO_2}, to our knowledge no previous study has examined the effect of changes in physiologic dead space on the P_{ETCO_2} and P_{aCO_2} relationship across a wide range of V_D/V_T ratios (from minimal to severe lung disease) in a diverse group of mechanically ventilated pediatric patients.

Methods

Subjects

This study is a retrospective cross-sectional analysis of data from a previous study at this institution (Donna S Hamel RRT FAARC and Ira M Cheifetz MD FAARC, personal communication, 2009). In the parent study, all children (ie, < 18 years of age) admitted to the pediatric ICU at Duke Children's Hospital with an anticipated need for mechanical ventilation of at least 24 hours and a functional indwelling arterial catheter were eligible for enrollment (Table 1). Enrollment occurred between November 2001 and June 2005. The study was approved by the Duke Medical Center institutional review board. Written informed consent was obtained from at least one parent or legal guardian prior to enrollment. Exclusion criteria included tracheostomy, need for high-frequency ventilation or extracorporeal life support, limitations on life support, baseline long-term invasive or noninvasive respiratory support, and intubation for known upper-airway obstruction.

Table 1. Subjects

	(*n* = 56)	%
Age (y)		
< 1	25	45
1–6	14	25
≥ 7	17	30
Primary Reason for Admission†		
Pulmonary	11	20
Cardiac	21	38
Bone marrow transplantation	4	7
Non-cardiac postoperative	7	13
Neurologic	9	16
Other	4	7

† Percentages do not sum to 100 because of rounding.

Ventilator Management

The mechanical ventilators (Avea, Viasys Healthcare, Yorba Linda, California, or Servo 300, Siemens, Solna, Sweden) were equipped with basic airway graphic monitors and were calibrated as per the manufacturer's recommendations. Ventilator management was directed by a standard pediatric ICU protocol. Of note, specific capnography parameters were not incorporated into the ventilator management protocol. Arterial blood gas analysis and chest radiographs were obtained and pharmacologic sedation administered as per standard clinical practice. A heterogeneous group of mechanically ventilated pediatric ICU patients was monitored with volumetric capnography (NICO Monitor, Philips-Respironics, Wallingford, Connecticut) from the initiation of mechanical ventilation in our pediatric ICU until extubation.

Data Collection

For every arterial blood gas obtained during routine medical care, P_{ETCO_2} and mixed exhaled carbon dioxide ($P_{\bar{E}CO_2}$) values were electronically collected at the proximal end of the endotracheal tube. The data acquisition rate of the NICO monitor is 100 Hz. The monitor continuously

checks factory calibration values to assure accuracy and alerts the clinician if there is a calibration error. V_D/V_T was calculated with the Enghoff modification[26] of the Bohr equation:

$$V_D/V_T = (P_{aCO_2} - P_{\bar{E}CO_2})/P_{aCO_2}$$

Corresponding arterial blood gas values were recorded.

Statistical Analysis

The relationship between P_{ETCO_2} and P_{aCO_2} within 4 V_D/V_T ranges (≤ 0.40, 0.41–0.55, 0.56–0.70, and > 0.7) was assessed with Pearson's correlation coefficient. We also calculated the mean P_{ETCO_2}-P_{aCO_2} difference within each V_D/V_T range. We used multivariable linear regression models to explore the relationships between all the dependent and independent variables and created Bland-Altman plots for each V_D/V_T range to further evaluate the agreement between P_{ETCO_2} and P_{aCO_2}. Analyses were done with statistics software (Stata 9, StataCorp, College Station, Texas).

Results

From a heterogeneous group of 56 mechanically ventilated pediatric patients (age range 0–17 y, mean weight 19.5 ± 24.5 kg), we obtained 493 data points for analysis. V_D/V_T was ≤ to 0.40 in 125 measurements (25%), 0.41–0.55 in 160 measurements (32%), 0.56–0.70 in 154 measurements (31%), and > 0.7 in 54 measurements (11%).

For $V_D/V_T \leq 0.40$ the correlation coefficient between P_{ETCO_2} and P_{aCO_2} was 0.95 and the mean P_{ETCO_2}-P_{aCO_2} difference was 0.3 ± 2.1 mm Hg. For V_D/V_T 0.41–0.55 the correlation coefficient was 0.88 and the mean P_{ETCO_2}-P_{aCO_2} difference was 5.9 ± 4.3 mm Hg. For V_D/V_T 0.56–0.70 the correlation coefficient was 0.86 and the mean P_{ETCO_2}-P_{aCO_2} difference was 13.6 ± 5.2 mm Hg. For $V_D/V_T > 0.7$ the correlation coefficient was 0.78 and the mean P_{ETCO_2}-P_{aCO_2} difference was 17.8 ± 6.7 mm Hg (Table 2).

For each V_D/V_T range, we used simple linear regression with weighted least squares to test the null hypothesis of no significant relationship between P_{ETCO_2} and P_{aCO_2}. In each V_D/V_T range there was a significant positive linear relationship between P_{ETCO_2} and P_{aCO_2} (Fig. 1).

Table 2. Correlation of P_{ETCO_2} and P_{aCO_2}

	V_D/V_T Range			
	≤ 0.40	0.41–0.55	0.56–0.70	> 0.7
Data points	125	160	154	54
Percent of total*	25	32	31	11
Correlation coefficient (ρ)	0.95	0.88	0.86	0.78
P_{ETCO_2}-P_{aCO_2} difference (mean ± SD mm Hg)	0.3 ± 2.1	5.9 ± 4.3	13.6 ± 5.2	17.8 ± 6.7

* Percentages do not sum to 100 because of rounding.
P_{ETCO_2} = end-tidal carbon dioxide
V_D = dead-space volume
V_T = tidal volume

Discussion

Capnography is accepted by some as an indispensable tool for mechanical ventilation to reduce the frequency of blood gas measurements in many clinical situations. However, there remains substantial debate as to whether capnography is useful as a continuous monitoring technique for mechanically ventilated patients. The goal of this study was to provide physiologic data to help clarify the relationship between P_{ETCO_2} and P_{aCO_2} in a heterogeneous pediatric ICU population.

There are potential benefits to the continuous monitoring of exhaled CO_2 in an ICU. Not only can continuous assessment of the patient's ventilatory status allow for early warning in case of a loss of integrity of the ventilator circuit or inadvertent extubation, it may help to optimize mechanical ventilation and shorten weaning time.[26] In addition, capnography can be a useful early indicator of changes in cardiopulmonary status due to alterations in pulmonary blood flow, respiratory effort, effective minute ventilation, and/or respiratory compliance.[27]

Previous reports suggest that P_{ETCO_2} may not be a reliable surrogate for measured arterial CO_2, which may cast doubt on the utility of capnography as a continuous monitor.[13-19] However, those studies generally did not include a comprehensive statistical analysis accounting for differences in physiologic dead-space ventilation and the resulting difference between P_{ETCO_2} and P_{aCO_2}. For example, the pediatric study by McDonald et al[19] in 2002 found an overall moderately strong correlation ($r^2 = 0.716$) between P_{aCO_2} and P_{ETCO_2} for all included patients, but that substantial lung disease (ie, ratio of P_{aO_2} to fraction of inspired oxygen < 200 mm Hg) negatively affected the correlation. However, the degree of physiologic dead space was not included in the analysis, which makes the results difficult to apply in the clinical setting. In contrast, our study incorporates the effect of physiologic dead space in patients with substantial lung disease.

Increased physiologic dead space lowers P_{ETCO_2} relative to P_{aCO_2} because of the mixing of gas from poorly perfused lung regions (devoid of CO_2) with that from well perfused areas, thus resulting in a larger difference between the 2 measurements. In this study we provide evidence that physiologic dead-space ventilation is a major factor in determining the relationship between P_{ETCO_2} and P_{aCO_2}. In patients with a $V_D/V_T \leq 0.40$ there was an excellent

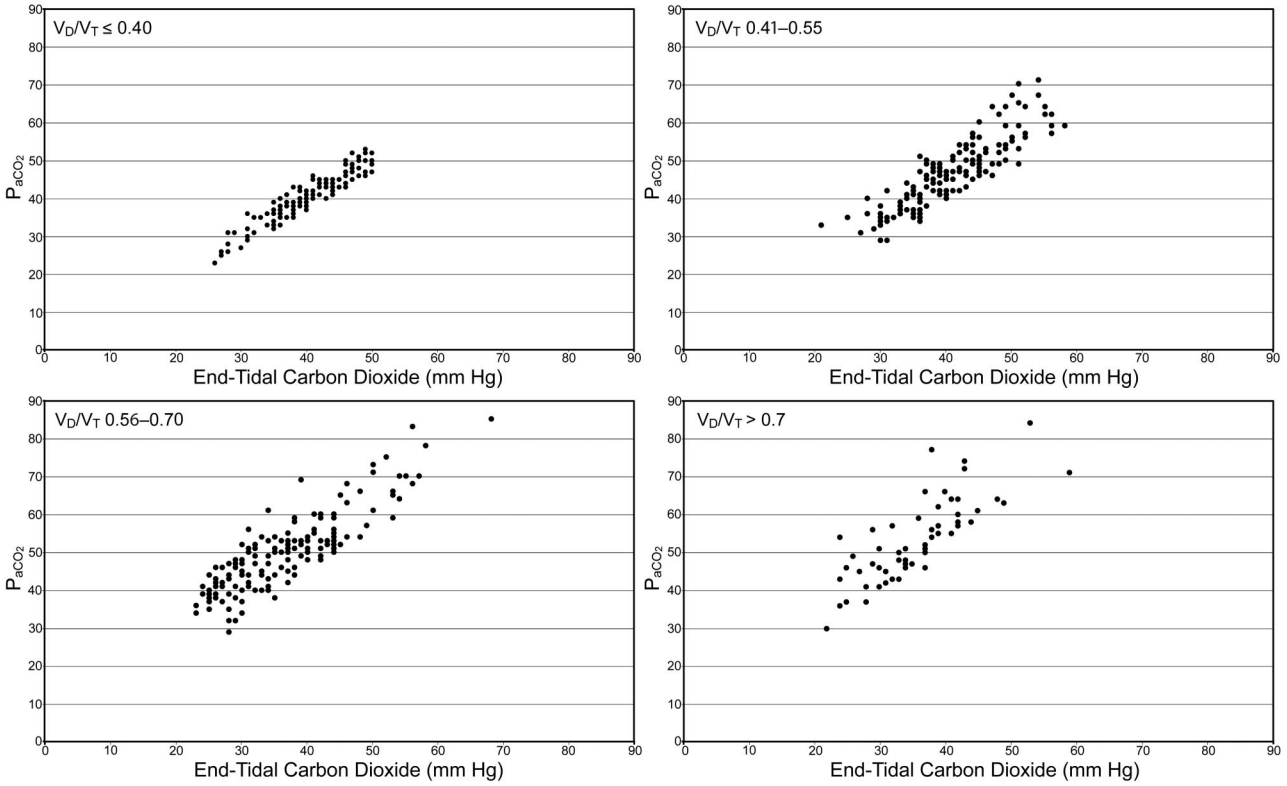

Fig. 1. End-tidal carbon dioxide versus arterial carbon dioxide in 4 ranges of physiologic dead space (ratio of dead space to tidal volume [V_D/V_T]). When V_D/V_T was ≤ 0.40 the correlation was very strong ($\rho = 0.95$). In the V_D/V_T range 0.41–0.55, $\rho = 0.88$. In the V_D/V_T range 0.56–0.70, $\rho = 0.86$. When V_D/V_T was > 0.7, $\rho = 0.78$. Thus, as V_D/V_T increases, the correlation coefficient decreases but remains moderately strong.

correlation ($\rho = 0.95$) between P_{ETCO_2} and P_{aCO_2}. Though the strength of the association diminishes slightly as V_D/V_T increases, the correlation remains strong ($\rho = 0.86$) even at V_D/V_T of 0.56–0.70, and moderately strong ($\rho = 0.78$) at $V_D/V_T > 0.7$. Thus, P_{ETCO_2} appears to be a useful indicator of P_{aCO_2}, even in patients with substantial lung disease, provided that the expected increase in the P_{ETCO_2}-P_{aCO_2} difference (from an average of 0.3 mm Hg at low V_D/V_T to an average of 18 mm Hg at high V_D/V_T) is taken into consideration (see Fig. 1).

For the purposes of the clinical application of our results, it is important to note that correlation is not the same as equality. Physiologically, as described above, the difference between P_{ETCO_2} and P_{aCO_2} is expected to increase at higher V_D/V_T. The decrease in the correlation coefficient between P_{ETCO_2} and P_{aCO_2} at high V_D/V_T is not due to that increased difference, but rather to the slightly increased variability of that difference at higher V_D/V_T. This is an important distinction, because the moderately strong correlation coefficient at high V_D/V_T values indicates that the expected larger difference between P_{ETCO_2} and P_{aCO_2} remains fairly predictable, despite the increased dead-space ventilation.

This distinction is very important in interpreting the Bland-Altman plots in Figure 2. Bland-Altman plots are a visual assessment of agreement between 2 methods of measurement, and demonstrate "good agreement" only when the difference between the 2 methods is consistent across all measurements. In a situation in which the difference between the 2 measurements is expected to change based on a third variable (in this case, V_D/V_T), the Bland-Altman plots lose importance. These plots do not take into account the expected change in the P_{ETCO_2}-P_{aCO_2} difference seen with increasing physiologic dead space, except insofar as we have divided the data set into 4 specific V_D/V_T ranges. Thus, it is impossible to tell whether the variation seen in these plots is due to variation in physiologic dead space within each subset or to unreliability of P_{ETCO_2} as a surrogate measure. We have included these plots for completeness, but they should be interpreted with an understanding of their shortcomings with regard to these data.

From a purely statistical standpoint, the best method to compare P_{ETCO_2} and P_{aCO_2} is a multiple linear regression equation using P_{ETCO_2} and V_D/V_T to predict P_{aCO_2}. From a clinical standpoint, however, we feel that this would not be practical. It is for that reason that we have grouped our

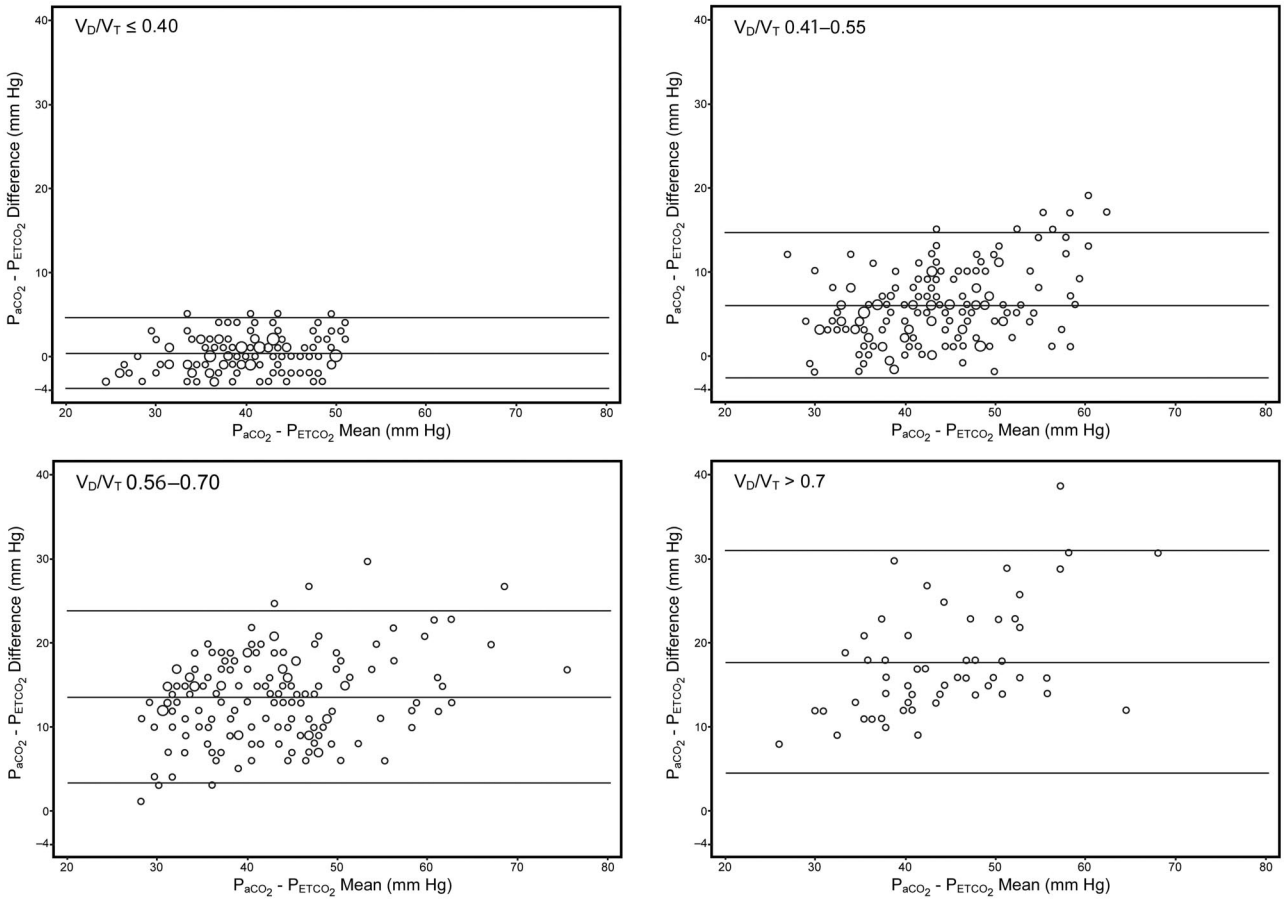

Fig. 2. Bland-Altman plot of end-tidal carbon dioxide (P_{ETCO_2}) versus P_{aCO_2}. These plots do not take into account the expected change in the P_{ETCO_2}-P_{aCO_2} difference with increasing physiologic dead space, so it is impossible to tell whether the variation seen in these plots is due to the predicted variation in physiologic dead space within each subset, or to unreliability of P_{ETCO_2} as a surrogate measure.

data into V_D/V_T ranges corresponding to normal, mildly elevated, moderately elevated, and severely elevated physiologic dead space. At the bedside it is easier to consider into what category of physiologic dead space a patient falls than it is to calculate a predicted P_{aCO_2} value using a derived equation.

Continuous P_{ETCO_2} monitoring in the pediatric ICU may help clinicians to more closely monitor mechanically ventilated infants and children. Our data support the view that P_{ETCO_2} does closely trend with P_{aCO_2}, potentially allowing for a reduction in the number of arterial blood gas analyses. At low dead-space values, P_{ETCO_2} closely matches P_{aCO_2}. As dead space increases, the trend between P_{ETCO_2} and P_{aCO_2} remains reliable in most patients; however, the difference between these values does increase, as physiology predicts.

Limitations

A key limitation of our study is the assumption that V_D/V_T is stable between blood gas analyses over time for an individual patient. Data on the stability of V_D/V_T and the P_{aCO_2}-P_{ETCO_2} difference over time in individual patients were not available for this study. As clinical status changes, dead space may change as well, and the relationship between P_{aCO_2} and P_{ETCO_2} becomes less predictable. Thus, the clinician should obtain periodic blood gas analyses, especially if there are important changes in the patient's overall pulmonary status, to reassess the correlation between P_{aCO_2} and P_{ETCO_2}.

The increased variation in the P_{aCO_2}-P_{ETCO_2} difference at highly elevated physiologic dead space must be noted. The data analysis does not allow us to determine whether the variation in the relationship at severely elevated physiologic dead space is present in individual patients. We expect there is less variation in the P_{aCO_2}-P_{ETCO_2} difference in individual patients, even at severely elevated V_D/V_T, and, thus, the increased variability of the P_{aCO_2}-P_{ETCO_2} difference in our data set is at least partly a function of combining data from different patients. Additionally, some of the variation in the highest V_D/V_T subgroup might be due to the slightly wider distribution of V_D/V_T (ie, the

largest grouping beyond the normal range). Since the P_{aCO_2}-P_{ETCO_2} difference should increase as V_D/V_T increases, a larger range of differences is expected given the larger V_D/V_T range. Despite these caveats, it is likely that P_{ETCO_2} does lose some capacity to predict P_{aCO_2} in patients with the most severe lung disease and, thus, the most severely elevated physiologic dead space—a fact that must be taken into consideration clinically.

Application of these results in the clinical setting may require additional clinician training and equipment. The capnography monitor we use automatically calculates V_D/V_T when blood gas data are entered, which obviates calculation by the clinician. In addition, the capnography sensors measure both gas flow and CO_2 concentration, so that only one endotracheal tube attachment is required.

The results of this study should, theoretically, allow fewer blood gas analyses per patient and enable more efficient management of the mechanical ventilator via continuous capnography. However, proof of this speculation is beyond the scope of this physiology-based study.

Conclusions

We found moderate to strong positive linear correlation coefficients between P_{ETCO_2} and P_{aCO_2} for all 4 V_D/V_T ranges, although the strength of the correlation decreased slightly as V_D/V_T increased. As expected physiologically, the absolute difference between P_{ETCO_2} and P_{aCO_2} consistently increased with increasing V_D/V_T.

REFERENCES

1. American Heart Association. 2005 American Heart Association (AHA) guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care (ECC) of pediatric and neonatal patients: pediatric advanced life support. Pediatrics 2006;117(5):e1005-e1028.
2. Birmingham PK, Cheney FW, Ward RJ. Esophageal intubation: a review of detection techniques. Anesth Analg 1986;65(8):886-891.
3. Knapp S, Kofler J, Stoiser B, Thalhammer F, Burgmann H, Posch M, et al. The assessment of four different methods to verify tracheal tube placement in the critical care setting. Anesth Analg 1999;88(4):766-770.
4. Roberts WA, Maniscalco WM, Cohen AR, Litman RS, Chhibber A. The use of capnography for recognition of esophageal intubation in the neonatal intensive care unit. Pediatr Pulmonol 1995;19(5):262-268.
5. Kannan S, Manji M. Survey of use of end-tidal carbon dioxide for confirming tracheal tube placement in intensive care units in the UK. Anaesthesia 2003;58(5):476-479.
6. Eichhorn JH, Cooper JB, Cullen DJ, Maier WR, Philip JH, Seeman RG. Standards for patient monitoring during anesthesia at Harvard Medical School. JAMA 1986;256(8):1017-1020.
7. Tinker JH, Dull DL, Caplan RA, Ward RJ, Cheney FW. Role of monitoring devices in prevention of anesthetic mishaps: a closed claims analysis. Anesthesiology 1989;71(4):541-546.
8. Williamson JA, Webb RK, Cockings J, Morgan C. The Australian Incident Monitoring Study. The capnograph: applications and limitations—an analysis of 2000 incident reports. Anaesth Intensive Care 1993;21(5):551-557.
9. Murray IP, Modell JH. Early detection of endotracheal tube accidents by monitoring carbon dioxide concentration in respiratory gas. Anesthesiology 1983;59(4):344-346.
10. Poirier MP, Gonzalez Del-Rey JA, McAneney CM, DiGiulio GA. Utility of monitoring capnography, pulse oximetry, and vital signs in the detection of airway mishaps: a hyperoxemic animal model. Am J Emerg Med 1998;16(4):350-352.
11. Ahrens T, Sona C. Capnography application in acute and critical care. AACN Clin Issues 2003;14(2):123-132.
12. Cheifetz IM, Myers TR. Should every mechanically ventilated patient be monitored with capnography from intubation to extubation? Respir Care 2007;52(4):423-438.
13. Grenier B, Verchere E, Mesli A, Dubreuil M, Siao D, Vandendriessche M, et al. Capnography monitoring during neurosurgery: reliability in relation to various intraoperative positions. Anesth Analg 1999;88(1):43-48.
14. Short JA, Paris ST, Booker PD, Fletcher R. Arterial to end-tidal carbon dioxide tension difference in children with congenital heart disease. Br J Anaesth 2001;86(3):349-353.
15. 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.
16. Kerr ME, Zempsky J, Sereika S, Orndoff P, Rudy EB. Relationship between arterial carbon dioxide and end-tidal carbon dioxide in mechanically ventilated adults with severe head trauma. Crit Care Med 1996;24(5):785-790.
17. Tobias JD, Meyer DJ. Noninvasive monitoring of carbon dioxide during respiratory failure in toddlers and infants: end-tidal versus transcutaneous carbon dioxide. Anesth Analg 1997;85(1):55-58.
18. Berkenbosch JW, Lam J, Burd RS, Tobias JD. Noninvasive monitoring of carbon dioxide during mechanical ventilation in older children: end-tidal versus transcutaneous techniques. Anesth Analg 2001;92(6):1427-1431.
19. McDonald MJ, Montgomery VL, Cerrito PB, Parrish CJ, Boland KA, Sullivan JE. Comparison of end-tidal CO_2 and P_{aCO2} in children receiving mechanical ventilation. Pediatr Crit Care Med 2002;3(3):244-249.
20. Yamanaka MK, Sue DY. Comparison of arterial-end tidal P_{CO2} difference and dead space/tidal volume ratio in respiratory failure. Chest 1987;92(5):832-835.
21. Burrows FA. Physiologic dead space, venous admixture, and the arterial to end-tidal carbon dioxide difference in infants and children undergoing cardiac surgery. Anesthesiology 1989;70(2):219-225.
22. Fletcher R. The arterial-end-tidal CO_2 difference during cardiothoracic surgery. J Cardiothorac Anesth 1990;4(1):105-117.
23. Sullivan KJ, Kissoon N, Goodwin SR. End-tidal carbon dioxide monitoring in pediatric emergencies. Pediatr Emerg Care 2005;21(5):327-332.
24. Sun XG, Hansen JE, Garatachea N, Storer TW, Wasserman K. Ventilatory efficiency during exercise in healthy subjects. Am J Respir Crit Care Med 2002;166(11):1443-1448.
25. Kallet RH, Alonso JA, Pittet J, Matthay MA. Prognostic value of the pulmonary dead-space fraction during the first 6 days of acute respiratory distress syndrome. Respir Care 2004;49(9):1008-1014.
26. Enghoff H. Volumen inefficax: Bemerkungen zur frage des schadlichen raumes. Upsala Lakareforen Forh 1938;44:191-218. *Article in German.*
27. Taskar V, John J, Larsson A, Wetterberg T, Jonson B. Dynamics of carbon dioxide elimination following ventilator resetting. Chest 1995;108(1):196-202.