Assessment of Bohr and Enghoff Dead Space Equations in Mechanically Ventilated Children

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BACKGROUND: Recent findings suggest that using alveolar P_{CO_2} (P_{ACO_2}) estimated by volumetric capnography in the Bohr equation instead of P_{aCO_2} (Enghoff modification) could be appropriate for the calculation of physiological dead space to tidal volume ratio ($V_D/V_{T\ Bohr}$ and $V_D/V_{T\ Enghoff}$, respectively). We aimed to describe the relationship between these 2 measurements in mechanically ventilated children and their significance in cases of ARDS. METHODS: From June 2013 to December 2013, mechanically ventilated children with various respiratory conditions were included in this study. Demographic data, medical history, and ventilatory parameters were recorded. Volumetric capnography indices (NM3 monitor) were obtained over a period of 5 min preceding a blood sample. Bohr's and Enghoff's dead space, S2 and S3 slopes, and the S2/S3 ratio were calculated breath-by-breath using dedicated software (FlowTool). This study was approved by Ste-Justine research ethics review board. RESULTS: Thirty-four subjects were analyzed. Mean $V_D/V_{T\ Bohr}$ was 0.39 ± 0.12, and $V_D/V_{T\ Enghoff}$ was 0.47 ± 0.13 (P = .02). The difference between $V_D/V_{T\ Bohr}$ and $V_D/V_{T\ Enghoff}$ was correlated with P_{aO_2}/F_{IO_2} and with S2/S3. In subjects without lung disease ($P_{aO_2}/F_{IO_2} \geq 300$), mean $V_D/V_{T\ Bohr}$ was 0.36 ± 0.11, and $V_D/V_{T\ Enghoff}$ was 0.39 ± 0.11 (P = .056). Two children with status asthmaticus had a major difference between $V_D/V_{T\ Bohr}$ and $V_D/V_{T\ Enghoff}$ in the absence of a low P_{aO_2}/F_{IO_2}. CONCLUSIONS: This study suggests that $V_D/V_{T\ Bohr}$ and $V_D/V_{T\ Enghoff}$ are not different when there is no hypoxemia ($P_{aO_2}/F_{IO_2} > 300$) except in the case of status asthmaticus. In subjects with a low P_{aO_2}/F_{IO_2}, the method to measure V_D/V_T must be reported, and results cannot be easily compared if the measurement methods are not the same. *Key words: respiratory physiological concepts; mechanical ventilation; pediatric ICU; ventilation-perfusion ratio; capnography; ARDS.* [Respir Care 2017;62(4):468–474. © 2017 Daedalus Enterprises]

Introduction

Lung physiologic dead space (V_D) is defined as the wasted tidal volume during respiration (ie, the volume remaining in the conducting airways [anatomical dead space] and in poorly perfused and non-perfused alveoli [alveolar dead space] that are not participating in gas exchange). Employing the law of mass conservation, Bohr proposed a formula using alveolar P_{CO_2} (P_{ACO_2}) to esti-

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mate physiologic dead space, expressed as a ratio of dead space volume (V_D) to tidal volume (V_T).[1] Later, Enghoff proposed a simplification of Bohr's formulae to calculate the physiologic dead space ratio at the bedside using arterial P_{CO_2} (P_{aCO_2}) instead of P_{ACO_2}.[1] Currently, physiologic dead space measurement is used by clinicians in the management of mechanical ventilation because CO_2 removal is inversely proportional to V_D/V_T, and V_D fluctuates considerably, depending upon the severity of lung disease.[2] The dead space on V_T (V_D/V_T) ratio informs caregivers as to the effect of therapeutic procedures such as prone positioning,[3] surfactant administration,[4] or lung recruitment maneuvers[5,6] and provides information useful in prognostication, depending on the severity of lung disease in adults and children.[7,8]

Recent findings suggest that using P_{ACO_2} estimated by volumetric capnography can be appropriate to calculate the Bohr physiological dead space/tidal volume ratio ($V_D/V_{T\ Bohr}$). P_{aCO_2} (Enghoff modification) can be used as well ($V_D/V_{T\ Enghoff}$). Especially in the case of lung injury, comparison of $V_D/V_{T\ Bohr}$ and $V_D/V_{T\ Enghoff}$ may have complementary physiological meaning, as recently suggested[9,10]: Bohr's equation estimates the true dead space (ie, high ventilation/perfusion [$\dot{V}/\dot{Q}$] units plus anatomical and mechanical dead space), whereas Enghoff's estimates not only the dead space but also the shunting and low $\dot{V}/\dot{Q}$ regions of the lungs (Fig. 1). We conducted a prospective observational study to compare Bohr's and Enghoff's measurements of V_D/V_T in mechanically ventilated children, and we hypothesized that a difference between these 2 measurements may be observed in cases of lung injury. If confirmed, a large difference between $V_D/V_{T\ Bohr}$ and $V_D/V_{T\ Enghoff}$ would indicate significant lung heterogeneity with regard to the degree of shunt and low $\dot{V}/\dot{Q}$ regions in the lungs.

QUICK LOOK

Current knowledge

Monitoring dead space ratio in critically ill patients is of prognostic value and may help to manage ventilator settings in patients with ARDS. Recent studies on the estimation of dead space using volumetric capnography validate a noninvasive estimation of alveolar CO_2 pressure (P_{ACO_2}) to calculate Bohr dead space, whereas most studies have used physiologic dead space (Enghoff dead space, replacing P_{ACO_2} with P_{aCO_2}).

What this paper contributes to our knowledge

Major variations existed between Bohr and Enghoff estimations of deadspace in cases of hypoxemic lung injury. The use of volumetric capnography explains these differences. The method of deadspace estimation should always be detailed to allow interpretation based on these findings.

Methods

Subjects

All patients admitted to the Pediatric ICU of Sainte-Justine Hospital (Montreal, Canada), <18 y old, mechanically ventilated with an endotracheal tube for ≥6 h were eligible for the study. They were included if they had an arterial line and a blood gas scheduled. Exclusion criteria were: gestational age <36 weeks, hemodynamic instability (fluid administration or increasing use of catecholamines in the last hour or serum lactate >2.2 mmol/L), high-frequency oscillatory ventilation, extracorporeal membrane oxygenation, air leak around the endotracheal tube >20%, cyanotic heart disease, primary pulmonary hypertension, palliative care, pregnancy, research assistant unavailable for the study, and volumetric capnograph monitor unavailable. The study was approved by the Sainte-Justine Hospital institutional review board (approval 3622 [November 26, 2012]) without the need for parental or subject consent.

Study Protocol

Once the subject reached inclusion criteria without any exclusion criteria, the subject's head was positioned to avoid air leak if any was detected. Then an infrared mainstream CO_2 sensor (Capnostat, Philips Healthcare, Markham, Ontario, Canada) was placed between the T-piece and the endotracheal tube. The sensor was connected to an NM3 volumetric capnograph (Philips Healthcare, Markham, Ontario, Canada). We used the neonatal sensor for children <5 kg and the pediatric sensor above that weight. Volumetric capnography data were electronically recorded over the 5 min before blood gas analysis. Only one blood gas per subject was analyzed. Blood gas values were corrected for body temperature.

Data Collected

Demographic characteristics of the subject, diagnosis, ventilatory parameters, blood gas results, blood hemoglobin level, sedation scale, and clinical severity scores [PRISM (Pediatric RISk of Mortality), PELOD (PEdiatric Logistic Organ Dysfunction)] were documented in a case report form. Severity of lung injury was assessed using both P_{aO_2}/F_{IO_2} ratio and oxygenation index F_{IO_2} × mean airway pressure/P_{aO_2} (mm Hg). Lung injury severity was classified using P_{aO_2}/F_{IO_2} ratio thresholds according to the Berlin definition.[11]

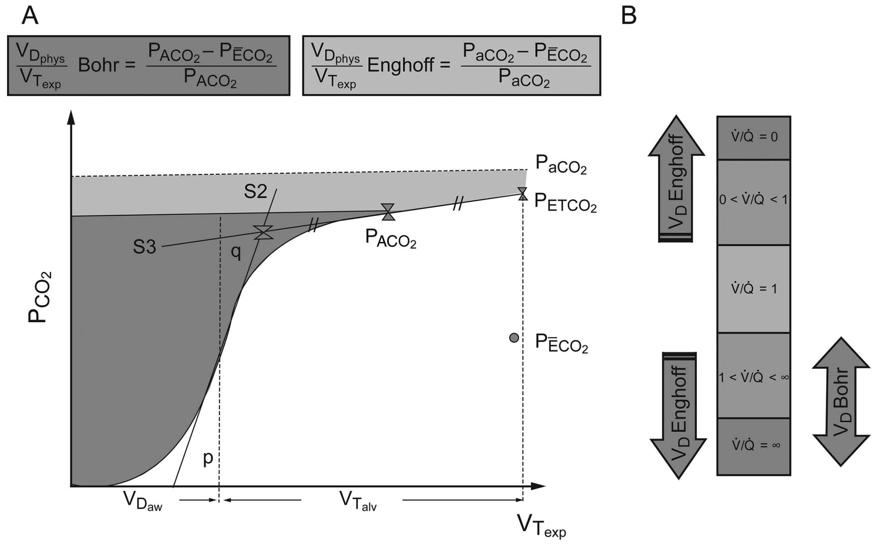

Fig. 1. A: Representation of a volumetric capnogram with a schematic approach for the measurement of dead space. Noninvasive estimation of dead space is related to Bohr's approach after estimation of alveolar P_{CO_2} (P_{ACO_2}), whereas Enghoff's method requires an invasive measurement of arterial P_{CO_2} (P_{aCO_2}). P_{ACO_2} is calculated as the middle point of a line joining the intersection of S2 and S3 slopes and end-tidal P_{CO_2} (P_{ETCO_2}). $P_{\bar{E}CO_2}$ is mixed expiratory P_{CO_2} that corresponds to the integration of the P_{CO_2} vs tidal volume curve. Airway dead space ($V_{D_{aw}}$) is calculated according Fowler's method (ie, the equality of area p and q). B: A representation of Riley's model of the lung with a superposition of Bohr and Enghoff dead space assessment formulas. In the bottom, the ventilation/perfusion ratio ($\dot{V}/\dot{Q}$) tends to infinity (dead space); in the top, $\dot{V}/\dot{Q}$ tends to zero and represents the amount of venous admixture or shunt. Enghoff's dead space (arrows on the left) is the addition of high $\dot{V}/\dot{Q}$ and low $\dot{V}/\dot{Q}$ units. It may be higher than Bohr's dead space (arrow on the right), which represents "pure dead space" (ie, high $\dot{V}/\dot{Q}$ units). Data from Reference 10.

Data were collected electronically from the volumetric capnograph and calculated via dedicated software (Flowtool Viewer 3.03, Philips Healthcare, Markham, Ontario, Canada). All recorded breaths were analyzed. Aberrant capnograms were manually deleted if V_T was <80% of the mean V_T or presented an aberrant aspect, such as a sharp increase in P_{CO_2} after phase 3 (named "phase 4"), or very different slopes of phase 2 or phase 3. Subjects were secondarily excluded if >30% of capnograms were aberrant. The following values are the average of values consecutively obtained during a period of 5 min preceding the blood sample: the slope of the phase 2 (S2) and phase 3 (S3) of the capnogram; P_{ACO_2} (alveolar partial pressure of CO_2 calculated at the midpoint of phase 3 starting from the S2-S3 intersection, ending at end-tidal carbon dioxide pressure); mixed partial pressure of CO_2 in the expired volume; $V_{D\ Bohr}$; $V_{D\ Enghoff}$; and the capnographic index, which is defined as the S3/S2 ratio. Airway dead space was automatically calculated (Fowler's method). See Figure 1 for details.

Statistical Analysis

Statistical analysis was performed using SPSS 19 (SPSS, Chicago, Illinois). Descriptive statistics are presented as mean ± SD. Comparisons of mean V_D/V_T values were performed using a *t* test for independent or paired samples. Analysis of variance and Bonferroni tests were used to compare 3 samples or more if variance homogeneity was achieved. The Pearson coefficient was used to describe correlation between 2 continuous variables with a linear correlation. $P < .05$ was considered as statistically significant.

Results

Subjects

Forty subjects were included in the study from December 2012 to June 2013. Subject characteristics and the distribution of P_{aO_2}/F_{IO_2} values are described in Table 1. Six subjects were secondarily excluded from analysis. All of them presented aberrant values of capnographic parameters. These findings were mostly associated with low V_T (<30 mL) (Fig. 2).

Dead Space Measurements and Relationship With Lung Injury Severity

Mean $V_D/V_{T\ Bohr}$ was 0.39 ± 0.12, and mean $V_D/V_{T\ Enghoff}$ was 0.47 ± 0.13 (P = .02). $V_D/V_{T\ Bohr}$ was correlated with P_{aO_2}/F_{IO_2} (r = −0.35, P = .031) and oxygenation index (r = 0.44, P = .005). Similar results were found for $V_D/V_{T\ Enghoff}$ with P_{aO_2}/F_{IO_2} (r = −0.62, P < .001) and

Table 1. Subject Characteristics

Characteristics	Values (N = 34)
Age, mean ± SD y	6.3 ± 5.6
Weight, mean ± SD kg	23 ± 20
Male/female sex, n	15/19
PELOD score, mean ± SD	8.7 ± 7.6
PRISM score, mean ± SD	9.8 ± 0.8
pH, mean ± SD	7.34 ± 0.34
P_{aO_2}, mean ± SD mm Hg	118 ± 18
Hb, mean ± SD g/L	98 ± 8
Reason for admission, n	
Cardiac postoperative care	6
Non-cardiac postoperative care	5
Medical	22
Trauma	1
Lung injury categories, n	
No ARDS ($P_{aO_2}/F_{IO_2} \geq 300$	12
Mild ARDS ($200 \leq P_{aO_2}/F_{IO_2} \leq 300$)	11
Moderate ARDS ($100 \leq P_{aO_2}/F_{IO_2} \leq 200$)	11
Severe ARDS ($P_{aO_2}/F_{IO_2} < 100$)	0

PRISM = Pediatric RISk of Mortality
PELOD = PEdiatric Logistic Organ Dysfunction

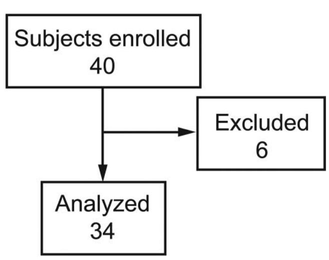

Fig. 2. Flow chart.

oxygenation index (r = 0.65, $P < .001$). Dead space assessment among different categories of severity of lung injury is represented in Figure 3. Analysis of variance showed significant $V_D/V_{T\ Enghoff}$ difference for each category of P_{aO_2}/F_{IO_2} (P = .003). However, no difference in $V_D/V_{T\ Bohr}$ was observed.

The percentage difference between $V_D/V_{T\ Enghoff}$ and $V_D/V_{T\ Bohr}$ ($V_D/V_{T\ Enghoff} - V_D/V_{T\ Bohr})/V_D/V_{T\ Enghoff}$ was 17 ± 16% (from −21 to +65%). Figure 4 represents the correlation between percentage difference and P_{aO_2}/F_{IO_2} (r = −0.50, P = .003). Subjects were divided into 3 quartiles of percentage difference: 0–5% (first quartile, n = 8), 5–25% (second and third quartiles, n = 16), and >25% (fourth quartile, n = 11). Table 2 shows the factors associated with percentage difference.

Discussion

Our study confirms that in mechanically ventilated children, dead space measurements using P_{ACO_2} from volumetric capnography ($V_{D\ Bohr}$) gave lower values compared with dead space measurements using P_{aCO_2} ($V_{D\ Enghoff}$). Major differences are found in subjects presenting the most severe lung injury. Furthermore, our results suggest that the shape of the capnogram itself (capnographic index) is predictive of major variations.

Based on the 3-compartment model of Riley, dead space represents the fraction of lung that is ventilated but unperfused ($\dot{V}/\dot{Q} = \infty$). However, Enghoff's equation, by using P_{aCO_2} instead of P_{ACO_2}, overestimates Riley's dead space (Fig. 1). Indeed, P_{aCO_2} differs from P_{ACO_2} in the case of right to left shunt or in subjects with high $\dot{V}/\dot{Q}$ heterogeneity and consequently high P3 slope.[12,13]

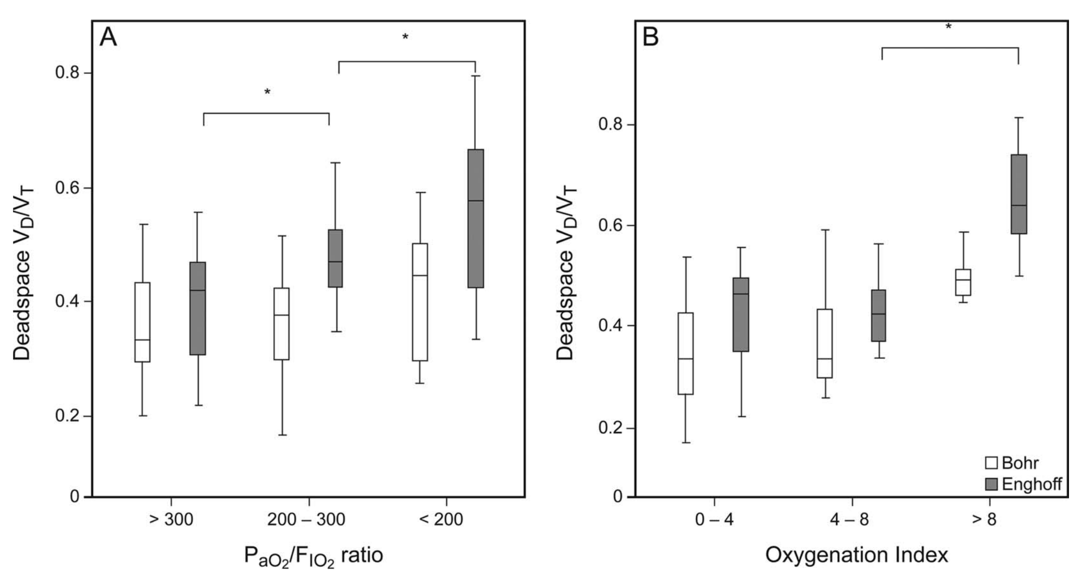

Fig. 3. V_D/V_T values according to different levels of lung injury severity. The asterisk shows interclass differences after analysis of variance (A: P = .03; B: P = .014).

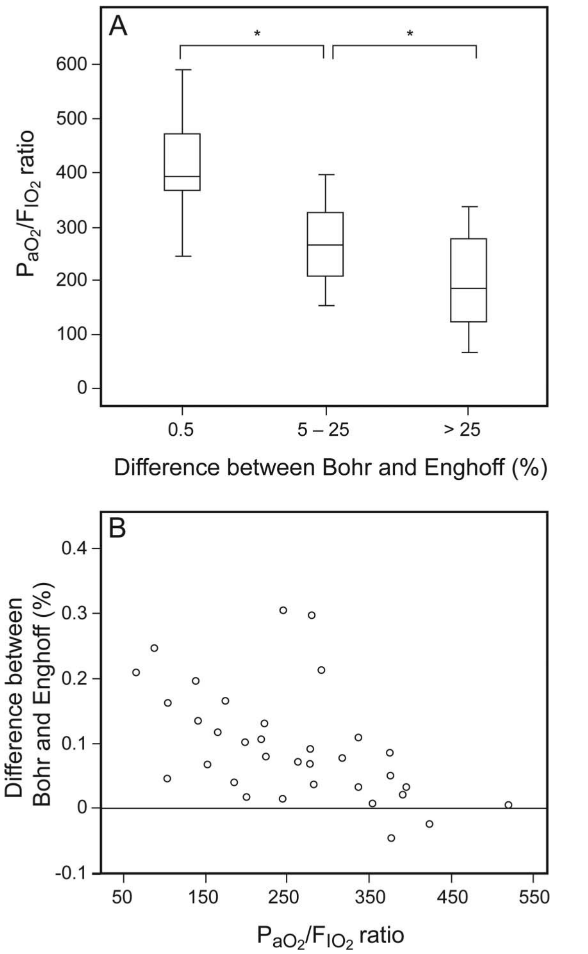

Fig. 4. A: P_{aCO_2}/F_{IO_2} values for 3 intervals of variations between Bohr's and Enghoff's calculation of dead space (percentage difference = $(V_D/V_{T\ Enghoff} - V_D/V_{T\ Bohr})/V_D/V_{T\ Enghoff}$). Asterisks indicate significant differences with P = .003 after analysis of variance/Bonferroni test. B: Representation of the correlation between P_{aCO_2}/F_{IO_2} and difference between Bohr and Enghoff.

Table 2. Factors Associated With an Increase in the Difference Between $V_{D\ Bohr}$ and $V_{D\ Enghoff}$ Measurement

Variables	r	*P*
P_{aO_2}/F_{IO_2}	−0.50	.003
Oxygenation index	0.233	.19
Capnographic index	0.479	.004
P2 slope	−0.279	.11
P3 slope	0.025	.89
$V_{D_{aw}}/V_T$	−0.249	.16

$V_{D_{aw}}$ = airway dead space

In our study, larger differences between Bohr's and Enghoff's dead space occurred as lung injury worsened. Such large differences between $V_D/V_{T\ Bohr}$ and $V_D/V_{T\ Enghoff}$ have been observed for intrapulmonary shunt fraction >20–30% (using Berggren's formula for shunt calculation) in an animal model of ARDS.[14] This study confirmed data obtained from computerized models with similar levels of shunt,[15] whereas older studies suggested that only contexts of high right to left shunt (50%), unlikely to occur in most critically ill patients, resulted in increased V_D/V_T.[16] In Suarez-Sipmann et al[14] again, the use of known algorithms to correct the effect of shunt leads to a better correlation of $V_{D\ Bohr}$ and $V_{D\ Enghoff}$, but this correction failed to explain the entire difference.

Apart from intrapulmonary shunt, the coexistence of a large variety of alveoli with very high and very low $\dot{V}/\dot{Q}$ can explain higher P3 slopes, because each $\dot{V}/\dot{Q}$ is associated with a given expiratory time constant. Thus, high-$\dot{V}/\dot{Q}$ alveoli (that contain a low quantity of CO_2) generate the first part of the phase 3 slope, whereas low-$\dot{V}/\dot{Q}$ alveoli generate the last part of the phase 3 slope due to higher concentration of CO_2. In an animal model of acute lung injury, a good correlation was observed between P3 slope and $\dot{V}/\dot{Q}$ dispersion (assessed by the multiple inert gas elimination technique).[17] In the clinical setting, this dispersion of $\dot{V}/\dot{Q}$ values is best described by S2/S3, elsewhere named the capnographic index or KPI, and this has been reported in children with chronic obstructive disease (cystic fibrosis, bronchopulmonary dysplasia, or asthma).[18-20] Our study is the first to report the statistically significant association of the capnographic index and the difference between Bohr's and Enghoff's calculation of dead space in the critical care setting, and our results are comparable with those found in children with cystic fibrosis versus controls[18] (ie, patients with major variations of dead space measurement also present with a higher capnographic index). These results suggest that the interpretation of the appearance of the capnogram itself may be appropriate and may guide decisions in the management of patients with ARDS.

One limitation of our study is the absence of evaluation of pulmonary blood flow. Apart from shunt and dispersion of $\dot{V}/\dot{Q}$ values, increases in dead space could be due to decreased blood flow in the pulmonary artery.[15,21,22] Pulmonary blood flow is not measured routinely in children, but we excluded patients with hemodynamic instability and intracardiac right to left shunt, allowing us to assume that pulmonary blood flow was near normal ranges. Furthermore, other parameters that influence dead space in ARDS computerized models were not necessarily controlled for in our study: Hemoglobin and pH are 2 variables that influence the amount of dissolved CO_2 and thus the calculation of dead space.[20] However, pH and hemoglobin were within normal ranges in the pediatric ICU subjects included (Table 1).

Another limitation of our study may be the choice to consider the effect of temperature on CO_2 partial pressure measurement. Indeed, because exhaled gas measurements reflect the in vivo alveolar P_{CO_2}, we chose to take into account corrected (for subject's temperature) values of P_{aCO_2}. This choice was suggested in previous studies.[23,24] However, the comparison of uncorrected versus corrected values of $V_D/V_{T\ Bohr}$ and $V_D/V_{T\ Enghoff}$ would be interesting to further analyze the impact of temperature on both measurements.

Apart from our main results, we identified subjects of special interest: those with high percentage difference in the absence of hypoxemia and those with low percentage difference and severe hypoxemia. Three subjects were isolated. One was a 6-month-old infant weighing 4 kg with dilated cardiomyopathy admitted after cardiac surgery having a P_{aO_2}/F_{IO_2} of 104 and an oxygenation index of 12. The percentage difference was only 6% despite severe hypoxemia. This subject had a V_T of 36 mL with an airway dead space equal to 18 mL that explained most of the V_D/V_T (0.66). This low difference was probably due to the proportional low influence of $\dot{V}/\dot{Q}$ mismatch when compared with instrumental + anatomical dead space (ie, airway dead space). Two children were intubated for severe status asthmaticus resistant to β_2 agonists who displayed severe hyperinflation without any consolidation on chest radiograph. In these subjects, $V_D/V_{T\ Enghoff}$ values were high (0.51 and 0.53) with a high percentage difference (65 and 55%) and high P_{aO_2}/F_{IO_2} (245 and 280 mm Hg, respectively). In such subjects, a large variation between Bohr and Enghoff dead space measurements may be observed without much hypoxemia, suggesting that Enghoff dead space measurements (including a P_{aCO_2} measurement) are required to measure dead space accurately.

Conclusions

Our results suggest that Bohr and Enghoff dead space measurements are not similar in cases of hypoxemia (P_{aO_2}/F_{IO_2} <300) except in the case of status asthmaticus. Our study confirmed that Enghoff dead space measurements are usually higher than Bohr dead space measurements. The method used to measure V_D/V_T must be reported, and the availability of volumetric capnography to assess both $V_{D\ Bohr}$ and $V_{D\ Enghoff}$ may be more informative than dead space monitoring alone in the management of patients with ARDS.

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