Accuracy of Physiologic Dead Space Measurements in Patients With Acute Respiratory Distress Syndrome Using Volumetric Capnography: Comparison With the Metabolic Monitor Method

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BACKGROUND: Volumetric capnography is an alternative method of measuring expired carbon dioxide partial pressure (P_{eCO_2}) and physiologic dead-space-to-tidal-volume ratio (V_D/V_T) during mechanical ventilation. In this method, P_{eCO_2} is measured at the Y-adapter of the ventilator circuit, thus eliminating the effects of compression volume contamination and the need to apply a correction factor. We investigated the accuracy of volumetric capnography in measuring V_D/V_T, compared to both uncorrected and corrected measurements, using a metabolic monitor in patients with acute respiratory distress syndrome (ARDS). METHODS: There were 90 measurements of V_D/V_T made in 23 patients with ARDS. The P_{eCO_2} was measured during a 5-min expired-gas collection period with a Delta-trac metabolic monitor, and was corrected for compression volume contamination using a standard formula. Simultaneous measurements of P_{eCO_2} and V_D/V_T were obtained using volumetric capnography. RESULTS: V_D/V_T measured by volumetric capnography was strongly correlated with both the uncorrected ($r^2 = 0.93$, $p < 0.0001$) and corrected ($r^2 = 0.89$, $p < 0.0001$) measurements of V_D/V_T made using the metabolic monitor technique. Measurements of V_D/V_T made with volumetric capnography had a bias of 0.02 and a precision of 0.05 when compared to the V_D/V_T corrected for estimated compression volume contamination. CONCLUSION: Volumetric capnography measurements of V_D/V_T in mechanically-ventilated patients with ARDS are as accurate as those obtained by metabolic monitor technique.
Key words: acute respiratory distress syndrome, dead-space fraction, dead-space-to-tidal volume ratio, volumetric capnography, metabolic, monitor. [Respir Care 2005;50(4):462–467.

Introduction

The measurement of physiologic dead-space-to-tidal volume ratio (V_D/V_T) requires the collection of expired gas to assess the mean expired carbon dioxide partial pressure (P_{eCO_2}). Traditionally, this has been accomplished by collecting expired gas over several minutes into a Douglas bag.[1] The advent of commercially available, indirect calorimeters permitted a more convenient but equally accurate and reliable method for measuring P_{eCO_2}.[2,3] Both the Douglas bag and the metabolic monitor methods have limitations, because during positive-pressure ventilation the expired gas collected in either the Douglas bag or the metabolic monitor also contains gas compressed within the ventilator circuit, which dilutes the fractional expired carbon dioxide concentration.[4] This artificially lowers the P_{eCO_2} and overestimates the true V_D/V_T. Dead-space measurements can be corrected for the effects of compression

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The NICO monitor and supplies were donated by Respironics Inc.

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Table 1. Demographic Information of Patients With Acute Respiratory Distress Syndome

Patient	Etiology of Lung Injury	Age (y)	Sex	LIS
1	Trauma	44	M	2.50
2	Trauma/sepsis	22	M	3.50
3	Pneumonia	56	F	3.00
4	Sepsis	65	F	3.00
5	Pneumonia	43	M	3.00
6	Aspiration/sepsis	43	M	2.75
7	Sepsis	62	F	2.25
8	Sepsis	55	M	2.00
9	Sepsis	50	M	2.75
10	Aspiration/sepsis	47	M	3.50
11	Sepsis	46	M	3.75
12	Sepsis/pneumonia	38	M	3.50
13	Sepsis/pneumonia	60	F	3.25
14	Trauma	71	F	2.75
15	Sepsis/pneumonia	22	M	3.75
16	Pneumonia	39	F	2.50
17	Pneumonia	58	F	3.00
18	Pneumonia	41	F	3.00
19	Sepsis/pneumonia	71	F	2.00
20	Sepsis	33	F	2.00
21	Pneumonia	44	M	2.50
22	Pneumonia/drug overdose	41	F	2.50
23	Trauma	30	M	3.50
Mean ± standard deviation		47 ± 14		2.88 ± 0.55

LIS = lung injury score

volume contamination, either by physical segregation of expired gases[5] or by use of a correction factor based upon the circuit compliance and peak inspiratory pressure (PIP).[6] Both techniques are equally reliable methods for adjusting P_{eCO_2} and V_D/V_T to account for the effects of compression volume contamination.[5]

Volumetric capnography is an alternative method of measuring P_{eCO_2} and V_D/V_T during mechanical ventilation.[7] In this method, expired CO_2 is measured at the Y-adapter of the ventilator circuit, thus eliminating the effects of compression volume contamination and the need to apply a correction factor. We investigated the accuracy of volumetric capnography in measuring V_D/V_T, compared to both uncorrected and corrected measurements, using a metabolic monitor in patients with acute respiratory distress syndrome (ARDS).

Methods

There were 90 measurements of V_D/V_T made in 23 patients who met American-European Consensus Conference criteria for ARDS (Table 1).[8] A comparison of methods was made as part of a larger observational study of dead-space fraction in patients with ARDS. The study was approved by the Committee on Human Research at the University of California, San Francisco. Signed informed consent was obtained from either the patient's relative or legally authorized representative. Patients were studied in the absence of nursing care activities and when they were observed to be reasonably calm and synchronous with the ventilator.

The fractional expired carbon dioxide concentration and the minute production of carbon dioxide ($\dot{V}_{CO_2}$) were measured with a metabolic monitor (Delta-trac, SensorMedics, Yorba Linda, California).[2] Both gas and barometric pressure calibrations were done prior to each measurement. Mean P_{eCO_2} was determined by multiplying the fractional expired carbon dioxide concentration by the barometric pressure (minus water vapor pressure). A 5-min expired gas collection period was used to determine P_{eCO_2} and $\dot{V}_{CO_2}$, with an arterial blood gas sample obtained at the mid-point to determine the P_{aCO_2}.[2] All arterial blood gas samples were obtained from an indwelling arterial catheter and placed on ice.

Dead-space fraction was calculated using the Enghoff modification of the Bohr equation:[9]

$$V_D/V_T = [P_{aCO_2} - P_{eCO_2}] \div P_{aCO_2}$$

Mean P_{eCO_2} was adjusted for compression volume dilution by a correction factor, which was the ratio of the observed V_T divided by the observed V_T minus the calculated compression volume:[4,6]

$$\text{Corrected } P_{eCO_2} = P_{eCO_2} \times (V_T \div [V_T - \text{compression volume}])$$

The compliance of the ventilator circuits was determined by a previously described method.[10] As in our original study,[11] we recorded both uncorrected and corrected values of V_D/V_T.

Simultaneous measurements of P_{eCO_2} and V_D/V_T were made using an automated volumetric capnograph and pulmonary mechanics monitor (NICO, Respironics, Wallingford, Connecticut). A one-point calibration was done on the capnograph sensor prior to each measurement. As both monitors use minute-to-minute measurement averaging, the internal clocks were synchronized. The mid-point of the 5-min gas collection was noted on the metabolic monitor, and that time was used for the subsequent determination of the P_{eCO_2} measured by the NICO monitor. The mechanical dead space of the ventilator circuits was minimized to 7.5 mL, and the dead space of the Capnostat CO_2/flow sensor (Respironics, Carlsbad, California) was < 8.5 mL.[12] Therefore, the estimated total mechanical dead space was approximately 15 mL.

Because this investigation was done as part of a larger observational study, mechanical ventilation settings were determined by the clinicians. Clinical practice for patients with acute lung injury at our institutions is governed by the low-V_T ventilation protocol of the ARDS Network.[13] However, there was variability in the mode used to achieve lung-protective ventilation during clinical practice. Of the 90 dead-space measurements, 42 (47%) were made on volume-control ventilation, 41 measurements (45%) were made on pressure-regulated volume-control ventilation, while 7 measurements (8%) were made on pressure-control ventilation. Only pressure-triggering or nonbias flow-triggering was used during the study. During the dead-space measurements, the mean ($\pm$ standard deviation) V_T was 6.7 $\pm$ 1.4 mL/kg predicted body weight, the mean inspiratory time was 0.73 $\pm$ 0.18 s, and the set level of positive end-expiratory pressure was 11.2 $\pm$ 4.6 cm H_2O.

Correlation was measured by Pearson product-moment coefficient (r), and bias/precision was assessed by Bland-Altman test.[14] Statistical analysis was done using commercially-available software (InStat, version 3.0, GraphPad Software, San Diego, California). Results were considered to be significant when $p < 0.05$.

Table 2. Comparison of Dead-Space Fraction and Mean Expired Carbon Dioxide Partial Pressure Made by Metabolic Monitor and Volumetric Capnography

	Delta-trac Uncorrected	Delta-trac Corrected	NICO Monitor
P_{eCO_2} (mm Hg)	15.7 ± 4.7	18.5 ± 5.7	17.5 ± 5.5
V_D/V_T	0.64 ± 0.11	0.58 ± 0.14	0.60 ± 0.12

P_{eCO_2} = mean expired carbon dioxide partial pressure
V_D/V_T = physiologic dead-space-to-tidal-volume ratio

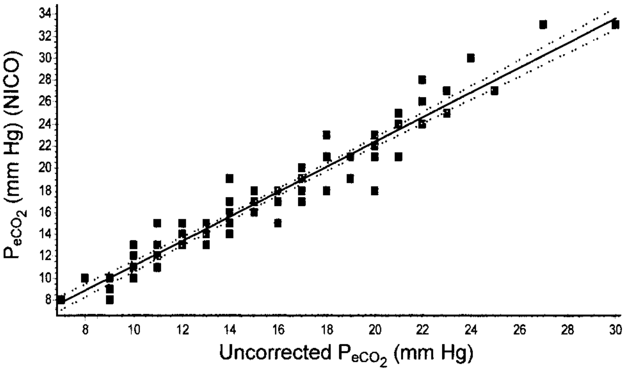

Fig. 1. Correlation between expired carbon dioxide partial pressure (P_{eCO_2}) measured by volumetric capnography (NICO pulmonary mechanics monitor) and uncorrected P_{eCO_2} measured with the metabolic monitor technique ($r = 0.96$, $r^2 = 0.93$, $p < 0.0001$).

Results

As expected, the P_{eCO_2} measured by volumetric capnography was higher than the uncorrected P_{eCO_2} measured with the metabolic monitor. Therefore, measurements of V_D/V_T by volumetric capnography were lower than those values obtained by the metabolic monitor (Table 2). When compared to the P_{eCO_2} corrected for the estimated effects of compression volume contamination, the P_{eCO_2} measured by volumetric capnography was slightly lower than metabolic monitor measurements. Thus, the resulting V_D/V_T measured by volumetric capnography was slightly higher than the corrected V_D/V_T obtained with the metabolic monitor (see Table 2). Volumetric capnography measurements of $\dot{V}_{CO_2}$ were 13% lower than measurements made with the metabolic monitor (214 $\pm$ 60 vs 240 $\pm$ 65 mL/min, respectively), and the mean difference was 27 $\pm$ 20 mL/min.

A strong correlation was found between the uncorrected P_{eCO_2} and the P_{eCO_2} measured by volumetric capnography ($r = 0.96$, $r^2 = 0.93$, $p < 0.0001$) and also between the corrected P_{eCO_2} and the P_{eCO_2} measured by volumetric capnography ($r = 0.94$, $r^2 = 0.88$, $p < 0.0001$) (Figs. 1 and 2, respectively). Likewise, the measurements of V_D/V_T made by volumetric capnography also had a strong cor-

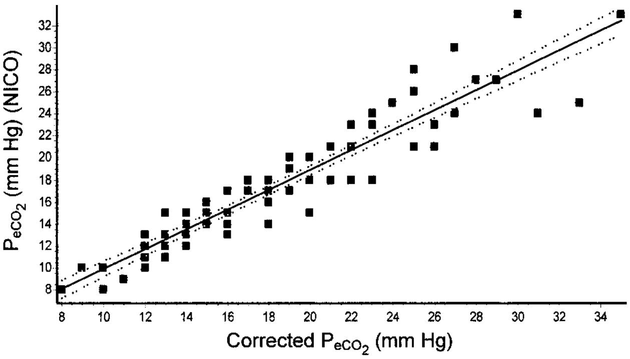

Fig. 2. Correlation between expired carbon dioxide partial pressure (P_{eCO_2}) measured by volumetric capnography (NICO pulmonary mechanics monitor) and P_{eCO_2} measured with the metabolic monitor technique and corrected for estimated compression volume dilution ($r = 0.94$, $r^2 = 0.88$, $p < 0.0001$).

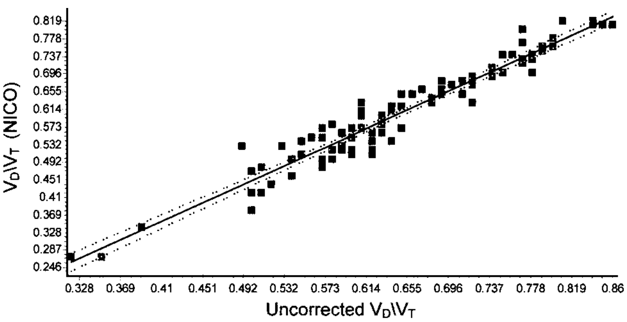

Fig. 3. Correlation between dead-space-to-tidal volume ratio (V_D/V_T) measured by volumetric capnography (NICO pulmonary mechanics monitor) and uncorrected V_D/V_T measured with the metabolic monitor technique ($r = 0.96$, $r^2 = 0.93$, $p < 0.0001$).

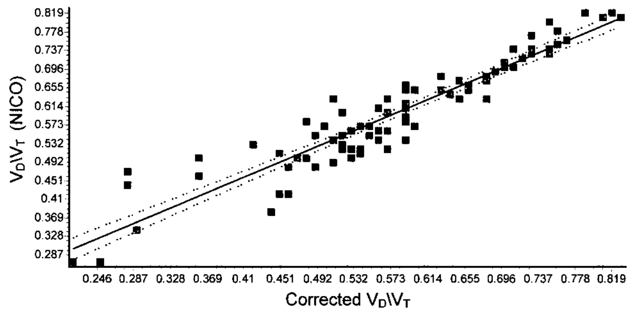

Fig. 4. Correlation between dead-space-to-tidal volume ratio (V_D/V_T) measured by volumetric capnography (NICO pulmonary mechanics monitor) and V_D/V_T measured with the metabolic monitor technique and corrected for estimated compression volume dilution ($r = 0.94$, $r^2 = 0.89$, $p < 0.0001$).

relation with both the uncorrected ($r = 0.96$, $r^2 = 0.93$, $p < 0.0001$) and the corrected V_D/V_T made with the metabolic monitor technique ($r = 0.94$, $r^2 = 0.89$, $p < 0.0001$) (Figs. 3 and 4, respectively). In addition, the $\dot{V}_{CO_2}$ measured by volumetric capnography had a strong correlation with the $\dot{V}_{CO_2}$ measured by the metabolic monitor ($r = 0.95$, $r^2 = 0.90$, $p < 0.0001$).

The bias and precision of the NICO volumetric capnograph was reasonable when compared against both the uncorrected and corrected measurements of P_{eCO_2} and V_D/V_T made with the metabolic monitor technique. When compared to the uncorrected P_{eCO_2} measured with the metabolic monitor technique, volumetric capnography measurements of P_{eCO_2} had a bias of 1.8 mm Hg and a precision of 1.6 mm Hg. When compared to the metabolic monitor technique corrected for compression volume contamination, the P_{eCO_2} measured by volumetric capnograph had a bias of −1 mm Hg and a precision of 2 mm Hg.

Similarly, V_D/V_T measured by volumetric capnography had a bias of −0.04 and a precision of 0.03, compared to the uncorrected V_D/V_T made with the metabolic monitor technique. When compared to the V_D/V_T corrected for estimated compression volume contamination, V_D/V_T measured by volumetric capnography had a bias of 0.02 and a precision of 0.05. In addition, the $\dot{V}_{CO_2}$ measured by volumetric capnography had a bias of −26 mL/min and a precision of 21 mL/min, compared to the $\dot{V}_{CO_2}$ measured with the metabolic monitor.

Of the 23 patients in the study, 13 (56%) had 2–4 comparisons made between techniques, whereas 2 patients (9%) had only 1 comparison, and 8 patients (35%) had 5 or more comparisons made. Because of the unequal number of measurements made in some patients, we controlled for potential bias by using only the first comparison made in each patient. Yet, when the number of comparisons was reduced to 23 observations, the correlation between the uncorrected P_{eCO_2} measured with the metabolic monitor and P_{eCO_2} measured by volumetric capnography was unchanged ($r^2 = 0.92$, $p < 0.0001$), as was the bias (1.8 mm Hg) and the precision (1.4 mm Hg). Comparisons between the corrected P_{eCO_2} measured with the metabolic monitor and P_{eCO_2} measured by volumetric capnography were somewhat lower ($r^2 = 0.83$, $p < 0.0001$), but the bias (−0.9 mm Hg) and precision (2 mm Hg) were essentially unchanged. The bias and precision between measurements of $\dot{V}_{CO_2}$ made with the metabolic monitor and those made with volumetric capnography also were not different (−23 mL and 21 mL, respectively).

Stability during the 5-min measurement period was assessed by the variability in the expired CO_2 concentration and in the variability in the mean P_{eCO_2}. The mean expired CO_2 concentration varied by only 0.06 ± 0.04%, resulting in variability in mean P_{eCO_2} of 0.45 ± 0.55 mm Hg (95% confidence interval of 0.33–0.57 mm Hg). As the mean P_{eCO_2} was always rounded off to the nearest whole number, in 51/90 measurements (57%) the variability in P_{eCO_2} was 0 mm Hg during the 5-min measurement period, whereas in 37/90 measurements (41%), the mean P_{eCO_2} was noted to vary by 1 mm Hg. In only 2 measurements

(2%) did the mean P_{eCO_2} vary by 2 mm Hg. All observed variations in P_{eCO_2} occurred in only one direction during the measurement period (ie, the variation was either +1 mm Hg or −1 mm Hg in any particular measurement, and not ±1 mm Hg).

Given that the mean P_{aCO_2} was 46 mm Hg and the mean uncorrected P_{eCO_2} was approximately 16 mm Hg, the ≤ 1 mm Hg variability noted in P_{eCO_2} in 98% of the samples would suggest that the estimated random error in V_D/V_T during the 5-min measurement period probably did not exceed ±0.02. Variability in mean P_{eCO_2} measured by volumetric capnography during the 5-min measurement period was essentially the same as that observed during the metabolic monitor measurements: there was no variability in P_{eCO_2} in 55% of measurements, a 1-mm Hg variability in 44% of the measurements, and only one measurement in which the P_{eCO_2} varied by 2 mm Hg.

Discussion

In this study we found that V_D/V_T measured by volumetric capnography produced results that were as accurate as those obtained using the metabolic monitor method in patients with ARDS. Thus, our results support the use of volumetric capnography to measure V_D/V_T in these patients. Furthermore, volumetric capnography provides a reasonable estimate of $\dot{V}_{CO_2}$, despite the incorporation of markedly different methods of volume measurement between the 2 techniques.

There were only small differences in measurements of P_{eCO_2} and V_D/V_T between volumetric capnography and the metabolic monitor method corrected for the estimated effects of compression volume contamination. Yet the correlation was not quite as strong as those results obtained when volumetric capnography was compared to the uncorrected measurements ($r^2 = 0.93$ vs $r^2 = 0.89$, respectively). We attributed this to errors in the calculation of the correction factor in one patient (number 7). Interestingly, this patient was ventilated on volume-control ventilation at a very low V_T (4.5 mL) and high PIP (> 50 cm H_2O). The corrected V_D/V_T measurements were markedly lower (0.26–0.36) from both the corresponding uncorrected measurements (0.50–0.57) and the volumetric capnography V_D/V_T measurements (0.44–0.50). In this patient, the correction factor used to estimate the corrected P_{eCO_2} was 1.47, whereas the average correction factor for the entire sample was only 1.18 (95% confidence interval 1.16–1.20). As a result, the average difference between uncorrected and corrected values of V_D/V_T was 0.21, whereas the average difference between the uncorrected and corrected metabolic monitor measurements was 0.06 (95% confidence interval 0.05–0.07) for the entire sample. When these 4 measurements were removed, r^2 increased from 0.89 to 0.93 ($p < 0.0001$), the bias decreased from 0.02 to 0.01, and the precision increased from 0.05 to 0.037.

The reliability of using a correction factor to estimate the degree of compression volume contamination primarily depends upon the accuracy of the recorded PIP and expired V_T used to determine the correction factor. This in turn is dependent upon the relative stability of these variables over the expired gas collection period. During a ventilator systems-check the expired V_T and PIP are typically observed over brief periods of time (usually 10–20 s) relative to the 5-min expired-gas collection period. The more expired V_T and PIP fluctuate during the expired gas collection period, the more likely that the observed values of expired V_T and PIP will not reflect the average expired V_T and PIP. In particular, when a small V_T is used during lung-protective ventilation, even small errors in the observed PIP and expired V_T may lead to more pronounced errors in the corrected P_{eCO_2} and V_D/V_T. These observational errors potentially may become more frequent when pressure-regulated volume-controlled ventilation is used, because both V_T and PIP may be more likely to vary on a breath-to-breath basis as respiratory system mechanics change. When very large differences between uncorrected and corrected measurements occur, particularly when the resultant V_D/V_T does not fit with other clinical data, errors in the correction calculations should be considered. Because volumetric capnography measures expired CO_2 at the airway Y-adapter, any potential errors caused by either compression volume contamination or in the calculation of compression volume are avoided.

Accuracy in the determination of pulmonary dead-space fraction may be particularly important in patients with ARDS, as both early and sustained elevations of V_D/V_T are associated with an increased risk of mortality when patients are ventilated at a traditional V_T size.[11,15] Recently, low-V_T ventilation was shown to lower mortality in patients with ARDS.[13] However, the adoption of low-V_T ventilation may introduce technical problems in the determination of dead-space fraction. Elevated minute ventilation and patient-ventilator asynchrony are common problems during lung-protective ventilation.[10] Attempting to maintain low-V_T ventilation in these situations may require high peak inspiratory flow rates that may result in high PIP and increased compression volume contamination of a relatively smaller V_T. This may further increase the V_D/V_T and make its prognostic value less certain. However, we have just described a circumstance when the correction factor for compression volume contamination apparently was in error and falsely decreased the V_D/V_T. The correction factor for compression volume contamination may be susceptible to error if the observed expired V_T and PIP during the ventilator systems-check does not reflect the average expired V_T and PIP over the expired-gas collection period.

An additional source of difference between measurement techniques may have been due to the research design. In our previous studies,[11,15] we used an expired collection time of 5 min. We wished to know whether the volumetric capnography measurement of V_D/V_T based upon a 1-min average P_{eCO_2} would produce satisfactory results, compared to our standard 5-min gas-collection technique. Although there was very little variation in P_{eCO_2} during the 5 min of gas collection, had we used the corresponding 1-min averages of P_{eCO_2} reported by both the metabolic monitor and the volumetric capnograph, the precision and correlation may have been stronger.

Conclusion

We found that V_D/V_T measurements made in mechanically-ventilated patients with ARDS by volumetric capnography produce results that are as accurate as those obtained by metabolic monitor. Furthermore, because volumetric capnography measures expired CO_2 at the proximal airway, the effects of compression volume contamination and the required calculations to account for this error are eliminated, thus simplifying the technique.

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