Anatomic Dead Space Cannot Be Predicted by Body Weight

Lara M Brewer MSc, Joseph A Orr PhD, and Nathan L Pace MD

BACKGROUND: Anatomic dead space (also called airway or tracheal dead space) is the part of the tidal volume that does not participate in gas exchange. Some contemporary ventilation protocols, such as the Acute Respiratory Distress Syndrome Network protocol, call for smaller tidal volumes than were traditionally delivered. With smaller tidal volumes, the percentage of each delivered breath that is wasted in the anatomic dead space is greater than it is with larger tidal volumes. Many respiratory and medical textbooks state that anatomic dead space can be estimated from the patient's weight by assuming there is approximately 1 mL of dead space for every pound of body weight. With a volumetric capnography monitor that measures on-airway flow and CO_2, the anatomic dead space can be automatically and directly measured with the Fowler method, in which dead space equals the exhaled volume up to the point when CO_2 rises above a threshold. METHODS: We analyzed data from 58 patients (43 male, 15 female) to assess the accuracy of 5 anatomic dead space estimation methods. Anatomic dead space was measured during the first 10 min of monitoring and compared to the estimates. RESULTS: The coefficient of determination (r^2) between the anatomic dead space estimate based on body weight and the measured anatomic dead space was $r^2 = 0.0002$. The mean $\pm$ SD error between the body weight estimate and the measured dead space was 60 $\pm$ 54 mL. CONCLUSIONS: It appears that the anatomic dead space estimate methods were sufficient when used (as originally intended) together with other assumptions to identify a starting point in a ventilation algorithm, but the poor agreement between an individual patient's measured and estimated anatomic dead space contradicts the assumption that dead space can be predicted from actual or ideal weight alone. *Key words: respiratory dead space, anatomic dead space, tidal volume, gas exchange, body weight, respiratory distress syndrome, mechanical ventilation, ventilator, capnography, lung volume, pulmonary ventilation, respiratory function tests, ventilation-perfusion ratio.* [Respir Care 2008;53(7):885–891. © 2008 Daedalus Enterprises]

Introduction

The anatomic dead space (also called airway, tracheal, or series dead space) is the part of the tidal volume (V_T)

Lara M Brewer MSc, Joseph A Orr PhD, and Nathan L Pace MD are affiliated with the Department of Anesthesiology, University of Utah Health Sciences Center, Salt Lake City, Utah.

Correspondence e-mail: lbrewer@abl.med.utah.edu.

that remains in the conducting passages at the end of inspiration and therefore does not participate in gas exchange. During expiration the gas from the conducting passages has the same composition it did during inspiration; it is commonly referred to as wasted ventilation. Anatomic dead space was first measured with a fast nitrogen analyzer, by Fowler[1] in 1948. In 1952 DuBois et al[2] described an

---

SEE THE RELATED EDITORIAL ON PAGE 860

---

anatomic-dead-space measurement technique that used a rapid CO_2 analyzer, and in 1954 Bartels et al[3] found that several indicator gases, including oxygen and carbon dioxide, all gave the same value for anatomic dead space and could therefore be used interchangeably.

Many current textbooks[4-7] suggest a simple method of estimating anatomic dead space based on the patient's body
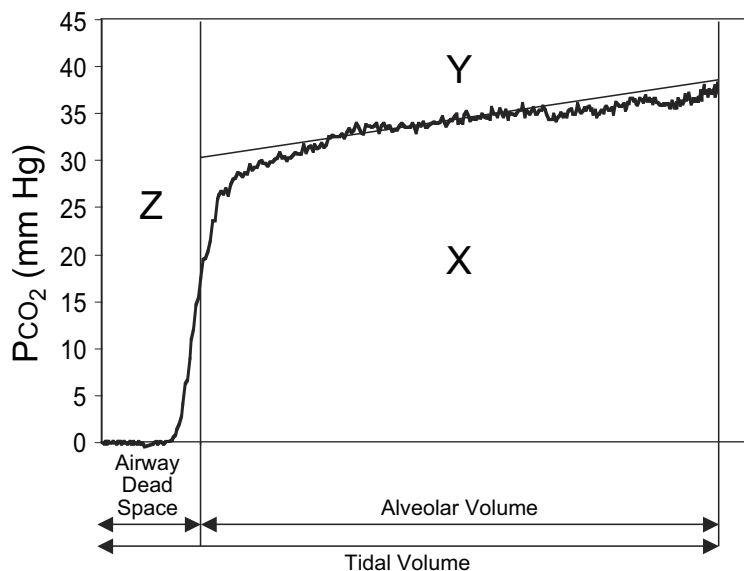
Fig. 1. Volumetric capnogram depicting the derivation of anatomic and alveolar dead space. Anatomic (or airway) dead space is represented by the vertical line that bisects the rise on the capnogram during exhalation. Alveolar dead space is identified by the letter Y.

weight or predicted body weight. Specifically, they suggest that anatomic dead space is approximately 1 mL per pound of body weight. Because this dead space estimation technique has been so widely disseminated, many clinicians apply the 1 lb = 1 mL rule in clinical practice.

The observation that anatomic dead space is roughly correlated with body weight seems to have been first put forth by Radford[8] in 1955. Radford's article described ventilation standards he had developed to predict an individual's required ventilation based on body weight and sex. As part of the development of the ventilation standard, he presented anatomic dead space data and estimated dead space values for 11 patient groups that comprised 131 subjects, ages newborn to 59.6 ± 6.3 y, mean body weight range 8–170 lb. Radford plotted the mean dead space as a function of mean body weight for each of the 11 groups, and observed a "remarkable, but approximate, rule that the respiratory dead space in milliliters (at body temperature and pressure saturated) equals the body weight in pounds."

Contemporary ventilation protocols such as that of the Acute Respiratory Distress Syndrome (ARDS) Network,[9] which call for smaller V_T as part of a lung-protection strategy for patients with ARDS or acute lung injury, result in a larger percentage of each breath being wasted in the anatomic dead space volume, compared to ventilation with larger V_T. When a weight-based estimate of anatomic dead space is incorrect, the assumed alveolar minute ventilation may be much smaller or larger than the actual alveolar minute volume, which can lead to unintentional hypoventilation if the dead space estimate is too small, or an unintentionally large alveolar V_T if the dead space es-

timate is too large. Unintentional hypoventilation could be made worse by a breathing circuit that includes excessive apparatus dead space.[10,11]

Anatomic dead space can be calculated with the Fowler equal-area method, which is based on volumetric capnography.[1] We analyzed data collected with a respiratory profile monitor that provides volumetric CO_2 analysis, to study how well the estimated anatomic dead space predicted the measured anatomic dead space in a group of mechanically ventilated patients.

Methods

The study was performed at the University of Utah Health Sciences Center. The study was approved by our institutional review board, and informed consent was not required. We analyzed data from 58 patients (43 male, 15 female) who were tracheally intubated, mechanically ventilated, and sedated, in either the operating room (42 patients) or the intensive care unit (16 patients), who had been admitted for coronary artery bypass graft or valve repair surgeries. The data set had been previously collected to measure end-tidal CO_2, carbon dioxide production, and Fick cardiac output. Mean ± standard deviation patient characteristics included: age 63.2 ± 13.8 y (range 14–81 y), body weight 188 ± 42 lb (range 110–301 lb), height 172.9 ± 9.8 cm (range 149–198 cm), predicted ideal body weight 149 lb, and body surface area 2.01 ± 0.26 m². Ventilation settings were left to the clinician's discretion.

The patients were monitored with a volumetric CO_2 monitor that has a combination CO_2 and flow sensor
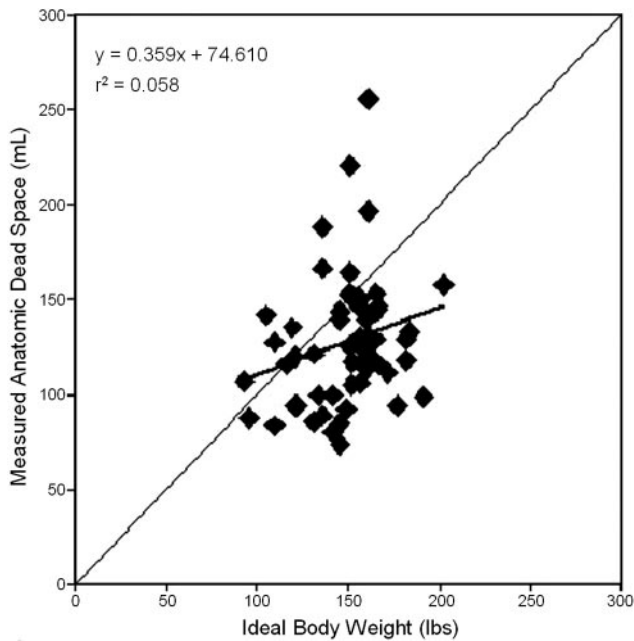
Fig. 2. Regression analysis of measured anatomic dead space versus ideal body weight.

(NICO$_2$, Respironics, Wallingford, Connecticut). This monitor calculates anatomic dead space on a breath-to-breath basis, by analyzing the expiratory volume at which the CO$_2$ signal transitions from anatomic to alveolar CO$_2$, using the Fowler method[1] (Fig. 1). For each patient the mean anatomic dead space was measured with data collected during the first 10 min of monitoring and compared to the values predicted by 5 published prediction methods,[8,12-16] which are based on actual body weight or ideal body weight and an allowance for the presence of an endotracheal tube (ETT).

In 21 patients there was an elbow placed in the breathing circuit between the ETT and the volumetric capnometry sensor. With those patients we subtracted a volume of 6 mL from the measured anatomic dead space, to compensate for the dead space added by the elbow. For all other patients the ETT was connected directly to the volumetric capnometry sensor, so no compensation was required.

The most frequently published anatomic dead space prediction equation is cited in many general and respiratory physiology texts.[4-7] This method was published by Radford[8] and simply states that 1 lb of actual body weight corresponds to 1 mL of anatomic dead space. A second, commonly used method, published by Nielsen,[12] uses the ideal body weight, based on the patient's height:

1 mL of dead space = 1 lb of ideal body weight

Ideal body weight is calculated as:

$$45.5 + (0.91 \times (\text{height in cm} - 152.4)) \times 2.2046$$

for females, and

$$50 + (0.91 \times (\text{height in cm} - 152.4)) \times 2.2046$$

for males.[9,13]

A refinement by Nunn and Hill[14] of the 1 mL = 1 lb method states that estimated anatomic dead space should be decreased by 72 mL if the patient is intubated, to account for the extrathoracic volume bypassed by the ETT:

$$1 \text{ mL} = 1 \text{ lb actual body weight} - 72 \text{ mL}$$

Casati et al[15] proposed reducing the estimate of 1 lb = 1 mL by 50% to account for the volume bypassed by the airway-maintenance devices:

$$1 \text{ mL} = 0.5 \times 1 \text{ lb of actual body weight}$$

The Suwa and Bendixen method[16] uses a similar, related approach that estimates dead space as two thirds of the patient's weight:

$$1 \text{ mL} = 0.66 \times 1 \text{ lb of actual body weight.}$$

We used spreadsheet software (Excel, Microsoft, Redmond, Washington) to conduct the linear regression analysis and to calculate all statistics. The mean and standard deviation were calculated for respiratory rate, number of dead space measurements, V_T (mL, mL/kg ideal body weight, and mL/kg measured body weight), positive end-expiratory pressure (PEEP), inspiratory time, measured anatomic dead space, and predicted dead space. With each of the published prediction methods, we calculated the coefficient of determination (r^2), mean bias ± 95% confidence interval (CI), standard deviation of the bias, and limits of agreement (mean bias ± 2 standard deviation) ± CI between the measured and estimated values.[17] For 2 methods to be used interchangeably, we defined clinically acceptable mean bias and limits of agreement to be small enough that the estimation allowed the patient to be ventilated within 10% of the intended delivered ventilation. For each method we also calculated the ratio of the mean measured anatomic dead space to predicted anatomic dead space.

Results

Figure 2 illustrates the regression analysis for measured anatomic dead space versus ideal body weight. The r^2 for the regression of the measured and predicted anatomic dead space was 0.0002 for each prediction method except the Nielsen method, which had an r^2 of 0.058.
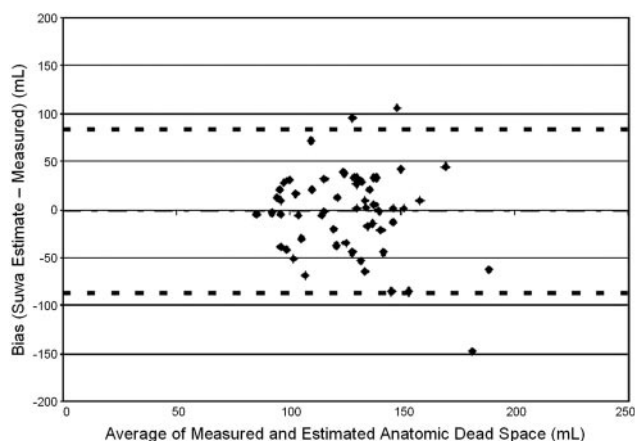
Fig. 3. Bland-Altman analysis of Suwa's estimate and measured anatomic dead space.

Table 1. Results From 5 Methods of Estimating Anatomic Dead Space

Method*	r^2	Mean Bias (mL)	95% CI of Bias (mL)	SD Bias (mL)	Limits of Agreement
Radford[8]	0.0002	59.9	45.7 to 74.1	53.9	−45.7 to 165.5
Nielsen[12]	0.058	20.9	11.5 to 30.3	35.9	−49.5 to 91.3
Nunn[13]	0.0002	−12.1	−26.3 to 2.1	53.9	−117.7 to 93.5
Casati[14]	0.0002	−34.1	−44.5 to −23.7	39.7	−111.9 to 43.7
Suwa[15]	0.0002	−2.7	−14.2 to 8.8	43.8	−88.6 to 83.1

*Methods:
Radford: anatomic dead space in mL = actual weight in pounds
Nielsen: anatomic dead space in mL = ideal weight in pounds
Nunn: anatomic dead space in mL = actual weight in pounds − 72 mL
Casati: anatomic dead space in mL = 0.5 × actual weight in pounds
Suwa: anatomic dead space in mL = 0.66 × actual weight in pounds
CI = confidence interval

Table 2. Results From 3 Methods of Estimating Anatomic Dead Space Using Ideal Body Weight Rather Than Actual Weight

Method*	r^2	Mean Bias (mL)	95% CI of Bias (mL)	SD Bias (mL)	Limits of Agreement
Nunn (IBW)	0.058	−51.1	−60.5 to −41.7	35.9	−121.5 to 19.3
Casati (IBW)	0.058	−53.6	−62.3 to −44.9	33.0	−118.3 to 11.1
Suwa (IBW)	0.058	−28.7	−37.5 to −19.9	33.6	−94.6 to 37.1

*Methods:
Nunn: anatomic dead space in mL = ideal weight in pounds − 72 mL
Casati: anatomic dead space in mL = 0.5 × ideal weight in pounds
Suwa: anatomic dead space in mL = 0.66 × ideal weight in pounds
CI = confidence interval
IBW = ideal body weight

Table 3. Respiratory Variables*

Variable	Mean ± SD
Respiratory rate (breaths/min)	10.3 ± 2.3
Measurements per subject	103.5 ± 23.0
V_T (mL)	770.8 ± 193.7
V_T (mL/Kg ideal weight)	11.5 ± 2.6
V_T (mL/Kg actual weight)	9.3 ± 2.5
PEEP (cm H_2O)	2.3 ± 2.0
Inspiratory time (s)	1.9 ± 0.5
Dead space (mL)	
Measured	128.0 ± 33.8
Radford method	187.9 ± 42.3
Nielsen method	148.9 ± 22.7
Nunn method	115.9 ± 42.3
Casati method	94.0 ± 21.2
Suwa method	125.3 ± 28.2

PEEP = positive end-expiratory pressure

Figure 3 illustrates the Bland-Altman analysis for the Suwa method, which was the method with the lowest bias. Table 1 reports the r^2 values, mean bias, standard deviation of the bias, and limits of agreement for the 5 methods.

When we used the ideal body weight instead of actual body weight in the Nunn, Casati, and Suwa methods, the r^2 was 0.058 (Table 2).

The mean and standard deviation of the measured anatomic dead space were calculated for each patient. The mean measured anatomic dead space was 128 mL, and the mean intrapatient standard deviation of the measurements was 4.3 mL (range 1.2–8.7 mL). Table 3 shows the measured and calculated respiratory variables.

The ratio of mean measured anatomic dead space to mean predicted anatomic dead space was 1:1.10 with Nunn's classic method (actual weight − 72 mL), and 1:1.7 for the method ideal body weight − 72 mL. The ratios that were the closest to 1:1 were the Suwa method (1:1.02, with actual weight) and the Nielsen method (1:1.29).

Discussion

The poor correlation in the present data set between patient weight and measured anatomic dead space appears to conflict with the common practice of estimating anatomic dead space from body weight. Generally, it appears that the mean anatomic dead space in milliliters corresponds to the mean body weight in pounds for the overall population, since the line of identity passes through the data cluster. However, based on the variability of the measured values in our data for a given weight or ideal weight, there is no basis for estimating an individual patient's anatomic dead space volume from the body weight or ideal body weight. The Bland-Altman analysis, with both mean bias and limits of agreement, confirms that estimation and measurement are not interchangeable methods. Even if we had defined clinically acceptable mean bias and limits of agreement to be within 25% of the intended

minute ventilation, for a V_T of 330 mL (121 lb person ventilated with 6 mL/kg), none of the estimates of anatomic dead space could have been used interchangeably with the measurement.

We also repeated the Bland-Altman analyses on log-transformed data to give the methods the best possible chance to agree. The repeated analysis did not change our conclusion that the methods are not interchangeable. Bear in mind that the standard deviation values in Table 3 for each of the dead space estimation methods are representative of the range of heights and weights observed in this data set. A limitation of our study is that we obtained measurements from a relatively small number of patients. The r^2, bias, and standard deviation may be different with a larger sample size.

In Radford's original paper,[8] which proposed the 1 lb = 1 mL rule, the anatomic dead space was plotted as a function of body weight. On his plot the error bars indicate that the standard deviation of the anatomic dead space measurements was approximately 40 mL, which is similar to what we observed with the Radford method. Radford emphasized that the rule of 1 mL dead space per pound of body weight gives only a rough approximation of anatomic dead space, as evidenced by the large standard deviations of the data he presented. He warned that it is probably not justifiable to extend the dead-space-to-body-weight relationship to patients who weigh more than 200 lb. Radford also elected to ignore the evidence that anatomic dead space increased with age, for the purpose of his ventilation guidelines, because it was a small effect and was offset by the decreased carbon dioxide production with age. In fact, Radford did not advocate the use of a dead space estimate for anything but a way to simplify the ventilation guidelines he was proposing. It appears that the practice of estimating dead space from body weight has become a matter of convenience, but it was not Radford's intended message. His proposed ventilation guidelines, on the other hand, have stood the test of time and are still in wide use today as a starting point for setting automatic support ventilation and weaning protocols.[18,19]

Radford's ventilation nomogram, which was based on body weight, sex, and breathing frequency, required adjustment for the change in anatomic dead space associated with endotracheal intubation. For intubated patients he recommended a rough correction of subtracting from the total V_T a volume corresponding to half the body weight. This was based on the observation that the volume of the oro-nasal dead space and upper part of the trachea are approximately 50% of the total anatomic dead space.[20] Clearly, Radford did not intend the approximate 1:1 correlation between weight and anatomic dead space in the overall population to be used as an independent estimate of an intubated patient's anatomic dead space.

Anatomic dead space is not a fixed value for each individual; it is influenced by several factors, most importantly, position of the neck and jaw, anesthesia, drugs that act on the bronchiolar musculature, and ventilator settings.[4] These factors are likely to change during a ventilated patient's hospital stay, which supports repeated measurement rather than a one-time estimation of the anatomic dead space.

Precise knowledge of the anatomic dead space is more important with a smaller V_T, as in the ARDS Network ventilation recommendations.[9] The percentage of each breath lost to anatomic dead space ventilation increases as the V_T decreases. As an example, consider the average patient in our data set, who weighed the predicted 149 lb. With the ARDS Network protocol of 6 mL/kg ideal body weight, the V_T would be set to 406 mL. Our mean measured anatomic dead space was 128 mL, so 32% of every breath would be lost to dead-space ventilation. If V_T were set at 12 mL/kg, only 16% of each breath would be lost to dead space.

The Nunn method (ideal body weight) had a mean bias of −51.1 mL, compared to the measured value. If the average subject in our data set had been ventilated at 6 mL/kg ideal body weight, the measured alveolar V_T would have been 15% smaller than the estimate. If a clinician were to use the estimated rather than the measured dead space value, a respiratory rate of 20 breaths/min (minute ventilation of 8 L/min) could unintentionally lead to hypoventilation, because the alveolar minute ventilation would be 1 L/min less than assumed.

The mean bias results from each of the estimation methods reveal that the effective alveolar ventilation can be greater or less than expected if the patient-to-patient variation in anatomic dead space is not considered. In other words, if 2 patients with the same height, weight, and metabolic rate had different anatomic dead space volumes, the same ventilation protocol could yield different P_{aCO_2} values simply because their effective alveolar ventilations were different.

In the present study the mean clinician-selected V_T was 11.5 ± 2.6 mL/kg of ideal body weight (see Table 3). We performed a linear regression analysis of the differences between the estimate methods and the measured dead space versus V_T in mL/kg ideal body weight. The r^2 range was 0.017–0.16, which correspond to p values (for r) of 0.33 and 0.002, respectively. For actual V_T the r^2 range was 0.0016–0.077, which correspond to p values (for r) of 0.77 and 0.035, respectively. Therefore, in the present data set, we observed a range of very small r^2 values, with a range of no association to weak statistical association for the relationship between the V_T size and the measurement error of the estimates.

We also analyzed the influence of outliers on ventilation settings. The r^2 for measured dead space and V_T (mL/kg

ideal weight) was originally 0.06, and it was 0.005 after outliers were removed. Similarly, when outliers of inspiratory time were removed, r^2 decreased from 0.19 to 0.12. We had previously tested the effect of PEEP on anatomic dead space and found a strong correlation between increased PEEP (from 0 cm H_2O to 20 cm H_2O) and increased measured anatomic dead space, but in the present data set, which has a small range of PEEP, removing the outliers changed r^2 from only 0.05 to 0.07.

Quantification of physiologic dead space is clinically important. Nuckton et al observed that an increased dead space fraction (V_D/V_T) is independently associated with mortality in patients with ARDS.[21] Unfortunately, that study reported only the total pulmonary dead space, so it is not possible to reanalyze their results to separate anatomic dead space and alveolar dead space. In a subsequent paper, Kallet et al[22] found that patients with ARDS who had lower V_D/V_T had a better survival rate: the difference in V_D/V_T between survivors and nonsurvivors was about 0.1. A large proportion of the total dead space is anatomic dead space. Our data show that when the contribution of the variability in the anatomic dead space is considered, the V_D/V_T can change by ± 0.13 solely because of patient-to-patient differences in anatomic dead space. This means that the variability in anatomic dead space contributes to V_D/V_T measurements by a similar magnitude as the difference observed between survivors and nonsurvivors. It is likely that the prognostic value of V_D/V_T measurements is related to ventilation-perfusion mismatch and not to the percent of each breath lost in anatomic dead space. However, if anatomic dead space variability is not considered, then the relationship between V_D/V_T and ventilation-perfusion mismatch is weakened.

Consider a patient with a low V_D/V_T and an abnormally small anatomic dead space. Based on the V_D/V_T this patient might be considered to have a favorable prognosis, when in fact serious ventilation-perfusion mismatch problems are masked by the small anatomic dead space. The solution proposed by Moppett et al[23] is to calculate the ratio of alveolar dead space to alveolar V_T, rather than the total V_D/V_T. That is, measure the anatomic dead space, then subtract the anatomic dead space from both the total dead space and the V_T before calculating the ratio. The resulting V_D/V_T would be a ratio of alveolar dead space to alveolar V_T. Moppett et al speculated that the association Nuckton[21] and Kallet[22] observed between dead space ratio and mortality was probably due to disturbed ventilation-perfusion matching, and that the alveolar dead space ratio would be even more strongly associated with mortality. Drummond and Fletcher[24] pointed out that right-to-left shunting (intrapulmonary or intracardiac) affects the total dead space measurement, but not the anatomic dead space measurement. The idea of measuring anatomic dead space to estimate the uniformity of alveolar ventilation goes back

to 1944.[25-28] We suggest the use of direct anatomic dead space measurement in future studies, to develop better descriptions of the changes that occur in the alveolar dead space with lung injury.

It is important to ensure that the patient receives adequate V_T by minimizing unnecessary apparatus dead space.[10,11] Apparatus dead space affects both alveolar V_T and V_D/V_T, and Nuckton[21] and Kallet[22] ensured their V_D/V_T analyses were carried out with minimal apparatus dead space. Correct assessment of the effect of all series dead space (anatomic and apparatus) requires calculating the apparatus dead space and adding that volume to the estimated anatomic dead space. Direct measurement with volumetric capnography should combine both anatomic and apparatus dead volume into a single volume.

Conclusions

All these issues point to the need to use direct measurements of anatomic dead space, rather than estimation. The errors associated with estimations are less important with a larger V_T, but with a smaller V_T the percentage of each breath lost to anatomic dead space ventilation is greater. With volumetric capnography it is simple to directly measure anatomic dead space under every condition and use that measurement to inform treatment.

REFERENCES

1. Fowler WS. Lung function studies II: the respiratory dead space. Am J Physiol 1948;154(3):405-416.
2. DuBois AB, Fowler RC, Soffer A, Fenn WO. Alveolar CO2 measured by expiration into the rapid infrared gas analyzer. J Appl Physiol 1952;4(7):526-534.
3. Bartels J, Severinghaus W, Forster RE, Briscoe WA, Bates DV. The respiratory dead space measured by single breath analysis of oxygen, carbon dioxide, nitrogen or helium. J Clin Invest 1954;33(1):41-48.
4. Nunn's applied respiratory physiology, 6th edition. Philadelphia: Elsevier; 2005:118-120.
5. Respiratory physiology: the essentials, 2nd edition. Baltimore: Lippincott Williams & Wilkins; 1979:19.
6. Hlastala MP, Berger AJ. Physiology of respiration. Oxford University Press; 1996:73-74.
7. Ganong WF. Review of medical physiology, 19th edition. Stamford, Connecticut: Appleton & Lange; 1999.
8. Radford EP Jr. Ventilation standards for use in artificial respiration. J Appl Physiol 1955;7(4):451-460.
9. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000;342(18):1301-1308.
10. Hinkson C, Benson M, Stephens L, Deem S. The effects of mechanical dead space on P_{aCO_2} in patients receiving lung-protective ventilation (abstract). Respir Care 2006;51(11):1140.
11. LeBourdellès G, Mier L, Fiquet B. Comparison of the effects of head and moisture exchangers and heated humidifiers on ventilation and gas exchange during weaning trials from mechanical ventilation. Chest 1996;110(5):1294-1298.

12. Nielsen L. Assessing patients' respiratory problems. Am J Nurs 1980; 80(12):2192-2196.

13. Devine BJ. Gentamicin therapy. Drug Intell Clin Pharm 1974;8:650-655.

14. Nunn JF, Hill DW. Respiratory dead space and arterial to end-tidal carbon dioxide tension difference in anesthetized man. J Appl Physiol 1960;15:383-389.

15. Casati A, Fanelli G, Torri G. Physiological dead space/tidal volume ratio during face mask, laryngeal mask and cuffed oropharyngeal airway spontaneous ventilation. J Clin Anesth 1998;10(8):652-655.

16. Suwa K, Bendixen HH. Change in P_{aCO_2} with mechanical dead space during artificial ventilation. J Appl Physiol 1968;24(4):556-562.

17. Mantha S, Roizen MF, Fleisher LA, Thisted R, Foss J. Comparing methods of clinical measurement: reporting standards for Bland and Altman analysis. Anesth Analg 2000;90(3):593-602.

18. Petter AH, Chioléro RL Cassina T, Chassot P, Müller XM, Revelly JP. Automatic "respirator/weaning" with adaptive support ventilation: The effect on duration of endotracheal intubation and patient management. Anesth Analg 2003;97(6):1743-1750.

19. Sulzer CF, Chioléro R, Chassot P, Mueller X, Revelly J. Adaptive support ventilation for fast tracheal extubation after cardiac surgery: a randomized controlled study. Anesthesiology 2001;95(6):1339-1345.

20. Rohrer F. [Der Strömungswiderstand in den menschlichen Atemwegen und der Einfluss der unregelmässigen Verzweigung des Bronchialsystems auf den Atmungsverlauf in verschiedenen Lungenbezirken]. Pflügers Archiv Euro J Physiol 1915;162(5-6):225-299. *Article in German.*

21. Nuckton TJ, Alonso JA, Kallet RH, Daniel BM, Pittet JF, Eisner MD, Matthay MA. Pulmonary dead-space fraction as a risk factor for death in the acute respiratory distress syndrome. N Engl J Med 2002;347(17):850-852.

22. Kallet RH, Alonso JA, Pittet JF, 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.

23. Moppett IK, Gornall CB, Hardman JG. The dependence of measured alveolar deadspace on anatomical deadspace volume. Brit J Anaesth 2005;95(3):400-405.

24. Drummond GB, Fletcher R. Editorial II: Dead space: invasive or not? (editorial) Brit J Anaesth 2006;96(1):4-7.

25. Bateman JB. The measurement of intrapulmonary mixing and pulmonary midcapacity ("functional residual air"). Proc Staff Meet Mayo Clin 1946;21:112.

26. Birath G. Lung volume and ventilation efficiency; changes in collapse-treated and non-collapse-treated pulmonary tuberculosis and in pulmonectomy and lobectomy. Acta Med Scand 1944; (Suppl):154S.

27. Darling RC, Cournand A, Richards DW Jr. Studies on intrapulmonary mixture of gases: forms of inadequate ventilation in normal and emphysematous lungs, analyzed by means of breathing pure oxygen. J Clin Invest 1944;23(1):55-67.

28. Riley RL, Cournand A. Ideal alveolar air and the analysis of ventilation-perfusion relationships in the lungs. J Appl Physiol 1949; 1(12):825-847.