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PHYSIOLOGICAL NOTE

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Dead space

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Introduction

Dead space is that part of the tidal volume that does not participate in gas exchange. Although the concept of pulmonary dead space was introduced more than a hundred years ago, current knowledge and technical advances have only recently lead to the adoption of dead space measurement as a potentially useful bedside clinical tool.

Concept of dead space

The homogeneity between ventilation and perfusion determines normal gas exchange. The concept of dead space accounts for those lung areas that are ventilated but not perfused. The volume of dead space (Vd) reflects the sum of two separate components of lung volume: 1) the nose, pharynx, and conduction airways do not contribute to gas exchange and are often referred to as anatomical Vd or herein as airway Vd (Vd_{aw}); 2) well-ventilated alveoli but receiving minimal blood flow comprise the alveolar Vd (Vd_{alv}). Mechanical ventilation, if present, adds additional Vd as part of the ventilator equipment (endotracheal tubes, humidification devices, and connectors). This instrumental dead space is considered to be part of the Vd_{aw}. Physiologic dead space (Vd_{phys}) is comprised of Vd_{aw} (instrumental and anatomic dead space) and Vd_{alv} and it is usually reported in mechanical ventilation as the portion of tidal volume (Vt) or minute ventilation that does not participate in gas exchange [1, 2].

A device that measures partial pressures (PCO_2) or fractions (FCO_2) of CO_2 during the breathing cycle is called a capnograph. The equation to transform FCO_2 into PCO_2 is $PCO_2 = FCO_2$ multiplied by the difference between barometric pressure minus water-vapour pressure. Time-based capnography expresses the CO_2 signal as a function of time and from this plot mean expiratory (Douglas bag method) or end-expiratory (end-tidal) CO_2 values can be obtained. The integration of the volume signal using an accurate flow sensor (pneumotachograph) and CO_2 signal (with a very fast CO_2 sensor) is known as volumetric capnography. Combined with the measurement of arterial PCO_2 ($PaCO_2$) it provides a precise quantification of the ratio of Vd_{phys} to Vt. The three phases of a volumetric capnogram are shown in Fig. 1 and Fig. 2. The combination of airflow and mainstream capnography monitoring allows calculation of breath by breath CO_2 production and pulmonary dead space. Therefore, the use of volumetric capnography is clinically more profitable than time-based capnography.

Measurement of dead space using CO_2 as a tracer gas

Bohr originally defined Vd/Vt [2] as: $Vd/Vt = (F_ACO_2 - F_ECO_2)/F_ACO_2$, where F_ACO_2 and F_ECO_2 are fractions of CO_2 in alveolar gas and in mixed expired gas, respectively. End-tidal CO_2 is used to approximate F_ACO_2,

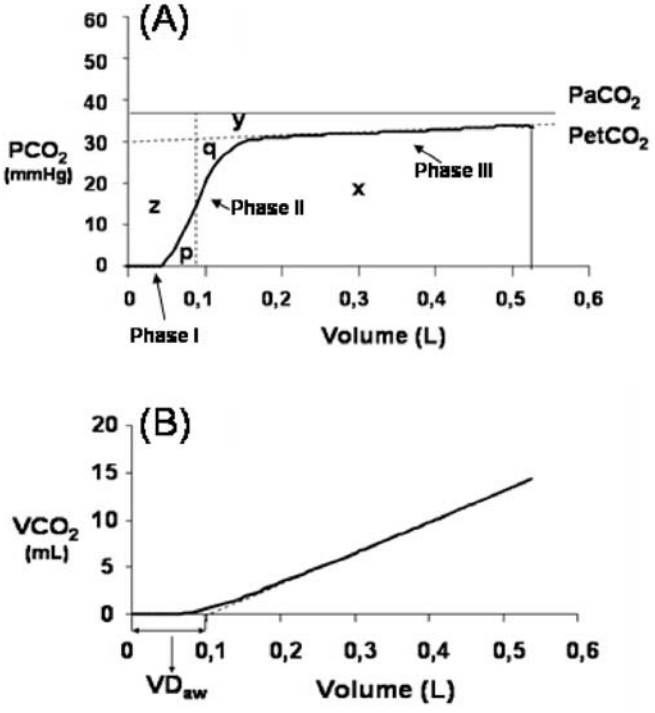

Fig. 1 **A** Single-breath expiratory volumetric capnogram recorded in a healthy patient receiving controlled mechanical ventilation. Dead-space components are shown graphically and equations are depicted and explained in the text. Phase I is the CO_2 free volume which corresponds to Vd_{aw}. Phase II represents the transition between airway and progressive emptying of alveoli. Phase III represents alveolar gas. $PaCO_2$ is arterial PCO_2; $PetCO_2$ is end-tidal PCO_2. Drawings adapted from [2]; **B** Single-breath expiratory carbon dioxide volume (VCO_2) plotted as a function of exhaled tidal volume. The alternative method to measure airway dead space (Vd_{aw}) described by Langley et al. [3] is graphically shown in a healthy patient receiving controlled mechanical ventilation

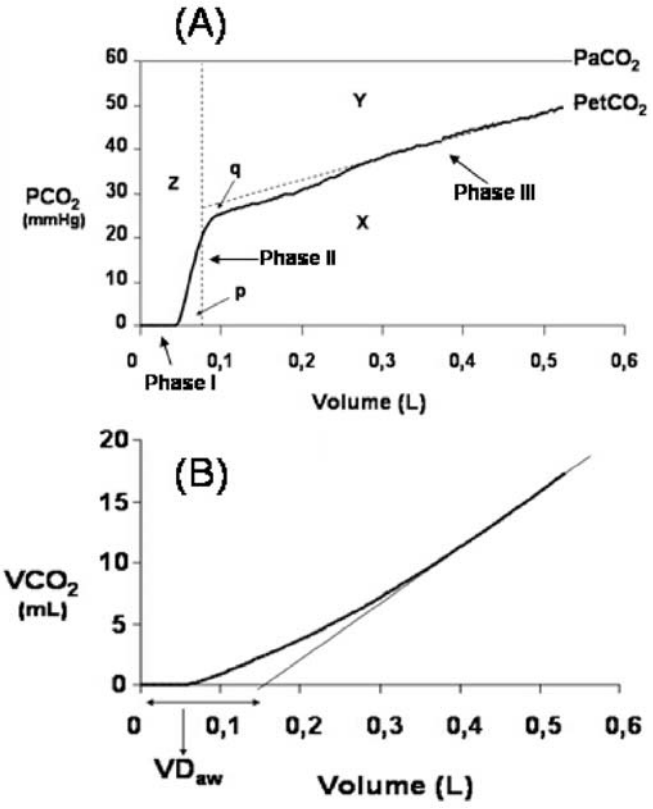

Fig. 2 **A** Single-breath expiratory volumetric capnogram recorded in a chronic obstructive pulmonary disease patient receiving controlled mechanical ventilation. The three phases of the volumetric capnogram are depicted. The transition from phase II to III is less evident due to heterogeneity of ventilation and perfusion ratios. Dead-space components are shown graphically and equations are depicted and explained in the text. $PaCO_2$ is arterial PCO_2; $PetCO_2$ is end-tidal PCO_2. Drawings adapted from [2]; **B** Single-breath expiratory carbon dioxide volume (VCO_2) plotted as a function of exhaled tidal volume. The alternative method to measure airway dead space (Vd_{aw}) described by Langley et al. [3] is graphically shown in a chronic obstructive pulmonary disease patient receiving controlled mechanical ventilation

assuming end-tidal and alveolar CO_2 fractions are identical. Physiologic dead space calculated from the Enghoff modification of the Bohr equation uses $PaCO_2$ with the assumption that $PaCO_2$ is similar to alveolar PCO_2 [2], such that: $Vd_{phys}/Vt = (PaCO_2 – P_ECO_2)/PaCO_2$, where P_ECO_2 is the partial pressure of CO_2 in mixed expired gas and is equal to the mean expired CO_2 fraction multiplied by the difference between the atmospheric pressure and the water-vapour pressure. Since Vd_{phys}/Vt measures the fraction of each tidal breath that is wasted on both Vd_{alv} and Vd_{aw}, the Vd_{aw} must be subtracted from Vd_{phys}/Vt to obtain the Vd_{alv}/Vt. Vd_{phys}/Vt is the most commonly and commercially (volumetric capnographs) formula used to estimate pulmonary dead space at the bedside.

Additional methods mostly used in research to calculate all the Vd components are shown in Fig. 1A and Fig. 2A. Fowler [1] introduced a procedure for measuring Vd_{aw} based on the geometric method of equivalent areas (p = q), obtained by crossing the back extrapolation of phase III of the expired CO_2 concentration over time with a vertical line traced so as to have equal p and q areas. Airway dead space is then measured from the beginning of expiration to the point where the vertical line crosses the volume axis [1]. By tracing a line parallel to the volume axis and equal to the $PaCO_2$, it is possible to determine the readings from areas y and z, which respectively represent the values of alveolar and airway dead space. Referring these values to the Vt, it is possible to single out several Vd components [2]:

$$Vd_{phys}/Vt = (Y + Z)/(X + Y + Z)$$

$$Vd_{alv}/Vt = Y/(X + Y + Z)$$

$$Vd_{aw}/Vt = Z/(X + Y + Z)$$

An alternative method to measure airway dead space introduced by Langley et al. [3] is based on determination of the VCO_2 value, which corresponds to the area inscribed within the CO_2 versus volume curve (indicated in Fig. 1A and Fig. 2A as X area). Figure 1B and Fig. 2B are examples of Vd_{aw} calculation using the Langley et al. [3] method. Briefly, VCO_2 is plotted versus expired breath volume. Thereafter, Vd_{aw} can be calculated from the value obtained on the volume axis by back extrapolation from the first linear part of the VCO_2 versus volume curve.

Although these indexes are clinically useful, they are always bound to visual criteria for the definition of phase III of the expired capnogram. Often, the geometric analysis establishing the separation between the phase II and phase III is hardly seen and the rate of CO_2 raising of the phase III is nonlinear in patients with lung inhomogeneities (Fig. 2A).

Utility of dead space in different clinical scenarios

The CO_2 tension difference between pulmonary capillary blood and alveolar gas is usually small in normal subjects and end-tidal PCO_2 is close to alveolar and arterial PCO_2. Physiologic dead space is the primary determinant of the difference between arterial and end-tidal PCO_2 (ΔPCO_2) in patients with a normal cardio-respiratory system. Patients with cardiopulmonary diseases have altered ventilation to perfusion (V_A/Q_T) ratios producing abnormalities of Vd, as well as in intrapulmonary shunt, and the latter may also affect the ΔPCO_2. A ΔPCO_2 beyond 5 mmHg is attributed to abnormalities in Vd_{phys}/Vt and/or by an increase in venous admixture (the fraction of the cardiac output that passes through the lungs without taking oxygen) or both. The increase in Vd_{phys}/Vt seen in normal patients when anaesthetised may be attributed to muscle paralysis, which causes a reduction of functional residual capacity and alters the normal distribution of ventilation and perfusion across the lung [2, 4, 5, 6].

Ventilation to regions having little or no blood flow (low alveolar PCO_2) affects pulmonary dead space. In patients with airflow obstruction, inhomogeneities in ventilation are responsible for the increase in Vd. Shunt increase VD_{phys}/Vt as the mixed venous PCO_2 from shunted blood elevates the $PaCO_2$, increasing VD_{phys}/Vt by the fraction that $PaCO_2$ exceeds the nonshunted pulmonary capillary PCO_2 [7]. Vd_{alv} is increased by shock states, systemic and pulmonary hypotension, obstruction of pulmonary vessels (massive pulmonary embolus and microthrombosis), even in the absence of a subsequent decrease in ventilation and low cardiac output. Vd_{aw} is increased by lung overdistension and additional ventilatory apparatus dead space. Endotracheal tubes, heat and moisture exchangers, and other common connectors may increase ventilator dead space and induce hypercapnia during low Vt or low minute ventilation. Vd_{aw} calculations include the ventilator dead space. Because the anatomic dead space remains relatively constant as Vt is reduced, very low Vt is associated with a high Vd/Vt ratio [1, 2, 7, 8, 9].

Positive end-expiratory pressure (PEEP) is used to increase lung volume and to improve oxygenation in patients with acute lung injury. Vd_{alv} is large in acute lung injury and does not vary systematically with PEEP. However, when the effect of PEEP is to recruit collapsed lung units resulting in an improvement of oxygenation, Vd_{alv} may decrease, and alveolar recruitment is associated with decreased arterial minus end-tidal CO_2 difference [4, 5, 6]. Conversely, PEEP-induced overdistension may increase Vdalv and widen this difference [7].

In patients with sudden pulmonary vascular occlusion due to pulmonary embolism, the resultant high V_A/Q_T mismatch produces an increase in Vd_{alv}. The association of a normal D-dimer assay result plus a normal Vd_{alv} is a highly sensitive screening test to rule out the diagnosis of pulmonary embolism [9].

Dead space and outcome prediction

Characteristic features of acute lung injury are alveolar and capillary endothelial cell injuries that result in alterations of pulmonary microcirculation. Consequently, adequate pulmonary ventilation and blood flow across the lungs are compromised and Vd_{phys}/Vt increases. A high dead-space fraction represents an impaired ability to excrete CO_2 due to any kind of V_A/Q_T mismatch [7]. Nuckton et al. [10] demonstrated that a high Vd_{phys}/Vt was independently associated with an increased risk of death in patients diagnosed with acute respiratory distress syndrome.

Conclusions

The advanced technology combination of airway flow monitoring and mainstream capnography allows breath-by-breath bedside calculation of pulmonary Vd and CO_2 elimination. For these reasons, the use of volumetric capnography is clinically more useful than time capnography. Measurement of dead-space fraction early in the course of acute respiratory failure may provide clinicians with important physiologic and prognostic information. Further studies are warranted to assess whether the continuous measurement of different derived capnographic indices is useful for risk identification and stratification, and to track the effect of a therapeutic intervention during the course of disease in critically ill patients.

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