

What Do Dead-Space Measurements Tell Us About the Lung With Acute Respiratory Distress Syndrome?

In this issue of *RESPIRATORY CARE*, Kallet et al¹ describe the prognostic value of sequential dead-space measurements in patients with acute respiratory distress syndrome (ARDS). The simple calculation using arterial and mixed expired partial pressures of carbon dioxide (the Enghoff modification of the Bohr dead-space equation: physiologic dead-space volume divided by tidal volume [V_D/V_T]) is more convenient to acquire the data for, and simpler than the calculation of shunt or venous admixture. The data from Kallet et al¹ show that dead space is a useful index of lung dysfunction and a predictor of survival.

SEE THE ORIGINAL STUDY ON PAGE 1008

However, interpreting the pathophysiology that leads to increased V_D/V_T in an ARDS patient is more complex than the simple concept of dead space that we introduce to students in beginning respiratory physiology. Nuckton et al² measured V_D/V_T during the first 24 hours of ARDS and found that the single initial V_D/V_T measurement outperformed other readily available bedside measurements as a predictor of mortality. However, a high V_D/V_T in ARDS does not primarily reflect increased ventilation to unperfused areas of lung, as Nuckton et al originally suggested. Though there is no question that ARDS is characterized by patchy areas of severe vascular damage, no studies have demonstrated that those heavily damaged areas receive any appreciable ventilation, as would be required for the existence of regions of high alveolar-ventilation-to-perfusion ratio (\dot{V}_A/\dot{Q}). In fact, 4 studies that used the multiple inert gas elimination technique (MIGET) with ARDS patients found that less than one quarter of the patients had discrete high- \dot{V}_A/\dot{Q} regions that could contribute substantially to elevated V_D/V_T .³⁻⁶ Nevertheless, Nuckton et al and Kallet et al document that elevated carbon dioxide V_D/V_T is a universal finding with ARDS patients from the onset of the illness. How can this apparent paradox be resolved?

In abnormal lungs an increased V_D/V_T reflects a global assessment of abnormal gas exchange, not simply the contribution of discrete high- \dot{V}_A/\dot{Q} regions and true anatomic dead space. Hence, V_D/V_T can be increased by shunt, \dot{V}_A/\dot{Q} heterogeneity across the entire spectrum from low to high \dot{V}_A/\dot{Q} regions, anemia, and by increased anatomic dead space. Hlastala and Robertson presented an inert gas model that demonstrated that the levels of shunt and mid-range \dot{V}_A/\dot{Q} heterogeneity commonly observed in ARDS substantially increase the carbon dioxide V_D/V_T , without high \dot{V}_A/\dot{Q} .⁷ In human ARDS studies that used MIGET, the primary gas exchange abnormalities were shunt and increased mid-range \dot{V}_A/\dot{Q} heterogeneity, with only an inconsistent component of ventilation to high- \dot{V}_A/\dot{Q} units.³⁻⁶ Severe anemia decreases the functional solubility of carbon dioxide in blood and increases the dead-space measurement, albeit by a lesser amount.

To analyze the various components of \dot{V}_A/\dot{Q} abnormality that contribute to elevated V_D/V_T , Coffey et al used MIGET to study dogs with acute oleic-acid injury.⁸ Various levels of positive end-expiratory pressure (PEEP) were used to alter the fractional contribution of each \dot{V}_A/\dot{Q} abnormality (shunt, mid-range \dot{V}_A/\dot{Q} heterogeneity, high \dot{V}_A/\dot{Q} peaks, and anatomic dead space) to the V_D/V_T . After injury, application of low-level PEEP reduced the overall V_D/V_T , primarily by reducing shunt. At the highest PEEP level, discrete high- \dot{V}_A/\dot{Q} regions developed, but that V_D/V_T augmentation was counterbalanced by reduced shunt and mid-range \dot{V}_A/\dot{Q} . The net result (reduced V_D/V_T) was relatively constant at all PEEP levels, despite there being different physiologic components contributing to the measurement. Ralph et al⁴ studied human ARDS responses to PEEP and found less predictable development of discrete high- \dot{V}_A/\dot{Q} peaks with the highest PEEP levels applied.⁴ The difference may have been because the human progressive-PEEP trials were stopped when a 20% reduction in cardiac output was observed, whereas the animals in the study by Coffey et al⁸ had a > 50% reduction in cardiac output at the highest PEEP level. The Coffey et al study⁸ demonstrated that animals with the same V_D/V_T at different PEEP levels had very different components of physiologic abnormalities. Likewise, it is plausible that 2 patients with ARDS who have identical V_D/V_T elevations might have

Correspondence: H Thomas Robertson MD, Box 356522, University of Washington Medical Center, Seattle WA 98195-6522. E-mail: tomrobt@u.washington.edu.

different physiological components explaining their V_D/V_T elevation. At this point we can only speculate as to whether knowledge of the physiologic components responsible for the elevated V_D/V_T in ARDS would provide additional prognostic information.

Kallet et al¹ demonstrate that, with patients who have ARDS, V_D/V_T is an easily obtained indicator of pulmonary gas exchange efficiency and that V_D/V_T has good clinical prediction characteristics. The value of V_D/V_T as a global index of lung dysfunction ought not be surprising, as it incorporates all the mechanisms by which gas exchange abnormalities can manifest in ARDS. Based on the most sophisticated MIGET measurements of gas exchange in patients with ARDS, an increased V_D/V_T (as calculated with the Bohr-Enghoff equation) usually represents a combination of shunt and mid-range- \dot{V}_A/\dot{Q} heterogeneity rather than discrete high- \dot{V}_A/\dot{Q} regions alone. However, regardless of the physiologic interpretation of the elevated V_D/V_T in a given patient, the clinical prognostic value of the measurement described by Kallet et al stands unchallenged.

H Thomas Robertson MD
Erik R Swenson MD

Division of Pulmonary and Critical Care Medicine
University of Washington
Seattle, Washington

REFERENCES

1. 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.
2. 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;346(17):1281–1286.
3. Dantzker DR, Brook CJ, Dehart P, Lynch JP, Weg JG. Ventilation-perfusion distributions in the adult respiratory distress syndrome. *Am Rev Respir Dis* 1979;120(5):1039–1052.
4. Ralph DD, Robertson HT, Weaver LJ, Hlastala MP, Carrico CJ, Hudson LD. Distribution of ventilation and perfusion during positive end-expiratory pressure in the adult respiratory distress syndrome. *Am Rev Respir Dis* 1985;131(1):54–60.
5. Melot C, Lejeune P, Leeman M, Moraine JJ, Naeije R. Prostaglandin E1 in the adult respiratory distress syndrome: benefit for pulmonary hypertension and cost for pulmonary gas exchange. *Am Rev Respir Dis* 1989;139(1):106–110.
6. Feihl F, Eckert P, Brimiouille S, Jacobs O, Schaller M-D, Melot C, Naeije R. Permissive hypercapnia impairs pulmonary gas exchange in the acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2000;162(1):209–215.
7. Hlastala MP, Robertson HT. Inert gas elimination characteristics of the normal and abnormal lung. *J Appl Physiol* 1978;44(2):258–266.
8. Coffey RL, Albert RK, Robertson HT. Mechanisms of physiological dead space response to PEEP after acute oleic acid lung injury. *J Appl Physiol* 1983;55(5):1550–1557.