Introduction

First described in 1967, acute respiratory distress syndrome (ARDS) is a difficult disease to manage and is associated with high mortality.1 Furthermore, laboratory and clinical research suggests that the use of a conventional tidal volume (V_T) (10–12 mL/kg) may result in ventilator-induced lung injury, which contributes to poor outcome.2 A recent large prospective randomized study found that the use of lower V_T (6 mL/kg predicted body weight versus conventional V_T of 12 mL/kg) reduced mortality from 39.8% to 31%.3 This lower-V_T method is known as lung-protective ventilation.

With the increased use of lung-protective ventilation in adult patients with ARDS/acute lung injury (ALI), new interest has arisen over the most efficacious configuration for the ventilator circuit. Of particular interest is the question of whether the dead space (V_D) of the apparatus in a standard ventilator circuit (such as the flexible tubing and heat-and-moisture exchanger [HME]) significantly affects the total V_D and ventilation requirements in patients with...
ARDS/ALI. When $V_T$ is in the 8–12 mL/kg range, apparatus $V_D$ may not be an important factor in determining total ventilatory requirements, but this may not be the case during low-$V_T$ ventilation. In addition, patients with ARDS have severe gas-exchange impairment, including compromised CO$_2$ elimination, which makes normalizing the $P_{CO_2}$ difficult or impossible in many cases.\cite{5} We hypothesized that the removal of all apparatus $V_D$ from a ventilator circuit during lung-protective ventilation would reduce $P_{aCO_2}$, increase pH, and allow a reduction in minute ventilation ($V_E$).

**Methods**

The study was conducted between September 28, 2004, and January 18, 2005, at Harborview Medical Center, which is a level-one trauma, burn, and acute-care hospital in Seattle, Washington. Patients who met the study criteria were managed according to a local protocol that is based on the ARDS Network protocol for lung-protective ventilation.\cite{3} The University of Washington investigational review board approved the study, and informed consent was obtained from each patient’s legal next of kin prior to any data collection. Patients were studied nonconsecutively.

At the time of the study, the patients were not undergoing any procedures and were reasonably calm and synchronous with the ventilator (Servo 300, Siemens/Maquet, Bridgewater, New Jersey). A respiratory monitor (CO$_2$SMO Plus 8100, Novametrix Medical Systems, Wallingford, Connecticut) was connected at the circuit Y-piece going any procedures and were reasonably calm and synchronous with the ventilator. The device was warmed and calibrated. Three ventilator-circuit configurations were tested:
1. Standard hygroscopic HME (Humid-Vent Filter Light, Hudson RCI, Research Triangle Park, North Carolina) with approximately 15-cm piece of flexible tubing (Tube-Flex, Puritan Bennett, Pleasanton, California)
2. Flexible tubing (approximately 15 cm) only
3. No HME or flexible tubing

The order of configuration was randomized for each patient, and the baseline configuration was the setup the patient had at the time of the study.

After 15 min on one of the circuit configurations, an arterial blood sample was drawn from an indwelling catheter, and, from the patient’s exhaled gas we measured end-tidal carbon dioxide, mixed expired carbon dioxide, and carbon-dioxide production. Blood pressure, heart rate, and respiratory rate were monitored. $V_T$, set respiratory rate, positive end-expiratory pressure, and fraction of inspired oxygen were maintained constant throughout the study period. Then the circuit was changed to the next configuration and, after 15 min elapsed, the data gathering was repeated with that circuit configuration.

The data were analyzed using spreadsheet software (Excel, Microsoft, Redmond, Washington) and graphing software (Prism, GraphPad Software, San Diego, California).

Physiologic $V_D$ ($V_D/V_T$) was calculated using the Enghoff modification of the Bohr equation:\cite{7}

$$V_D/V_T = (P_{aCO_2} - P_{eCO_2})/P_{aCO_2}$$

in which $P_{eCO_2}$ is the mixed expired pressure of carbon dioxide.

The data are presented as mean ± standard deviation. Differences between conditions were compared using a paired $t$ test with the Bonferroni correction for multiple comparisons. Differences were considered significant when $p < 0.05$. Linear regression was performed to determine the correlation coefficient between the fraction of apparatus $V_D$ (normalized to the maximum [HME + flexible tubing]) and the mean of measured variables, with linearity confirmed with the runs test.

**Results**

Seven patients were enrolled in the study (Table 1). The volume of the HME was 60 mL, and that of the flexible tubing was 55 mL, for a total maximum apparatus $V_D$ of 115 mL. Removal of the HME from the circuit decreased $V_D/V_T$ by approximately 6% ($p = 0.01$) and decreased $P_{aCO_2}$ by 5 mm Hg ($p = 0.007$) (Fig. 1). Removing both the HME and the flexible tubing decreased $V_D/V_T$ by an additional 5% ($p = 0.007$) and decreased $P_{aCO_2}$ by an additional 6 mm Hg ($p = 0.03$). Removing both the HME and the flexible tubing allowed for a $V_E$ decrease, from a mean of 11.51 L/min to 10.35 L/min ($p = 0.02$) and increased pH from 7.30 to 7.38 ($p = 0.005$) (Fig. 2). The relationships between apparatus $V_D$ and $V_D/V_T$ and $V_E$ were linear, with correlation coefficients of 0.99 and 0.94, respectively. With removal of apparatus $V_D$ there was a trend toward increased carbon-dioxide production, but there were no significant changes in mean arterial pressure, $P_{aO_2}$, or heart rate (Table 2).

Four of the studied patients were receiving $V_T$ of 6 mL/kg, whereas the other 3 patients were receiving 4 mL/kg. Reductions in $V_D/V_T$ and $P_{aCO_2}$ occurred in both groups, although the effects tended to be larger among the patients receiving 4 mL/kg. For example, comparing the maximum and minimum apparatus $V_D$, $P_{aCO_2}$ fell from 68 ± 10 mm Hg to 51.7 ± 8.4 mm Hg in patients who received $V_T$ of 4 mL/kg, whereas $P_{aCO_2}$ fell from 59.5 ± 14.5 mm Hg to...
ARDs/ALI is characterized by severe ventilation-perfusion mismatch, due to increased pulmonary vascular permeability and alveolar injury, leading to alveolar flooding, disruption of the hypoxic vasoconstriction response, and shunting due to collapsed alveolar units. The result is severe compromise of pulmonary gas exchange, with resulting hypoxemia and hypercapnia, which is frequently resistant to conventional oxygen therapy and mechanical ventilatory support. The gas-exchange abnormality can be further demonstrated by an increase in the Enghoff modification of the Bohr VD/VT (physiologic VD/VT). The increased VD/VT is believed to be due primarily to areas of shunt and low alveolar ventilation-perfusion rather than areas of high alveolar ventilation-perfusion, but the net result remains impaired CO₂ elimination, with consequent hypercapnia and respiratory acidosis, despite increased intensity of ventilatory support.

### Discussion

52.7 ± 15.3 mm Hg in patients who received 6 mL/kg (ie, 25% versus 17% relative change, p = 0.007 for difference between groups).
In patients who received low VT as part of a lung-protective strategy, the apparatus V_D of the ventilator circuit may also contribute to impaired CO2 elimination and hypercapnia. For example, the HME used in our study had a V_D of 60 mL and the flexible tubing had a V_D of 55 mL. The baseline apparatus V_D was 15 mL for the CO2 monitor and inline suction catheter, whereas the VT ranged from 270 mL to 465 mL, with a mean of 337 ± 80 mL. The apparatus V_D with both the HME and the flexible tubing accounted for 40.3 ± 8.5% of the VT, and the apparatus V_D of the flexible tubing alone accounted for 21.7 ± 4.6% of VT. The baseline apparatus V_D accounted for 4.6 ± 1.0%. Indeed, we found that removal of the HME and flexible tubing from the ventilator circuit reduced V_D/VT, which significantly reduced PaCO2 at a lower total VE. Removal of apparatus V_D was also associated with a clinically relevant increase in arterial-blood pH.

Patients on lung-protective ventilation with impaired CO2 elimination may benefit from the removal of all possible apparatus V_D, for 3 reasons. First, removal of apparatus V_D reduces hypercapnia and increases arterial-blood pH. Second, a reduction in ventilatory demand, with an associated decrease in VE, may decrease air trapping and intrinsic positive end-expiratory pressure, with consequent reduced intrathoracic pressure, improved hemodynamics, and lower intracranial pressure. The latter is supported by observations of the effects of HMEs on ventilatory mechanics in spontaneously breathing patients. Third, the improved CO2 elimination may allow reducing VT or respiratory rate, which may reduce gas trapping and ventilator-induced lung injury.

There is ongoing debate regarding the harm or benefits of hypercapnia on gas exchange and lung injury. Experimental models suggest that inhalation of CO2 to induce hypercapnic acidosis improves PaO2 in animals with normal lungs. Inhaled CO2 attenuated lung injury in experimental models. In contrast, inducing hypercapnia by reducing VE increased lung injury in rabbits treated with lipopolysaccharide. In addition, the benefits of therapeutic or passive hypercapnia on gas exchange or lung injury have not been reproduced in patients with severe lung injury. A recent retrospective analysis of data from the original ARDS Network lung-protective-ventilation trial found that hypercapnia did not affect mortality in patients ventilated with low VT (6 mL/kg) but was associated with a mortality reduction in the high-VT group.

Similar to other investigators, we found no PaO2 effect from manipulation of apparatus V_D and the associated changes in PaCO2. Thus it would be premature to recommend hypercapnic acidosis as a protective or therapeutic strategy in patients with ARDS and ALI, particularly when induced by a reduction in VE.

Two other studies have examined the effects of apparatus V_D on ventilation in ARDS. Prin et al studied 11 patients with ARDS. In that study the HME, which had an apparatus V_D of 100 mL, was removed when PaCO2 exceeded 55 mm Hg. That study found a pH increase, from 7.20 ± 0.08 to 7.26 ± 0.06 (p < 0.005) and PaCO2 reduction from 67 ± 9 mm Hg to 56 ± 6 mm Hg (p < 0.003). In another study Prat et al studied the effects of various-size apparatus V_D, ranging from 120 mL to 0 mL. They found a pH increase, from 7.18 ± 0.08 to 7.28 ± 0.08 (p < 0.05), and PaCO2 reduction, from 80.3 ± 20 mm Hg to 63.6 ± 13 mm Hg (p < 0.05).

Our study differs from the latter 2 studies in a couple of ways. First, we did not modify the patients’ ability to control their ventilation. Prin et al administered cisatracurium during the study procedure, and Prat et al maintained their patients’ sedation level to achieve a Ramsey score of 6, resulting in a fixed VE in both studies. In our study the patients were able to adjust VE with the changes in apparatus V_D, and V_D removal significantly reduced VE, which may reduce air trapping and allow reduction in the intensity of ventilation. We found pH and PaCO2 improvements comparable to the previous studies, despite the fact that we reduced the VE. Second, the VT in our study (5.3 ± 1 mL/kg) was lower than in the studies by Prin et al (7.6 ± 0.6 mL/kg) and Prat et al (6.9 ± 1.8 mL/kg).

| Table 2. Effect of Circuit Configuration on Gas Exchange and Vital Signs* |
|-----------------|-----------------|-----------------|
| Variable        | Flexible Tubing and HME | Flexible Tubing Only | No Flexible Tubing or HME |
| Arterial pressure (mm Hg) | 85 ± 12 | 81 ± 16 | 80 ± 13 |
| Heart rate (beats/min) | 104 ± 21 | 101 ± 20 | 95 ± 20 |
| PaO2 (mm Hg) | 77 ± 17 | 80 ± 23 | 81 ± 23 |
| VCO2 (mL/min) | 147 ± 56 | 172 ± 59 | 175 ± 51 |
| f (breaths/min) | 35.4 ± 6.6 | 34.3 ± 6.8† | 31.9 ± 6.3‡ |

*Values are mean ± SD
†p < 0.05 versus no flexible tubing, no HME
‡p < 0.05 versus flexible tubing and HME
HME = heat-and-moisture exchanger
VT = carbon dioxide production
The routine removal of apparatus VD from the ventilator circuit during lung-protective ventilation has some theoretical disadvantages. The absence of the flexible tubing can increase tension on the ventilator circuit and potentially increase the risk of inadvertent extubation. Removing the HME from the circuit necessitates the use of a more costly active heated humidifier device. However, for patients with severe gas-exchange abnormalities and associated hypercapnia and respiratory acidosis, removal of apparatus VD offers an important clinical benefit and should be routinely considered.

Conclusion

In patients with ARDS or ALI receiving lung-protective ventilation, removing all possible apparatus VD reduces PaCO2 and increases pH, at a lower VE. We recommend a circuit with the minimum possible apparatus VD for adults, and practice guidelines that trigger removal of VD from the circuit.

REFERENCES