Effect of Interfacing between Spontaneous Breathing and Mechanical Cycles on the Ventilation-Perfusion Distribution in Canine Lung Injury

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Background: Improved matching between ventilation and perfusion (V\textsubscript{A}/Q) has been proposed to be a major advantage of partial ventilatory support compared with controlled mechanical ventilation. This study was designed to determine whether a difference in gas exchange exists between partial ventilatory support techniques that allow unsupported spontaneous breathing to occur during any phase of the mechanical ventilatory cycle and those that provide mechanical support for each spontaneous inspiratory effort.

Methods: Ten anesthetized dogs with oleic acid–induced lung injury received, in random order, pressure-support ventilation (PSV) and airway pressure–release ventilation (APRV) with and without spontaneous breathing using equivalent airway pressure limits. Gas exchange was assessed by conventional blood gas analysis and by estimating the V\textsubscript{A}/Q distributions using the multiple inert-gas elimination technique.

Results: During APRV, spontaneous breathing accounted for 10 ± 1% of the total expiratory minute ventilation. Breath-to-breath ventilatory support with PSV resulted in the highest total expiratory minute ventilation (P < 0.05). During spontaneous breathing with APRV, cardiac output increased from 3.9 ± 0.3 to 4.6 ± 0.4 1·min\textsuperscript{-1} (P < 0.05), arterial oxygen tension from 75 ± 3 to 107 ± 8 mmHg (P < 0.05), and oxygen delivery from 507 ± 47 to 719 ± 73 ml·kg\textsuperscript{-1}·min\textsuperscript{-1} (P < 0.05). PSV did not increase cardiac output, arterial oxygen tension, and oxygen delivery. Spontaneous breathing did not increase oxygen consumption. During APRV spontaneous breathing accounted for a 13 ± 2% decrease (P < 0.05) in blood flow to shunt units (V\textsubscript{A}/Q < 0.005) and a 14 ± 2% increase (P < 0.05) in the perfusion of normal V\textsubscript{A}/Q units (0.1 < V\textsubscript{A}/Q < 10). Pulmonary blood flow distribution to shunt and normal V\textsubscript{A}/Q units was similar during PSV and APRV without spontaneous breathing. Dead space (V\textsubscript{A}/Q > 100) ventilation decreased by 6% during APRV with spontaneous breathing compared with PSV (P < 0.05).

Conclusions: Spontaneous breathing superimposed on mechanical ventilation contributes to improved V\textsubscript{A}/Q matching and increased systemic blood flow. Apparently, the spontaneous contribution to a mechanically assisted breath during PSV is not sufficient to counteract the V\textsubscript{A}/Q maldistribution of positive pressure lung insufflation during acute lung injury. (Key words: Lungs: ventilation–perfusion distribution. Measurement techniques: multiple inert-gas elimination. Ventilation, mechanical: airway pressure–release; pressure-support.)

PARTIAL ventilatory support is commonly used, not only to separate patients from mechanical ventilation, but also to provide stable ventilatory assistance of a desired degree. An improvement in matching between ventilation and perfusion (V\textsubscript{A}/Q) is commonly considered a major advantage of partial ventilatory support compared with controlled mechanical ventilation.¹ This presumably results from augmented distribution of ventilation to dependent, well-perfused lung regions during diaphragmatic contraction.²,³ Wolff et al.⁴ have shown that during synchronized intermittent mandatory ventilation, the efficiency of alveolar carbon dioxide removal of an assisted breath is no better than that of a purely mechanical one. Therefore, the advantage of partial ventilatory support rests completely on the efficiency of the unsupported spontaneous breathes.⁴ Furthermore, no improvement in overall V\textsubscript{A}/Q matching has been observed during breath-to-breath partial ventilatory support with pressure-support ventilation (PSV) compared with controlled mechanical ventilation.⁵ Previous results from our laboratory indicate that a significant improvement in pulmonary gas exchange occurs if even minimal spontaneous ventilation is allowed during airway pres-

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sure--release ventilation (APRV) and biphasic positive airway pressure. These techniques allow unsupported spontaneous breathing in any phase of the mechanical ventilatory cycle, which is accomplished with periodic switching between two levels of continuous positive airway pressure.\textsuperscript{7-10}

We hypothesized that uncoupling of spontaneous and mechanical breaths would provide better $V_{A}/Q$ matching than breath-to-breath, synchronized, partial ventilatory support. To test this hypothesis, we examined the $V_{A}/Q$ distributions with the multiple inert-gas elimination technique during APRV, with and without spontaneous breathing, and during PSV, using equivalent airway pressures, in dogs with oleic acid--induced lung injury.

**Materials and Methods**

**Instrumentation**

After approval by the local Laboratory Animal Care and Use Committee, ten mongrel dogs weighing 22–28 kg (24.6 ± 2.4 kg, mean ± SD), were anesthetized with intravenous sodium pentobarbital; a bolus of 12 mg kg$^{-1}$, followed by an infusion of 20 $\mu$g kg$^{-1}$·min$^{-1}$. The animals were placed supine, and their tracheas intubated with a 9-mm internal diameter cuffed tracheal tube (Mallinckrodt, Argyle, NY). All dogs breathed room air spontaneously at ambient airway pressure throughout instrumentation. A catheter was inserted in a femoral artery and a 7-French thermostistor-tipped triple-lumen pulmonary artery catheter (93A-131-7F, Baxter Edwards Critical Care, Irvine, CA) was placed through a femoral vein.

**Cardiovascular Measurements**

Systemic blood pressure and central venous, pulmonary artery, and pulmonary artery occlusion pressures were transduced (Transpac II, Abbott Critical Care, Chicago, IL) and recorded (TA 2600, Statham Gould, Oxnard, CA). A horizontal plane through the shoulder was taken as zero reference point for blood pressure measurements. Cardiac output was measured with the thermal dilution technique (Oximetrix 3, Abbott Critical Care). Ten milliliters of iced 5% dextrose solution was used as indicator, and an average of three determinations were performed at random moments during the ventilatory cycle.

**Ventilatory Measurements**

Gas flow was measured between the proximal end of the tracheal tube with a heated pneumotachograph (3791, Hans Rudolph, Kansas City, MO), connected to a differential pressure transducer (DP 1030871, Validyne, Northridge, CA). Tidal volume ($V_t$) and expiratory minute ventilation ($\dot{V}e$) were derived from the integrated gas flow signal. In addition, $V_t$ was measured with a calibrated Wright respirometer at the outlet of the gas mixing chamber, which was connected to the expiratory port of the ventilator (Evita, Dräger, Chantilly, VA). The breathing circuit had an internal compliance of 0.9 ml·cmH$_2$O$^{-1}$. Airway pressure was measured at the proximal end of the tracheal tube with a differential gas-pressure transducer (MP45-871, Validyne, Northridge, CA). Esophageal pressure ($P_{eo}$) was measured with a balloon catheter (length 10 cm and internal diameter 1.4 cm; Mallinckrodt, Argyle, NY) filled with ≤0.5 ml air and connected to a differential pressure transducer connected to a differential pressure transducer (MP45-871, Validyne, Northridge, CA). The esophageal balloon had a flat pressure–volume curve over a volume range of 0.2–7 ml air. The validity of the esophageal balloon technique for measuring respiratory mechanics in the supine subject was tested with the occlusion method of Baydur et al.\textsuperscript{11} Intrinsic positive end-expiratory pressure was estimated as negative deflection in $P_{eo}$ from the onset of inspiratory effort to the point of zero flow as described previously.\textsuperscript{12} All pressures were averaged over a period of 5 min.

**Physiologic Gas Analysis**

Arterial and venous blood oxygen and carbon dioxide tensions and $\text{pH}$ were determined immediately after sampling with standard blood gas electrodes (1303, Instrumentation Laboratories, Lexington, MA). Oxygen saturation of the arterial and mixed venous blood and total hemoglobin, carboxyhemoglobin, and methemoglobin concentrations were determined by spectrophotometry with a CO-oximeter (282, Instrumentation Laboratories). Fractions of inspired oxygen, carbon dioxide, and nitrogen and fractions of mixed expired oxygen, carbon dioxide, and nitrogen were determined with a Raman scattering gas analyzer (Rascal II, Ohmeda, Louisville, CO).\textsuperscript{13}

**Inert Gas Analysis**

The method for estimating the distributions of continuous $V_{A}/Q$ ratios was described by Wagner et al.\textsuperscript{14,15} Six inert gases (sulfur hexafluoride, ethane, cyclopropane, enflurane, diethyl ether, and acetone) were dissolved in lactated Ringer's solution and infused into a peripheral vein with a constant rate set at about 0.05%
of $\dot{V}e$ for at least 40 min. Arterial and mixed venous blood samples were collected during stable conditions confirmed by constancy of $\dot{V}e$, fraction of mixed expired oxygen, fraction of mixed expired carbon dioxide, and cardiac output. Expired gas samples were collected after blood samples with an appropriate time delay from the heated mixing chamber. Inert gases were extracted, their concentrations measured with a gas chromatograph (HP 5890, Hewlett-Packard, Waltham, MA) and their blood–gas partition coefficients determined as described previously.

**Data Analysis**

Arterial to mixed venous (retention) and mixed expired to mixed venous (excretion) concentration ratios of the inert gases were used to obtain retention and excretion solubility curves. By formal mathematical analysis with enforced smoothing, these relations were transformed into a 50-compartmental distribution plot of blood flow and ventilation against $\dot{V}a/\dot{Q}$. Intrapulmonary shunt defined as fraction of pulmonary blood flow ($\dot{Q}p$) perfusing essentially nonventilated alveoli ($\dot{V}a/\dot{Q} < 0.005$), low $\dot{V}a/\dot{Q}$ as fraction of $\dot{Q}p$ perfusing poorly ventilated lung areas ($0.005 < \dot{V}a/\dot{Q} < 0.1$), high $\dot{V}a/\dot{Q}$ as fraction of $\dot{V}e$ ventilating poorly perfused lung areas ($10 < \dot{V}a/\dot{Q} < 100$), dead space as fraction of $\dot{V}e$ ventilating nonperfused lung areas ($\dot{V}a/\dot{Q} > 100$), mean $\dot{V}a/\dot{Q}$ ratio of perfusion and ventilation, and logarithmic standard deviations of perfusion ($\log SD_{P}$) and ventilation ($\log SD_{V}$) were derived from the 50-compartment model. Predicted values for arterial oxygen tension ($P_{aO_2}$) were calculated from the recovered $\dot{V}a/\dot{Q}$ distributions as described. The index $DISP_{R-E}$ is the root mean square difference of measured retentions (R) and excretions (E) corrected for intrapulmonary shunt and dead space. It is an overall index of $\dot{V}a/\dot{Q}$ heterogeneity with a minimum value of zero (homogeneous lung) and a maximum value of 100 (100% shunt, 100% dead space).

Transmural central venous pressure, pulmonary artery pressure, pulmonary artery occlusion pressure, were derived by subtracting $P_{es}$ from the blood pressures. Average pressures were calculated over a period of 5 min. Systemic vascular resistance was calculated as (mean systemic blood pressure – mean central venous pressure) × 80/cardiac output and pulmonary vascular resistance as (mean transmural pulmonary artery pressure – transmural pulmonary artery occlusion pressure) × 80/cardiac output.

Oxygen content was determined for arterial, mixed venous, and pulmonary capillary blood as $(1.34 \times $ oxygen saturation $\times$ total hemoglobin) + $(0.0031 \times$ oxygen tension). Capillary oxygen saturation corresponding to an alveolar oxygen tension derived by the alveolar gas equation was calculated as described by Ruiz et al. and corrected for methemoglobin and carboxyhemoglobin. Venous admixture ($Q_{w}/Q_{r}$) was calculated as (pulmonary capillary oxygen content – arterial oxygen content)/(pulmonary capillary oxygen content – mixed venous oxygen content); physiologic dead space-to-tidal volume ratio ($V_{d}/V_{T}$) as (arterial carbon dioxide tension – mixed expired carbon dioxide tension)/arterial carbon dioxide tension; oxygen consumption ($\dot{V}O_{2}$) as $\dot{V}e \times ($fraction of inspired oxygen $\times ($fraction of mixed expired nitrogen/fraction of inspired nitrogen$) – $fraction of mixed expired oxygen$)); oxygen delivery ($\dot{DO}_{2}$) as arterial oxygen content × cardiac output; and oxygen extraction ratio as (arterial oxygen content – mixed venous oxygen content)/arterial oxygen content.

**Experimental Procedure**

After instrumentation, the dogs remained supine. Body temperature was kept at 37–38°C with a heating pad. Adequate hydration and energy supply (25 kcal·kg⁻¹·day⁻¹) was ensured with an infusion of 5% dextrose and lactated Ringer's solution to achieve a transmural pulmonary artery occlusion pressure of 8 mmHg.

Acute lung injury was induced by injection of 0.08 ml·kg⁻¹ purified oleic acid (J. T. Baker, Phillipsburg, NJ) into the right atrial catheter over 15 min. Additional 0.2 ml increments of oleic acid were administered every 30 min until $P_{aO_2}$ was between 50 and 60 mmHg while breathing room air at ambient airway pressure. Then, the fraction of inspired oxygen was set to 0.3 and the lung injury was allowed to stabilize for 90 min before baseline values were taken.

Pressure-limited ventilatory support was then provided with a demand-valve continuous positive airway pressure circuit of a standard microprocessor-controlled ventilator (Evita, Dräger). A pressure decrease of 0.5 cmH₂O was required to open the demand valve with a delay of 80 ms; the static pressure decrease at a flow of 120 l·min⁻¹ was 2 cmH₂O, and the expiratory resistance of the breathing circuit was 2 cmH₂O·l⁻¹·s⁻¹. The low-pressure level was set at 5 cmH₂O, and the high-pressure level was adjusted to the value that produced a tidal volume of 15 ml·kg⁻¹.
corresponding to the highest pulmonary compliance during transient neuromuscular blockade with an intravenous bolus of succinylcholine (0.5 mg·kg\(^{-1}\)·min\(^{-1}\)). During APRV the inspiratory-to-expiratory time ratio was set at 1:1 and the ventilator rate to maintain \(P_{aCO_2}\) between 40 and 50 mmHg in the absence of spontaneous breathing. PSV was administered with the same ventilator circuit using identical low- and high-pressure levels. Each inspiratory effort triggered an isovolumetric and the preset high-pressure level was maintained until inspiratory gas flow decreased to 25% of its peak value.

All animals maintained spontaneous breathing during ventilatory support with the settings described above. To assess cardiopulmonary function during APRV in the absence of spontaneous breathing the animals were paralyzed with intravenous succinylcholine 50 \(\mu\)g·kg\(^{-1}\)·min\(^{-1}\). APRV without spontaneous breathing is identical to conventional pressure-limited, time-cycled ventilation. The sequencing of the measurements with PSV, APRV with and without spontaneous breathing (fig. 1) was randomized using a computer-generated Latin square design. Forty minutes of equilibration was allowed on each ventilatory modality before measurements. After each measurement dogs breathed 30% oxygen at ambient pressure for at least 20 min until \(V_e\), fraction of mixed expired oxygen, fraction of mixed expired carbon dioxide, cardiac output, transmural pulmonary artery pressure, systemic blood pressure, \(P_{aO_2}\), and \(P_{aCO_2}\) returned to baseline values (±5%). To restore the lungs to baseline condition, the animals' lungs were inflated manually to an airway pressure of 30 cmH\(_2\)O for 10 s after each measurement before the ventilatory modality was changed.

**Statistical Analysis**

Results are expressed as mean ± standard error of the mean (SE). Data were analyzed by using repeated-measures analysis of variance. When a significant F ratio was obtained, differences between the means were isolated with the post hoc Scheffé's multiple range test. The relation between measured and predicted \(P_{aO_2}\), and between changes in cardiac output and \(P_e\) were assessed with a linear regression analysis. \(P < 0.05\) was considered to indicate statistical significance.

**Results**

During APRV, the animals breathed spontaneously with a tidal volume of 68 ± 7 ml and a respiratory rate of 9 ± 1 breaths/min, which accounted for 10 ± 1% of the total \(V_e\) (table 1). Spontaneous breathing during APRV did not significantly increase total \(V_e\). Breath-to-breath ventilatory support with PSV increased ventilator rate (\(P < 0.05\)) and reduced tidal volume (\(P < 0.05\)) compared with APRV with and without spontaneous breathing. Total \(V_e\) was significantly greater during PSV than during the other modalities (\(P < 0.05\)). Mean \(P_e\) was lowest during APRV with spontaneous breathing.

**Table 1. Ventilatory Variables**

<table>
<thead>
<tr>
<th></th>
<th>APRV without Spontaneous Breathing</th>
<th>APRV with Spontaneous Breathing</th>
<th>PSV</th>
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<tbody>
<tr>
<td><strong>Paw</strong> (cmH(_2)O)</td>
<td>22 ± 1</td>
<td>22 ± 1</td>
<td>22 ± 1</td>
</tr>
<tr>
<td><strong>Paw low</strong> (cmH(_2)O)</td>
<td>5.7 ± 1</td>
<td>5.7 ± 1</td>
<td>5.7 ± 1</td>
</tr>
<tr>
<td><strong>Paw mean</strong> (cmH(_2)O)</td>
<td>14.2 ± 1.1</td>
<td>14.2 ± 1.1</td>
<td>12.9 ± 1.5</td>
</tr>
<tr>
<td><strong>Pes mean</strong> (cmH(_2)O)</td>
<td>11.2 ± 1.3</td>
<td>7.8 ± 0.7*</td>
<td>8.9 ± 0.9*</td>
</tr>
<tr>
<td><strong>PEEP</strong> (cmH(_2)O)</td>
<td>2.2 ± 0.9</td>
<td>1.8 ± 0.7</td>
<td>2.0 ± 0.9</td>
</tr>
<tr>
<td><strong>RRspon (min)</strong></td>
<td>NA</td>
<td>9 ± 1</td>
<td>NA</td>
</tr>
<tr>
<td><strong>V_{espon} (L/min)</strong></td>
<td>NA</td>
<td>0.61 ± 0.10</td>
<td>NA</td>
</tr>
<tr>
<td><strong>RR (min)</strong></td>
<td>15 ± 0</td>
<td>15 ± 0</td>
<td>25 ± 3*</td>
</tr>
<tr>
<td><strong>V_{e} (L/min)</strong></td>
<td>5.8 ± 0.4</td>
<td>6.1 ± 0.4</td>
<td>7.4 ± 0.9*</td>
</tr>
</tbody>
</table>

APRV = airway pressure release ventilation; PSV = pressure support ventilation; Paw = airway pressure; Pes = esophageal pressure; PEEP = intrinsic positive end-expiratory pressure; RRspon = rate of unsupported spontaneous breaths; V_{espon} = unsupported spontaneous minute ventilation; RR = rate of mechanical cycles; \(V_e\) = total minute ventilation; NA = not applicable.

Values are mean ± SE.

* \(P < 0.05\) versus APRV without spontaneous breathing.

† \(P < 0.05\) versus APRV with spontaneous breathing.
(P < 0.05). Mean airway pressure did not vary significantly during the tested ventilatory support modalities.

Changes in cardiovascular variables are shown in table 2. Spontaneous breathing during APRV increased cardiac output (P < 0.05), whereas heart rate, mean systemic blood pressure, transmural central venous pressure, mean transmural pulmonary artery pressure, transmural pulmonary artery occlusion pressure, systemic vascular resistance, and pulmonary vascular resistance remained unchanged. Increase in cardiac output correlated inversely with the change in Paco2 (R² = −0.65; P < 0.001). Cardiovascular function during PSV was similar to that during APRV without spontaneous breathing.

Spontaneous breathing during APRV resulted in an increase in Paco2 (P < 0.05) (table 3), an increased cardiac output, and a higher Do2 (P < 0.05). Despite spontaneous breathing, VO2 remained unchanged and oxygen extraction ratio decreased (P < 0.05). Breath-to-breath synchronized ventilatory support with PSV did not increase Paco2 or Do2 significantly. Arterial pH, Paco2, and Paco2 did not vary significantly during the tested ventilatory support modalities. Calculated Qva/Qt and VO2/VO2 decreased when spontaneous breathing occurred during APRV (P < 0.05).

Results of the multiple inert-gas elimination analysis are summarized in table 4 and illustrated for a representative dog in figure 2. Spontaneous breathing during APRV accounted for a decrease (P < 0.05) in the blood flow to shunt units (Vα/Q < 0.005) from 31% to 16%

<table>
<thead>
<tr>
<th>Table 2. Hemodynamic Variables</th>
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<tbody>
<tr>
<td>APRV without Spontaneous Breathing</td>
</tr>
<tr>
<td>--------------------------------</td>
</tr>
<tr>
<td>HR (min)</td>
</tr>
<tr>
<td>Paco2 (mmHg)</td>
</tr>
<tr>
<td>Ppaw (mmHg)</td>
</tr>
<tr>
<td>Pvo2 (mmHg)</td>
</tr>
<tr>
<td>Paco2 (mmHg)</td>
</tr>
<tr>
<td>CO (l/min)</td>
</tr>
<tr>
<td>SVR (dyne · s · cm⁻²)</td>
</tr>
<tr>
<td>PVR (dyne · s · cm⁻²)</td>
</tr>
</tbody>
</table>

APRV = airway pressure release ventilation; PSV = pressure support ventilation; HR = heart rate; Paco2 = mean systemic arterial pressure; Ppaw = transmural mean pulmonary artery pressure; Pvo2 = transmural mean central venous pressure; Paco2 = arterial oxygen tension; Paco2 = arterial carbon dioxide tension; PVO2 = arterial oxygen consumption; HD = hemoglobin; Qva/Qt = calculated venous admixture; VO2/VO2 = dead space to tidal volume ratio; Do2 = oxygen delivery; VO2 = oxygen consumption; OER = oxygen extraction ratio.

Values are mean ± SE.

* P = 0.05 versus APRV without spontaneous breathing.
† P = 0.05 versus PSV with spontaneous breathing.

and an increase (P < 0.05) in the fraction of cardiac output to units with a normal Vα/Q ratio (0.1 < Vα/Q < 0.10) from 75% to 88%. Pulmonary blood flow distribution to shunt and normal Vα/Q units remained essentially unchanged during PSV, compared with APRV without spontaneous breathing. Blood flow distribution curves were centered, and their dispersions (log SDQ) were increased (log SDQ > 0.6). Ventilation distributions were shifted to the right, and the dispersion of the curves (log SDQ) was above the upper normal limit (log SDQ > 0.6). Dead space (Vα/Q > 100) was lowest during APRV with spontaneous breathing (P < 0.05). Breath-to-breath synchronized ventilatory support with PSV showed no statistically significant difference in dead space compared with APRV without spontaneous breathing. The index DISP increased during APRV with spontaneous breathing (P < 0.05) compared with APRV without spontaneous breathing and PSV. Predicted Paco2 was close to measured Paco2 for all tested ventilatory modalities (table 5).

**Discussion**

This study was designed to evaluate the effect of the interfacing of spontaneous breathing and mechanical
ventilation on pulmonary gas exchange in subjects with acute lung injury. We found that breath-to-breath synchronized ventilatory support with PSV did not improve $V_a/Q$ distributions when compared with controlled mechanical ventilation. In contrast, uncoupling of spontaneous and mechanical breaths during APRV improved overall $V_a/Q$ matching, as reflected by decrease in intrapulmonary shunt and dead space. A concomitant increase in cardiac output and $D_{O_2}$ improved tissue oxygen supply and demand balance, whereas $V_{O_2}$ remained essentially unaffected by the work of spontaneous breathing.

When comparing our results with those of previous human and animal studies, it should be emphasized that our observations were made in anesthetized dogs with oleic acid–induced lung injury. However, although pathophysiologically different, oleic acid–induced lung injury is a well-established animal model of human acute lung injury. The essentially unimodal $V_a/Q$ distribution with $23 \pm 2\%$ of the pulmonary blood flow perfusing shunt units indicated lung injury in our dogs and is consistent with previous observations in the canine oleic acid model. 

Induction of anesthesia with neuromuscular blockade and mechanical ventilation has been observed to cause decrease in lung volumes, expiratory airway closure, formation of atelectasis with $V_a/Q$ mismatch and a small increase in intrapulmonary shunt by $0.9–5.1\%$. However, in a previous study we distinguished between the effects of anesthesia and neuromuscular blockade on the $V_a/Q$ distributions. Neuromuscular blockade did not affect $V_a/Q$ distributions in dogs with oleic acid lung injury who had been rendered apneic by lowering $P_{aCO_2}$. Therefore, the use of neuromuscular blockade to guarantee controlled mechanical ventilation cannot explain the changes in the $V_a/Q$ distributions associated with spontaneous breathing during APRV. High $P_{aCO_2}$ and low $pH$ in our animals may have contributed to the observed $V_a/Q$ mismatch.

Pressure-support ventilation and APRV, which is equivalent to biphasic positive airway pressure, are similar in their pressure-limited delivery of tidal volume, but differ in their interfacing with spontaneous ventilation. Spontaneous breathing in any phase of the mechanical ventilator cycle is possible with APRV that ventilates by time-cycled switching between two pres-
sure levels in a continuous positive airway pressure circuit.\textsuperscript{7–10} Thus, the degree of ventilatory support is constant during APRV. Pressure-support ventilation provides breath to breath, patient-triggered insufflation, which in the ventilator is terminated when inspiratory gas flow decreases to 25% of the peak flow value.\textsuperscript{26} Consequently, during PSV the degree of ventilatory support is determined by the respiratory rate and the inspiratory-to-expiratory time ratio as a result of the interaction between spontaneous and mechanical ventilation. Because insufflation is not completed during PSV, equivalent low- and high-pressure levels are likely to result in a lower tidal volume during PSV compared with APRV. The observed increase in respiratory rate during PSV caused a sustained increase in ventilatory support to maintain P\textsubscript{aco2}.

Previous studies corroborated findings regarding the V\textsubscript{A}/Q matching between conventional controlled mechanical ventilation and breath-to-breath synchronized partial ventilatory support. Beydon \textit{et al.}\textsuperscript{5} observed no improvement in overall V\textsubscript{A}/Q matching during PSV compared with controlled mechanical ventilation. Intrapulmonary shunt remained unchanged, whereas dead space ventilation increased with PSV. Santak \textit{et al.}\textsuperscript{27} observed similar changes in the V\textsubscript{A}/Q distributions when comparing controlled mechanical ventilation with a combination of synchronized intermittent mandatory and PSV. Our results appear to be in contrast with those of Valentine \textit{et al.}\textsuperscript{28} who compared APRV and PSV in patients recovering from open-heart operations. Although they also found dead space to be considerably lower during APRV, intrapulmonary shunt was not affected.\textsuperscript{28} However, it is difficult to evaluate the effect of the different ventilatory support modalities on V\textsubscript{A}/Q matching on the basis of previous studies, because the degree of the mechanical lung inflation was changed significantly during the course of previous investigations.\textsuperscript{5,27,28} In our study, ventilatory support was provided using equivalent low- and high-pressure levels for both PSV and APRV. Therefore, our results should only reflect the effect of interfacing spontaneous and mechanical breaths during partial ventilatory support.

Spontaneous breathing during APRV resulted in a marked decrease in blood flow to shunt units. Two mechanisms may explain this decrease in intrapulmonary shunt. First, shunt units were recruited and became ventilated, thereby converting to low or normal V\textsubscript{A}/Q units. Second, perfusion of shunt units was reduced by redistribution of the blood flow to normal V\textsubscript{A}/Q, high V\textsubscript{A}/Q, or previously nonperfused areas. The first explanation is supported by radiographic observations in supine patients with normal lungs contractions of the diaphragm during unsupported spontaneous breathing improve the ventilation of dependent, well perfused lung regions.\textsuperscript{29} Recent three-dimensional x-ray computer tomography studies have indicated that during spontaneous breathing in the supine position, anatomic differences between the crural and costal diaphragm cause the dependent portion of the diaphragm to move more than the nondependent

\begin{table}[h]
\centering
\caption{Predicted Versus Measured Arterial Oxygen Tension}
\begin{tabular}{lccc}
\hline
 & APRV without & APRV with & PSV \\
Spontaneous & Spontaneous & Spontaneous & \\
Breathing & Breathing & Breathing & \\
\hline
Predicted P\textsubscript{aO2} (mmHg) & 74 ± 2 & 105 ± 4 & 86 ± 5 \\
Measured P\textsubscript{aO2} (mmHg) & 75 ± 3 & 107 ± 8 & 87 ± 5 \\
r\textsuperscript{2} & 0.93 & 0.90 & 0.92 \\
\hline
\end{tabular}
\end{table}

APRV = airway pressure release ventilation; PSV = pressure support ventilation; P\textsubscript{aO2} = arterial oxygen tension.
Values are mean ± SE.
portion which increases ventilation of the dependent lung regions. By contrast, during controlled mechanical ventilation in supine subjects displacement of the nondependent diaphragm and ventilation of the nondependent lung regions increased relative to dependent regions. Controlled mechanical ventilation has been observed to decrease lung volumes, cause expiratory airway closure and promote the formation of atelectasis in the dependent lung areas thereby contributing to \(\dot{V}_a/Q\) mismatch and intrapulmonary shunting. The second explanation is supported by the periodic decreases in intrathoracic pressure observed during spontaneous breathing with APRV which may increase cardiac output and may support the perfusion of nondependent high \(\dot{V}_a/Q\) and dead space regions. Our results allow not to distinguish between these two possible mechanisms.

Conversion of shunt units directly to normal \(\dot{V}_a/Q\) units without creating regions of low \(\dot{V}_a/Q\) indicates that spontaneous breathing during APRV recruited nonventilated lung areas. A similar phenomenon has been observed previously when positive end-expiratory pressure was applied to patients with adult respiratory distress syndrome. The decrease in intrapulmonary shunt may indicate an improved end-expiratory lung volume during spontaneous breathing with APRV. Intrinsic positive end-expiratory pressure did not change significantly and thus did not affect end-expiratory lung volume during the tested ventilatory support modalities. Conversion of shunt to normal \(\dot{V}_a/Q\) units has not been observed in studies comparing controlled mechanical ventilation with synchronized partial ventilatory support of each breath. Apparently the spontaneous contribution on a mechanically assisted breath is not sufficient to counteract the \(\dot{V}_a/Q\) maldistribution of positive pressure lung insufflation.

Calculated \(Q_{va}/Q_{T}\) always exceeded inert-gas shunt (\(\dot{V}_a/Q < 0.005\)) by 10% of the cardiac output, in accordance with previous observations. Consistent with our data, no difference has been observed between \(Q_{va}/Q_{T}\) and the inert gas–measured fraction of perfusion to shunt plus low \(\dot{V}_a/Q\) at an inspired oxygen fraction of 0.3–0.6.

The dead space ventilation was lowest during spontaneous breathing with APRV which can be explained by perfusion of previously not perfused units or redistribution of ventilation to less ventilated lung areas. Breath-to-breath synchronized ventilatory support with PSV was associated with a higher \(\dot{V}_E\) and dead space ventilation compared with spontaneous breathing with APRV. Previous studies have reported increased dead space and \(\dot{V}_E\) during changeover from controlled mechanical ventilation to PSV. Valentine et al. observed a lower inert-gas dead space during unrestricted spontaneous breathing with APRV when compared with PSV at similar \(\dot{V}_E\). Wolff et al. investigated the effect of unsupported spontaneous breaths and mechanical cycles on the alveolar CO₂ elimination during intermittent mandatory ventilation. The efficiency of alveolar CO₂ elimination was significantly higher during unsupported spontaneous breaths than during mechanical cycles. Similarly, the uncoupling of spontaneous and mechanical breaths during APRV may have contributed to decrease in dead space ventilation.

Calculated \(V_{D}/V_T\) was decreased by spontaneous breathing during APRV. The lack of a decrease in PaCO₂ may be explained by minimal increase in ventilation to high \(\dot{V}_a/Q\) units during spontaneous breathing with APRV. Similarly, PaCO₂ was unaffected during PSV, although total \(\dot{V}_E\) was considerably greater in the presence of an essentially unchanged \(V_{D}/V_T\). This may result from small changes in the ventilation distribution indicated by minimal increases in log SDv during PSV. In accordance with previous observations inert-gas dead space was lower, because \(V_{D}/V_T\) includes in part high \(\dot{V}_a/Q\) units with alveolar carbon dioxide tension less than PaCO₂.

Corresponding to the improvement of overall \(\dot{V}_a/Q\) distributions, pulmonary oxygen transfer increased during spontaneous breathing with APRV. The lack of a change in \(\dot{V}_a/Q\) matching during PSV did not result in a statistically significant improvement in arterial blood oxygenation compared with APRV in the absence of spontaneous breathing.

Cardiac output and stroke volume may be larger during partial than during full ventilatory support, because spontaneous breaths cause periodic decreases in intrathoracic pressure and an increase in abdominal pressure which may increase venous return. The belief that increase in transdiaphragmatic pressure caused by a fall in intrathoracic pressure during spontaneous inspiration improves venous return and cardiac output is supported by the inverse correlation between the change in cardiac output and Pao. We observed an increase in cardiac output and stroke volume, only in the presence of spontaneous breathing during APRV. A similar increase in cardiac output has been documented during intermittent mandatory ventilation, which adds mechanical cycles to unsupported spontaneous breathing. In contrast, no change in cardiac output.
was observed during PSV when compared with APRV without spontaneous breathing, using equivalent low- and high-pressure levels. This indicates that cardiovascular function during ventilatory support with PSV was influenced by a lack of a sufficient decrease in mean intrathoracic pressure, as observed during controlled mechanical ventilation. Changes in cardiac output have been reported to correlate positively with the intrapulmonary shunt fraction. In our study, increase in pulmonary blood flow during spontaneous breathing with APRV was preferentially distributed to normal V\textsubscript{A}/Q units. Consequently, increased cardiac output was associated with significantly lower intrapulmonary shunting of blood, increased PaO\textsubscript{2} and considerably higher Do\textsubscript{2}.

The work of spontaneous breathing during APRV and PSV did not affect V\textsubscript{O\textsubscript{2}}. This is in accordance with previous experimental and clinical findings indicating that total V\textsubscript{O\textsubscript{2}} may not be measurably altered by spontaneous breathing, even in the presence of altered lung function. In the presence of spontaneous breathing during APRV, an increased Do\textsubscript{2} and unchanged V\textsubscript{O\textsubscript{2}} resulted in an improved relation between tissue oxygen supply and demand, as reflected by a significant decrease in tissue oxygen extraction ratio.

Mechanical ventilatory support techniques should allow unrestricted breathing throughout the mechanical cycle. The results of this study demonstrate that uncoupling of spontaneous and mechanical breaths during partial ventilatory support contributes to improved V\textsubscript{A}/Q matching and increased systemic blood flow. Mechanical assistance of every breath during PSV did not provide any advantage in cardiopulmonary function or gas exchange compared with controlled mechanical ventilation. Controlled clinical trials and long-term investigations are warranted to evaluate the validity of these results in critically ill patients.

References

14. Wagner PD, Larusolo RB, Uhl RR, West JB: Continuous distributions of ventilation-perfusion ratios in normal subjects breathing air and 100 per cent O\textsubscript{2}. J Cell Invest 54:54-68, 1974
22. Domino KB, Lu Y, Eisenblt BL, Hlastala MP: Hypocapnia worsens arterial blood oxygenation and increases V\textsubscript{A}/Q heterogeneity in canine pulmonary edema. Anesthesiology 78:91-99, 1993


