Long-Term Effects of Spontaneous Breathing During Ventilatory Support in Patients with Acute Lung Injury

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Improved gas exchange has been observed during spontaneous breathing with airway pressure release ventilation (APRV) as compared with controlled mechanical ventilation. This study was designed to determine whether use of APRV with spontaneous breathing as a primary ventilatory support modality better prevents deterioration of cardiopulmonary function than does initial controlled mechanical ventilation in patients at risk for acute respiratory distress syndrome (ARDS). Thirty patients with multiple trauma were randomly assigned to either breathe spontaneously with APRV (APRV Group) (n = 15) or to receive pressure-controlled, time-cycled mechanical ventilation (PCV) for 72 h followed by weaning with APRV (PCV Group) (n = 15). Patients maintained spontaneous breathing during APRV with continuous infusion of sufentanil and midazolam (Ramsey sedation score [RSS] of 3). Absence of spontaneous breathing (PCV Group) was induced with sufentanil and midazolam (RSS of 5) and neuromuscular blockade. Primary use of APRV was associated with increases (p < 0.05) in respiratory system compliance (Crs), arterial oxygen tension (PaO2), cardiac index (CI), and oxygen delivery (DO2), and with reductions (p < 0.05) in venous admixture (Qva/Qt), and oxygen extraction. In contrast, patients who received 72 h of PCV had lower Crs, PaO2, CI, DO2, and Qva/Qt values (p < 0.05) and required higher doses of sufentanil (p < 0.05), midazolam (p < 0.05), noradrenaline (p < 0.05), and dobutamine (p < 0.05). Crs, PaO2, CI and DO2 were lowest (p < 0.05) and Qva/Qt was highest (p < 0.05) during PCV. Primary use of APRV was consistently associated with a shorter duration of ventilatory support (APRV Group: 15 ± 2 d [mean ± SEM]; PCV Group: 21 ± 2 d) (p < 0.05) and length of intensive care unit (ICU) stay (APRV Group: 23 ± 2 d; PCV Group: 30 ± 2 d) (p < 0.05). These findings indicate that maintaining spontaneous breathing during APRV requires less sedation and improves cardiopulmonary function, presumably by recruiting nonventilated lung units, requiring a shorter duration of ventilatory support and ICU stay.

Acute respiratory distress syndrome (ARDS) causes alveolar collapse primarily in dependent lung regions adjacent to the diaphragm, resulting in intrapulmonary venous admixture of blood (Qva/Qt) and severe arterial hypoxemia (1). Mechanical ventilation with positive end-expiratory pressure (PEEP) and low tidal volume (VT) is commonly applied during ARDS to recruit collapsed alveoli for gas exchange without hyperinflation of the lungs (2, 3). Despite early mechanical ventilation with PEEP, a high number of patients at risk have been observed to develop ARDS (4).

An improvement in ventilation-perfusion (V̇A/Q̇) matching has been considered an advantage of partial ventilatory support as compared with controlled mechanical ventilation (5–7), presumably because the diaphragmatic contraction augments distribution of ventilation to dependent, poorly aerated but perfused lung regions (8). Spontaneous breathing in any phase of the mechanical ventilator cycle is possible with airway pressure release ventilation (APRV), which ventilates by periodic switching between two levels of continuous positive airway pressure (CPAP) (9, 10). Recently, we observed that patients with severe ARDS exhibited better V̇A/Q̇ matching and arterial oxygenation, during spontaneous breathing with APRV than during controlled mechanical ventilation (11). However, it is not known whether maintaining spontaneous breathing from the very beginning of ventilatory support may prevent alveolar collapse and thereby reduce Qva/Qt and hypoxemia in patients at risk for ARDS.

We hypothesized that in patients at risk for ARDS, spontaneous breathing with APRV prevents deterioration of gas exchange or allows it to recover faster than does controlled mechanical ventilation. To test this hypothesis, we examined cardiopulmonary function in patients with severe multiple trauma who were either allowed to breathe spontaneously during APRV or were given full ventilatory support for 72 h and then weaned with APRV.

METHODS

The study protocol was approved by the Innsbruck Ethics Committee. In accordance with Austrian federal law, the independent Innsbruck Ethics Committee waived the need for informed consent by the patients in the study, given that all were unconscious and approved ventilatory modalities were used.

Thirty mechanically ventilated patients with severe multiple trauma, as indicated by an injury severity score (ISS) (12) above 40, were studied. Patients were not included in the study if they had chronic lung or heart disease, bronchopleural fistula, or severe cerebral injury. The criteria of the American–European Consensus Conference were used to define acute lung injury (ALI) and ARDS (13). Sepsis was defined by the criteria of the American College of Chest Physician and the Society of Critical Care Medicine Consensus Conference Committee of 1992 (14). Organ failure was defined with the scoring system described by Knaus and colleagues (15). Severity of illness was assessed with the Simplified Acute Physiologic Score (16).

Routine clinical management of the patients included the use of a radial artery catheter and a thermodilution-tipped quadrupule-lumen pulmonary artery catheter (CCO 746HF8; Baxter Edwards Critical Care, Irvine, CA).

Cardiovascular Measurements

Heart rate (HR) was obtained from the electrocardiogram. Systemic blood pressure (Psa), central venous pressure (Pcv), pulmonary artery pressure (Ppa), and pulmonary artery occlusion pressure (Ppao) were transduced (PS0; Gould, Oxnard, CA) and recorded. Cardiac output (CO) was continuously estimated with the thermal dilution technique (Vigilance; Baxter Edwards Critical Care, Irvine, CA). In addition, intermittent determinations of CO were made with 10 ml of iced 0.9% saline solution as indicator and by averaging seven determinations made at random moments during the ventilatory cycle.
Ventilatory and Lung Mechanics Measurements

Gas flow and airway pressure were measured at the proximal end of the tracheal tube with a heated pneumotachograph (No. 2; Fleisch, Lausanne, Switzerland) connected to a differential pressure transducer (P130; Statham, Oxnard, CA). Vt was derived from the integrated gas flow signal. End-inspiratory pressures were measured after a 5-s end-inspiratory occlusion, and intrinsic positive end-expiratory pressures (PEEPi) were measured after a 5-s end-expiratory occlusion of the airway as described previously (17). Respiratory system compliance (Crs) was obtained during transient neuromuscular blockade with intravenous vecuronium bromide in a dose of 0.1 mg/kg by dividing expiratory Vt by the difference between end-inspiratory Paw and PEEPi. A static pressure–volume (P–V) curve of the total respiratory system was constructed on a daily basis for each patient during transient neuromuscular blockade (18, 19). The lower inflection pressure (LIP) was defined as the lowest and the upper inflection pressure (UIP) as the highest Paw at which the slope of the static inflation P–V curve was maximal (18, 19). A computerized step-by-step regression analysis was used to quantify LIP and UIP as described previously (20).

Gas Analysis

Arterial and mixed venous blood gases (oxygen tension [P\text{O}_2], carbon dioxide tension [P\text{CO}_2], and pH were determined in duplicate, immediately after sampling, with standard blood gas electrodes (STATSProfil; Nova Biomedical, Waltham, MA). Each sample had oxygen saturation and hemoglobin analyzed spectrophotometrically (OSM3; Radiometer, Copenhagen, Denmark). Fractions of inspired and expired O\text{2} and CO\text{2} (FiO\text{2} and FeO\text{2}, and FiCO\text{2} and FeCO\text{2}, respectively) were continuously measured (Deltatrac; Datex, Helsinki, Finland).

Data Analysis

Standard formulas were used to calculate cardiac index (CI), systemic vascular resistance (SVR), \(\dot{Q}_{VA}/\dot{Q}_T\), oxygen delivery (DO\text{2}), and oxygen extraction ratio (O\text{2ER}). Oxygen consumption (VO\text{2}) was calculated as \((Vt \cdot F_{\text{IO2}}) - (Vt \cdot F_{\text{ECO2}})\). Protocol

After inclusion in the study, all patients remained supine. Adequate fluid supply was ensured with infusion of lactated Ringer’s solution to achieve a Pao\text{2} of 14 to 18 mm Hg. Albumin 5% solution was given to maintain serum albumin concentrations above 2.0 g/dl, and packed red blood cells were given to achieve a hemoglobin of at least 10 g/dl. Dobutamine was infused when, despite fluid replacement, CI fell below 3.0 L/min/m\text{2}, and was given to achieve a CI of 3.5 to 4.0 L/min/m\text{2}. Norepinephrine infusion was added if Sv\text{2} was below 600 dyn- s/ cm\text{5}/m\text{2}. to restore a mean Psa\text{2} of 70 to 80 mm Hg. In the absence of oliguria, dopamine infusion was added at a fixed rate of 3 \mu g/kg/min.

Pressure-limited ventilatory support was provided with the demand-valve CPAP circuit of a standard ventilator (Evia; Dräger, Lübeck, Germany). The low pressure level was set at 2 cm H\text{2}O above LIP on a static P–V curve, and the upper pressure level was adjusted to the value below UIP that produced a V\text{pao} of 14 to 18 mm Hg. The upper and lower pressure levels were always adjusted to allow flow to decelerate to zero, and the resulting inspiratory-to-expiratory ratio was kept constant. FiO\text{2} was adjusted to maintain Pao\text{2} above 60 mm Hg.

After obtaining baseline measurements, we randomly assigned patients to receive APRV with spontaneous breathing (APRV Group) or pressure-limited, time-cycled, controlled mechanical ventilation (PCV) for 72 h followed by weaning with APRV (PCV Group). Note that from a mechanical standpoint, APRV without spontaneous breathing, we gave patients to the PCV Group continuous infusions of sufentanil and midazolam as required to achieve a Ramsay sedation score (RSS) of 3 (21). To assess cardiopulmonary function during APRV in the absence of spontaneous breathing, we gave patients in the PCV Group continuous infusions of sufentanil and midazolam as required to achieve an RSS of 5 to 6, and paralyzed them with intravenous vecuronium bromide at 0.1 mg/kg for 72 h. Neuro-muscular blockade was considered sufficient with disappearance of the twitch response to a train of four supramaximal ulnar nerve stimulations at 2.0 Hz for 1.5 s every 2 min (Myograph 2000; Organon Teknika, Boxtel, The Netherlands). Then, in patients of the PCV Group, infusion of midazolam and sufentanil was reduced to achieve an RSS of 3, and spontaneous breathing was allowed with APRV.

All patients were weaned according to a strict protocol by decreasing the APRV rate twice daily. Clinical tolerance of weaning was considered poor and ventilatory support was increased when patients developed a respiratory rate > 35 breaths/min, pH < 7.25, Sa\text{2} < 90%, HR > 140 beats/min or a sustained increase or decrease in HR of more than 20%, systolic Psa\text{2} > 180 mm Hg or < 90 mm Hg, increased accessory muscle activity, diaphoresis, and facial signs of distress (22). Patients were extubated when they breathed comfortably with 5 cm H\text{2}O CPAP for 6 h.

Measurements including arterial blood gas analysis and data collection were made under stable conditions as confirmed by constancy (± 5%) of V\text{e}, Sa\text{2}, Fi\text{CO2}, Psa, Pao, and CI for at least 30 min at 8-h intervals over a period of 10 d. Cardiopulmonary variables were averaged for each 24-h period.

Endpoints and Statistical Analysis

The primary endpoints of the study were the effects of primarily partial ventilatory support on cardiorespiratory function within 10 d after ICU admission. The secondary endpoints were duration of ventilatory support, intubation, and ICU stay.

Results are expressed as mean ± SEM. Data were tested for normal distribution with the Shapiro–Wilk Test and were analyzed by two-way analysis of variance (ANOVA), with the initial ventilatory modality as the between-group factor and time after randomization as the repeated-measures factor. When a significant F ratio was obtained, differences between the means were isolated with the post hoc Newman–Keuls multiple comparison test. Clinical characteristics of the two groups were compared through a one-way ANOVA. Differences were considered statistically significant if p < 0.05.

RESULTS

There were no statistically significant differences between the two study groups in their demographic (Table 1) or clinical data (Figures 1 through 4) at baseline.

In all patients, LIP and UIP could be identified on the static P–V curve (Figure 1). Ventilatory variables, ventilator settings, and lung mechanics are shown in Figure 2. Patients were initially mechanically ventilated with an essentially identical low Paw limit (APRV Group: 12 ± 1 cm H\text{2}O; PCV Group: 12 ± 1 cm H\text{2}O).

| TABLE 1. DEMOGRAPHIC DATA AND CLINICAL CHARACTERISTICS AT INCLUSION INTO THE STUDY* |
|--------------------|-----------------|-----------------|
|                  | APRV Group   | PCV Group   | p Value |
| Number of patients, n (%)  | 15 (100)  | 15 (100)  |          |
| Age, yr            | 40 ± 5      | 42 ± 6      | ns       |
| Gender, M/F        | 11/4        | 13/2        | ns       |
| ISS                | 50 ± 2      | 49 ± 2      | ns       |
| SAPS               | 18 ± 1      | 18 ± 1      | ns       |
| ARDS, n (%)        | 2 (14)      | 3 (21)      | ns       |
| ALI non ARDS, n (%)| 6 (40)      | 5 (33)      | ns       |
| Extrapulmonary organ failure, n (%)*| 1 | 6 (30) | 5 (30) | ns |
| Ventilatory support before entry, h | 6 ± 1 | 6 ± 1 | ns |

Definition of abbreviations: ALI = acute lung injury (13); ARDS = acute respiratory distress syndrome (13); F = female; ISS = injury severity score (12); M = male; SAPS = simplified acute physiologic score (16).

* Values are mean ± SEM.

† Defined by the multi-organ failure score described by Knaus and colleagues (15).
cm H₂O), upper Paw limit (APRV Group: 26 ± 1 cm H₂O; PCV Group: 26 ± 1 cm H₂O), and ventilatory rate (APRV Group: 16 ± 2 breaths/min; PCV Group: 16 ± 2 breaths/min), resulting in similar values of $V_E$ (APRV Group: 9.9 ± 0.4 L; PCV Group: 10.2 ± 0.3 L) and $C_{RS}$ (APRV Group: 40 ± 3 ml/cm H₂O; PCV Group: 40 ± 2 ml/cm H₂O). In the APRV Group, a lower upper limit of Paw and ventilatory rate ($p < 0.05$) and an unchanged lower limit of Paw resulted in an essentially equal total $V_E$ and a higher compliance ($p < 0.05$) than in the PCV group. The highest upper Paw limit ($p < 0.05$) and lowest compliance ($p < 0.05$) were observed in the absence of spontaneous breathing. When patients in the PCV group were switched to APRV with spontaneous breathing after the initial 72-h period, the upper Paw limit and ventilatory rate could be reduced ($p < 0.05$), whereas total $V_E$ remained unchanged and $C_{RS}$ increased ($p < 0.05$). In the APRV-group, spontaneous breathing during APRV accounted for 10 ± 2% of the total $V_E$ on Day 1, which increased to 35 ± 9% by Day 10 ($p < 0.05$). In the PCV Group, spontaneous breathing began by accounting for 8 ± 2% of total $V_E$ on Day 4, which increased to 20 ± 3% by Day 10 ($p < 0.05$). Spontaneous $V_E$ and respiratory rate were always higher in the APRV Group than in the PCV Group ($p < 0.05$). PEEP and $V_r$ were not significantly different for the two groups.

Changes in cardiovascular variables are shown in Figure 3. CI was higher ($p < 0.05$) and SVR and PVR lower ($p < 0.05$) in the APRV Group than in the PCV Group. CI was lowest in the absence of spontaneous breathing ($p < 0.05$). When spontaneous breathing was allowed during APRV on Day 4 in the PCV Group, CI increased ($p < 0.05$). HR, Psa, Pcv, Ppa, and Ppao were not significantly different in the two groups.

Maintaining spontaneous breathing with APRV was associated with a lower $\dot{Q}_{VA}/\dot{Q}_T$ ($p < 0.05$) and a higher $P_{AaO_2}/FIO_2$ ($p < 0.05$) and $D_O_2$ ($p < 0.05$) than was seen in the PCV Group (Figure 4). Despite spontaneous breathing in the APRV Group, $V_O_2$ was comparable to that of patients receiving full ventilatory support, and $O_2$ER was lower ($p < 0.05$). $P_{AaO_2}/FIO_2$ ($p < 0.05$) and $D_O_2$ ($p < 0.05$) were lowest and $\dot{Q}_{VA}/\dot{Q}_T$ was highest in the absence of spontaneous breathing ($p < 0.05$). Arterial pH, $P_{aCO_2}$, $S_aO_2$, $S_vO_2$, and $V_O_2$ were comparable in the two groups.

Less sufentanil ($p < 0.05$) and midazolam ($p < 0.05$) was administered to patients breathing spontaneously with APRV than to patients receiving full ventilatory support in the initial 72 h (Figure 5). The highest doses of sufentanil and midazolam
were required to adapt patients to controlled mechanical ventilation during the first 3 d in the PCV Group (p < 0.05). Similarly, less noradrenaline (p < 0.05) and dobutamine (p < 0.05) were required to achieve the desired cardiovascular function in the APRV Group.

The incidence of ARDS was highest in the PCV Group within the first 10 d after admission to the ICU. In contrast, the incidence of ALI was higher in patients who from the beginning breathed spontaneously with APRV. Durations of ventilatory support (p < 0.05), intubation (p < 0.05), and ICU stay (p < 0.05) were shorter in patients in whom spontaneous breathing with APRV was used as the primary ventilatory modality (Table 2).

**DISCUSSION**

This study was designed to evaluate the effect of spontaneous breathing with APRV on gas exchange and cardiovascular function in patients at risk for ARDS. When spontaneous breathing was allowed from the beginning of ventilatory support, gas exchange improved, as reflected by a higher PaO₂/FIO₂.
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Maintaining Spontaneous Breathing During APRV

The concomitant increase in CI and arterial oxygenation improved the relationship between tissue oxygen supply and demand; $\dot{V}_O2$ remained unchanged despite the work of spontaneous breathing. In contrast, controlled mechanical ventilation for 72 h followed by weaning with APRV effected slower improvement in cardiopulmonary function and was associated with an increased duration of ventilatory support and stay in the ICU.

Patients with multiple trauma are considered at risk for development of ARDS. Hudson and coworkers (4) observed a 50% incidence of ARDS in trauma victims with an ISS above 50. The high incidence of ALI and ARDS in our trauma patients, who had an average ISS of 50, is in agreement with these findings. Controlled mechanical ventilation has been claimed superior to unsupported spontaneous breathing in the prevention of severe pulmonary dysfunction and arterial hypoxemia following trauma (23). On the other hand, arterial hypoxemia caused by $\dot{Q}_{VA}/\dot{Q}_T$ during ARDS has been found to correlate directly with the quantity of nonaerated tissue observed by computed tomography in dependent lung regions adjacent to the diaphragm. These observations have been attributed to alveolar collapse caused by the superimposed pressure on the lung and a cephalad shift of the diaphragm most evident in dependent lung areas during mechanical ventilation (1). Persisting spontaneous breathing during ventilatory support has been considered to improve both the distribution of ventilation to dependent lung areas and gas exchange, presumably by diaphragmatic contraction opposing alveolar compression (8, 11). This may explain why our patients, during full ventilatory support, had a lower $P_{A_{CO2}}/P_{A_{O2}}$ ratio and thereby fulfilled the criteria for ARDS. However, ALI and ARDS only represent different levels of pulmonary gas exchange disturbance caused by the same inflammatory reaction leading to increased vascular and alveolar permeability, interstitial edema formation, and alveolar collapse (13).

Partial ventilatory support is used increasingly, not only to wean patients from mechanical ventilation, but to provide stable ventilatory assistance of a desired degree during ventilatory failure (11, 24). Spontaneous breathing in any phase of the mechanical ventilator cycle is possible with APRV that provides ventilatory support by time-cycled switching between two levels of CPAP (9, 10). When spontaneous breathing is abolished, APRV is not different from conventional PCV (9–11). Ventila-

![Figure 5. Daily dose of intravenously administered norepinephrine, dobutamine, sufentanil, and midazolam at baseline (BL) and for 10 d in patients immediately breathing spontaneously with APRV (APRV Group) (open circles) or ventilated with a pressure-controlled, time-cycled mechanical mode for 72 h and then weaned with APRV (PCV Group) (closed squares). Values are mean ± SEM. †p < 0.05 between groups, *p < 0.05 between groups at the same time point, ‡p < 0.05 compared with Days 1, 2, or 3 within the same group.](image)

![Table 2. OUTCOME DATA*](image)

<table>
<thead>
<tr>
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<th>APRV Group</th>
<th>PCV Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients, n (%)</td>
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<td>15 (100)</td>
<td>–</td>
</tr>
<tr>
<td>Survivors, n (%)</td>
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<td>ARDS, n (%)</td>
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<td>11 (74)</td>
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<tr>
<td>ALI non ARDS, n (%)</td>
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<td>4 (27)</td>
<td>0.019</td>
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<td>Extrapulmonary organ failure, n (%)†</td>
<td>1 8 (53) 10 (67)</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 6 (38) 7 (47)</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt; 3 1 (9) 0 (0)</td>
<td>ns</td>
<td></td>
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<tr>
<td>Sepsis, n (%)</td>
<td>9 (75)</td>
<td>10 (30)</td>
<td>ns</td>
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<tr>
<td>Length of ventilatory support, d</td>
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<tr>
<td>Length of intubation, d</td>
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<tr>
<td>Length of ICU stay, d</td>
<td>23 ± 2 30 ± 2</td>
<td>0.032</td>
<td></td>
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Definition of abbreviations: ALI = acute lung injury (13); ARDS = acute respiratory distress syndrome (13); F = female; M = male.

* Values are mean ± SEM.
† Defined by the multi-organ failure score described by Knaus and colleagues (15).
tory support during APRV is determined by pulmonary mechanics, ventilatory rate, and the degree of spontaneous breathing. Consequently, in the absence of spontaneous breathing during APRV, lower alveolar ventilation results in a high PaCO₂ and low pH unless the airway pressure limits are adjusted to produce a larger VT and acceptable PaCO₂ and pH. Therefore, to maintain, V̇E, PaCO₂, and pH in the absence of spontaneous breathing, the pressure support level had to be significantly increased, and to prevent upper airway pressure from exceeding UIP, the ventilatory rate had to be significantly increased. Primarily partial ventilatory support with APRV allowed earlier discontinuation of ventilatory support, which was achieved by decreasing the ventilatory rate. Recent in vitro experiments suggest that decreasing ventilatory rates may even play a role in preventing ventilator-associated lung damage (25).

Several studies have documented improved pulmonary gas exchange upon changeover from full to partial ventilatory support (11, 24, 26). Prospective randomized trials indicate that the type of partial ventilatory support has little or no effect on the efficiency of weaning from mechanically ventilation (22, 27). Previous investigations have compared different partial ventilatory support modalities after prolonged mechanical ventilation in patients whose pulmonary function and gas exchange had essentially recovered (22, 27). Furthermore, the effects of full versus partial ventilatory support on cardiopulmonary function are difficult to evaluate on the basis of previous studies, because the modalities of mechanical ventilation were changed during the investigations (22, 27). In our study, the type of ventilatory support remained unchanged while the presence of spontaneous breathing was controlled with sedation and neuromuscular blockade and V̇E remained constant. Therefore, our results should reflect essentially the effect of persisting spontaneous breathing, not that of a change in mechanical ventilatory support modality.

Early spontaneous breathing during APRV consistently resulted in improved Q̇VA/QT and arterial oxygenation. These observations are in agreement with experimental (5, 6) and clinical (11, 24) findings that spontaneous breathing with APRV improves arterial blood oxygenation by decreasing intrapulmonary shunting. Previous radiographic observations have demonstrated that contractions of the diaphragm favor distribution of ventilation to dependent, well-perfused lung areas (8). Reduction of Q̇VA/QT in the presence of an increasing lung compliance indicates that spontaneous breathing with APRV improved the ventilation of initially nonventilated or poorly ventilated lung areas. In accordance with our findings, diaphragmatic contractions have been shown to reduce the size of atelectasis in dependent lung areas during general anesthesia (28). Spontaneous breathing should be associated with an increase in transpulmonary pressure caused by diaphragmatic contractions, and should therefore effectively recruit atelectatic lung regions or prevent progressive alveolar collapse in patients at risk for ARDS.

By contrast, full ventilatory support in anesthetized and paralyzed patients with normal lung function has been shown to result in atelectasis in dependent lung regions, which contributes considerably to Q̇VA/QT (29). In accord with these observations (29), absence of spontaneous breathing during mechanical ventilation, induced by deep sedation and neuromuscular blockade in our patients, promoted formation of atelectasis, presumably by a cephalad shift of the diaphragm and reflected by worsened lung compliance, Q̇VA/QT, and arterial oxygenation. After 72 h of mechanical ventilation, spontaneous breathing with APRV improved but did not restore gas exchange and lung mechanics.

Deep sedation with neuromuscular blockade is generally used to adapt patients to controlled mechanical ventilation (30). In a previous study we distinguished between the effects of sedation and neuromuscular blockade on gas exchange. Neuromuscular blockade did not affect gas exchange in patients with severe ARDS who had been rendered apneic by reducing their PaCO₂ (11). Therefore, the use of neuromuscular blockade to guarantee controlled mechanical ventilation cannot entirely explain the changes in cardiopulmonary function observed with persistent spontaneous breathing during APRV. Sedation in our patients was titrated to suppress spontaneous breathing. Under this condition, midazolam and sufentanil inhibited respiratory muscle activity and should have reduced the tension of the diaphragm (31). The cephalad shift of the diaphragm caused by its reduced tension during deep sedation or anesthesia is not aggravated by neuromuscular blockade (32). In agreement with observations during anesthesia, even higher airway pressures during controlled mechanical ventilation cannot prevent the development of atelectasis and deterioration of gas exchange (33). This may explain the deterioration in gas exchange observed in our patients who received initial PCV with deep sedation. However, the results of our study do not allow us to precisely distinguish the effects on cardiopulmonary function of deep sedation from those of controlled mechanical ventilation.

In our patients, spontaneous breathing was associated with an increase in CI. This is in agreement with the concept that a decrease in intrathoracic pressure during spontaneous inspiration with APRV may improve venous return and CI (11, 34). The highest CI values and lowest required doses of vasopressors and positive inotropes in our study occurred with persisting spontaneous breathing during APRV. The smaller increase in CI found when spontaneous breathing occurred after a period of controlled mechanical ventilation may be attributed to higher airway pressure support levels or deeper sedation. End-expiratory lung hyperinflation cannot explain this cardiovascular finding, because PEEP remained unchanged in both of our study groups. This indicates that during APRV, spontaneous respiratory activity may not decrease intrathoracic pressures sufficiently to entirely counteract the cardiovascular depression caused by higher airway pressures or deeper sedation.

Changes in CI caused by mechanical ventilation have been reported to correlate positively with Q̇VA/QT (35). In contrast, during spontaneous breathing with APRV, an increased CI was associated with a smaller Q̇VA/QT, an increased PaO₂, and a considerably higher ḊO₂. This effect was less pronounced when spontaneous breathing with APRV was allowed after 72 h of controlled mechanical ventilation. In accordance with previous findings (11, 24, 36), total V̇O₂ was not measurably altered by spontaneous breathing in our patients. The comparable total V̇O₂ indicates appropriate sedation levels in both of our study groups. An increased ḊO₂ with unchanged V̇O₂ resulted in an improved relationship between tissue oxygen supply and demand, as reflected by a significant decrease in O₂ER, which also may have contributed to the higher PaO₂ during APRV with spontaneous breathing.

Primarily partial ventilatory support with APRV was consistently associated with a shorter duration of ventilatory support, intubation, and ICU stay. This presumably results from the improvement in cardiopulmonary function with persisting spontaneous breathing without excessive sedation. Previous investigations demonstrated that standardized weaning protocols allow early identification of patients for spontaneous breathing trials, and thereby reduce the duration of mechanical ventilation (22). Because identical protocols were used to discontinue ventilatory support in both of our study groups, our results suggest that persisting spontaneous breathing with APRV is efficient for reducing the duration of ventilatory support. Hsiang
and coworkers reported that deep sedation and neuromuscular blockade in patients with head injury was associated with a higher incidence of pulmonary dysfunction and a prolonged ICU stay (37). Recently, Kress and coworkers (38) observed that daily interruption of sedative-drug infusions shortened the duration of ventilatory support and length of ICU stay. In accord with these findings, our results suggest that primarily spontaneous breathing with APRV avoided unnecessary deep sedation and thereby the reduced duration of ventilatory support and length of ICU stay. Because spontaneous breathing during APRV persisted only with less deep sedation, we cannot precisely distinguish the effects of sedation from those of spontaneous ventilation on duration of ventilatory support.

The results of this study show that partial ventilatory support with APRV, when used as a primary modality, allows reduction in sedation, contributes to improved arterial oxygenation, pulmonary compliance, and systemic blood flow, and is associated with a decreased duration of ventilatory support and ICU stay in patients at risk for ARDS. An initial period of controlled mechanical ventilation required unnecessary deep sedation and did not provide any advantage in cardiopulmonary function or clinical course.

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References


