Acute Hemodynamic Changes of Pressure-controlled Inverse Ratio Ventilation in the Adult Respiratory Distress Syndrome*  

A Transesophageal Echocardiographic and Doppler Study

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Twelve patients with the adult respiratory distress syndrome were included in this study and evaluated by transesophageal echocardiography and Doppler, assessing right and left ventricular intracardiac blood flow alterations with progressive increase of inspiration-to-expiration (I-E) ratios. Whereas midpulmonary artery flow parameters did not show any change, early left ventricular filling demonstrated a significant increase after switching the ventilatory mode from volume to pressure-controlled ventilation with 2:1 I-E ratio (end-inspiration: 39 ± 26 cm with positive end-expiratory pressure [PEEP]; ventilation to 68 ± 56 cm with pressure-controlled inverse-ratio ventilation, 2:1; p<0.01; at end-expiration, from 67 ± 21 cm with PEEP-ventilation to 83 ± 36 cm with pressure-controlled ventilation 1:1; p≤0.05), resulting probably from different ventilatory flow and pressure curves. In the meanwhile, cardiac index demonstrated a significant augmentation (from 4.73 ± 1.71 L/min·m² to 5.56 ± 1.66 L/min·m²; p<0.05). Pressure-controlled inverse ratio ventilation results in both respiratory and hemodynamic advantages as is demonstrated by this study.

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Continuous positive pressure ventilation (CPPV) has been used for many years as ventilatory support in patients with the adult respiratory distress syndrome (ARDS).1,3 Notwithstanding, the mortality of these patients apparently has not been affected until now, not even with extracorporeal assist technology.3 Therefore, trials with other ventilatory supportive techniques have been proposed. Pressure-controlled inverse ratio ventilation (Pc-IRV) seems to become of more than usual importance as supporting ventilatory therapy for ARDS.3-11 This mode of ventilation appears to increase mean airway pressure (Paw) with lower peak inspiratory pressure, yielding better oxygenation in conjunction with improved surfactant stabilization.12 Apart from these pulmonary advantages, the hemodynamic effects of this ventilation mode have not yet been fully evaluated.

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Using transesophageal echocardiography (TEE) and Doppler echocardiography, we therefore investigated hemodynamics of different settings of mechanical ventilation (volume-controlled ventilation with PEEP compared with Pc-IRV. Special interest was paid to evaluation of right ventricular function, pulmonary artery flow, and effects on left ventricular preload.

Materials and Methods

Patients

Twelve ARDS patients (8 male and 4 female; mean age, 40 years) were enrolled in the study over a 4-month period. Etiology of ARDS includes the following: polytrauma, 7; cytomegalovirus pneumonia, 2; burns including trachea, 1; postoperation, 2. According to the criteria of Rocker et al.,10 patients were accepted in the study when severe hypoxemia (PaO₂ <70 mm Hg) was present despite ventilation with 10 cm H₂O PEEP in combination with a forced inspiratory oxygen value of more than 0.6, which was held constant throughout the protocol for each patient. Furthermore, evidence of bilateral pulmonary infiltrates on the chest x-ray film and low filling pressures (pulmonary capillary wedge pressure, <18 mm Hg) were necessary. All patients yielded a lung injury score of more than 2.5.11 Patients were not permitted to be in the study if there was intracardiac shunting, valvular insufficiency, dysrhythmia, or hemodynamic instability. Patients with left ventricular wall motion abnormalities, as observed with TEE on the midpapillary muscle level, in conjunction with a fractional area contraction of
more than 0.50 also were excluded. Finally, patients with craniocerebral trauma, associated with increased intracranial pressure (measured by ventriculostomy), were not enrolled in the study.

The protocol was approved by the Local Ethics Committee. Before entering the study, a member of the family gave informed consent.

Methods

All patients received sedation with intravenously administered fentanyl, up to 7.5 μg/kg/h, and intravenously administered diazepam, 10 mg/kg 4 times a day, and muscle relaxation with intravenously administered pancuronium bromide, (50 μg/kg/h). Heart rate and blood pressure were monitored carefully in order to minimize central sympathetic outflow.  

The experimental setup of the study consisted of a ventilatory protocol in association with a TEE investigation.

Ventilation Protocol: A Servo 900C (Siemens Elema, Sweden) was used to deliver a constant tidal volume. Baseline values of both hemodynamic and echocardiographic variables were simultaneously measured at 10 cm H₂O PEEP with an inspiration-expiration (I:E) ratio of 1:1 and without pause time. Then ventilation was switched to the pressure-controlled mode with again an I:E ratio of 1:1 but without external PEEP and pause time. Changing from volume-controlled ventilation with PEEP to pressure-controlled ventilation with an I:E ratio of 1:1, the pressure preset on the ventilator was set in such a manner that the inspiratory tidal volume (V̇̇) and PaCO₂ remained constant compared with the volume-controlled ventilation mode. Furthermore, the I:E ratio was increased to 2:1 (without external PEEP and pause time) and finally to 4:1. Measurements were obtained at the end of each stabilization period of 30 min.

The following respiratory variables were measured: V̇̇, expiratory minute volume, peak inspiratory airway pressure and Paw. Alveolar PEEP was measured in the pressure-controlled ventilation modes on the ventilator using the expiratory hold function. Hemodynamic parameters were determined: heart rate, mean arterial pressure, right atrial pressure, mean pulmonary artery pressure, and pulmonary capillary wedge pressure; cardiac output and index were calculated as the mean of four measurements obtained by injection of 10 ml of a cold dextrose 5 percent solution. Analysis of arterial blood gas samples was performed in the laboratory (Corning 2500 CO-oximeter).

Transesophageal Echocardiographic protocol: Connected to an ultrasound system (Vingmed CFM 700, Trondheim, Norway), TEE was performed using a 5-MHz transducer mounted on a flexible probe. All echocardiographic and Doppler data were recorded on a videotape and reviewed in real time and stop-frame format later.

Throughout the study protocol, three levels were consecutively investigated with each ventilation mode. Both right and left ventricles were viewed at the mid-papillary muscle level (transgastric short-axis view) in order to study changes in these areas.  

End-diastolic and end-systolic boundaries were traced off line. The R wave was used to select end-diastolic frames; end-systole was defined as the minimal cross-sectional area of both ventricles. Care was taken that measurements were made at the end of expiration. Fractional area contraction was obtained according the following formula:

\[
\text{Fractional area contraction} = \frac{\text{end-diastolic area} - \text{end-systolic area}}{\text{end-diastolic area}} \times 100
\]

Furthermore, transmitial flow was obtained with the sample volume at the annulus of the mitral valve. Early left ventricular peak flow velocity and the late peak flow velocity were measured; for this purpose, the best signal-to-noise ratio and least spectral dispersion were used. For each case the early to late peak flow velocity ratio and time velocity integral (TVI) of the transmitial flow were assessed.

Finally, flow velocity of the pulmonary artery was obtained with the sample volume just between the pulmonary valve and the bifurcation and TVI again was measured.

Calculations for both transmitial flow and pulmonary artery variables were averaged over three consecutive expiratory phases. All echocardiographic measurements were performed off line with a commercially available analyzing system (Aloka SSD570, Tokyo, Japan).

Statistical Analysis

Overall statistical analysis was performed with analysis of variance. The Wilcoxon signed rank matched pair test was used to assign statistical differences. Statistical significance was accepted if probability was less than 0.05.

Results

In all patients, adequate short-axis views were obtained of both left and right ventricles. Furthermore, in all patients transmitial flow and mid-pulmonary artery flow were easily obtained.

Cardiorespiratory Parameters

A progressive decline in expiratory minute volume and V̇̇ was observed when switching the ventilation mode from CPPV to pressure-controlled ventilation with an I:E ratio of 4:1 (Table 1). Peak inspiratory airway pressure and Paw decreased significantly (p<0.05) from CPPV to pressure-controlled ventilation with an I:E ratio of 1:1 (from 37 ± 7 to 24 ± 7 cm H₂O and from 19 ± 3 to 12 ± 4 cm H₂O, respectively).

Total PEEP showed a decline from 10 cm H₂O with

### Table 1 — Respiratory Parameters With Continuous Positive Pressure Ventilation and Pressure-Controlled Ventilation With Increasing Inspiratory-to-Expiratory Ratios in 12 Patients With Adult Respiratory Distress Syndrome

<table>
<thead>
<tr>
<th></th>
<th>Expiratory Minute Volume</th>
<th>Peak Inspiratory Airway Pressure</th>
<th>Paw</th>
<th>PEEP*</th>
<th>PaCO₂</th>
<th>Oxygen Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPPV</td>
<td>899 ± 214</td>
<td>13.0 ± 3.4</td>
<td>37 ± 7</td>
<td>19 ± 3</td>
<td>10</td>
<td>40 ± 4</td>
</tr>
<tr>
<td>1:1</td>
<td>851 ± 243</td>
<td>12.9 ± 3.7</td>
<td>24 ± 7$</td>
<td>12 ± 4$</td>
<td>3</td>
<td>41 ± 6</td>
</tr>
<tr>
<td>2:1</td>
<td>756 ± 205</td>
<td>11.7 ± 3.0</td>
<td>25 ± 8$</td>
<td>17 ± 6</td>
<td>6</td>
<td>43 ± 5</td>
</tr>
<tr>
<td>4:1</td>
<td>606 ± 160$</td>
<td>9.3 ± 3.2$</td>
<td>24 ± 8$</td>
<td>19 ± 7</td>
<td>10</td>
<td>52 ± 10$</td>
</tr>
</tbody>
</table>

*PEEP = total PEEP (sum of intrinsic PEEP and external PEEP).
†: = pressure-controlled ventilation with I:E ratio 1:1, etc.
$ p<0.05 in relation to CPPV.
$ p<0.01 in relation to CPPV.
CPPV to 3 cm H₂O (alveolar PEEP) with pressure-controlled ventilation (I-E ratio, 1:1) but increased up to 10 cm H₂O with the Pc-IRV 4:1 mode.

Heart rate, mean artery pressure, right atrial pressure, pulmonary capillary wedge pressure, and mean pulmonary artery pressure did not change significantly throughout the study (Fig 1). Cardiac index showed a significant increase by switching the ventilation mode from CPPV to pressure-controlled ventilation (from 4.73 ± 1.71 to 5.56 ± 1.66 L/min/m², p<0.05). From arterial, mixed venous and pulmonary capillary blood gases, the respiratory profile was calculated: oxygen delivery and oxygen consumption did not show any change (Table 1).

| Table 2—Early to Late Peak Flow Parameters and Pulmonary Artery Flow Parameters in Relation to Continuous Positive Pressure Ventilation and Pressure-Controlled Inverse Ratio Ventilation With Augmenting Inspiratory-to-Expiratory Ratio in 12 Patients With Adult Respiratory Distress Syndrome |
|---------------------------------|-----------------|-------------------|
| TVI, E-A Ratio* | TVI, Pulmonary |
| CPPV | 1:1† | 2:1 | 4:1 |
| TVI | 13.2 ± 2.7 | 14.4 ± 4.1 | 17.0 ± 4.9 | 15.2 ± 5.2 |
| E-A | 12.8 ± 2.8 | 13.4 ± 3.2 | 14.7 ± 5.2 | 14.4 ± 7.4 |

*E-A: ratio of early left ventricular diastolic filling and atrial contraction wave.
†1:1 = pressure-controlled ventilation with I-E ratio of 1:1, etc.
‡p<0.05 in relation to CPPV.

**Echocardiographic and Doppler Parameters**

Concerning pulmonary artery flow, there were no changes at any time of the study (Table 2). At the transmural level, the A wave did not show any significant change throughout the study period in any patient in contrast to the E wave. At end-inspiration, early left ventricular filling velocity increased significantly, as shown in Figure 2, *top* (from 0.35 ± 0.16 m/s with PEEP ventilation to 0.43 ± 0.18 m/s with the Pc-IRV 2:1 mode; p<0.05). Significant increase was also found observing TVI of the E wave (39 ± 26 cm with PEEP ventilation to 68 ± 56 cm with the Pc-IRV 2:1 mode; p<0.01). At end-expiration, TVI of the E wave also increased significantly, as is demonstrated in Figure 2, *bottom* (from 67 ± 21 cm with PEEP ventilation to 93 ± 36 cm with pressure-controlled ventilation 1:1, p<0.05). Transmural flow increased significantly with Pc-IRV 2:1 compared to volume-controlled PEEP ventilation (Table 2). At baseline, no significant differences of right ventricular fractional area contraction were observed (Table 3). The end-diastolic areas of the right ventricle showed a significant increase with the Pc-IRV 4:1 mode (Table 3).

**DISCUSSION**

The ability of tranesophageal color Doppler echocardiography to obtain high quality images in the critically ill appears to be of importance in many clinical situations, especially in the case of nontrans-
Table 3—Fractional Area Contraction (%) and Right Ventricular End-Diastolic Area in 12 Adult Respiratory Distress Patients Ventilated Consecutively With Continuous Positive Pressure Ventilation and With Pressure-Controlled Ventilation With Increasing Inspiratory-to-Expiratory Ratio

<table>
<thead>
<tr>
<th>Right Ventricular Fractional Area Contraction</th>
<th>Right Ventricular End-Diastolic Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPPV</td>
<td>36 ± 12</td>
</tr>
<tr>
<td>1:1</td>
<td>38 ± 11</td>
</tr>
<tr>
<td>2:1</td>
<td>39 ± 9</td>
</tr>
<tr>
<td>4:1</td>
<td>36 ± 9</td>
</tr>
<tr>
<td>1:1*</td>
<td>79 ± 46</td>
</tr>
<tr>
<td>1:1†</td>
<td>83 ± 43</td>
</tr>
<tr>
<td>2:1</td>
<td>85 ± 36</td>
</tr>
<tr>
<td>4:1</td>
<td>117 ± 33†</td>
</tr>
</tbody>
</table>

*1:1 = pressure-controlled ventilation with I-E ratio of 1:1, etc.
†p<0.05 in relation to baseline conditions.

Ventricular ejection fraction catheter, Edwards Lab, Santa Ana, Calif) and was used to assess hemodynamic effects of different ventilation modes.19,23

The possibility of evaluating hemodynamics of PEEP ventilation with TEE and Doppler has been discussed recently.24-28 With respect to hemodynamic assessment of mechanical ventilation, the usefulness of this technique already has been demonstrated in earlier studies: a beat-to-beat analysis becomes possible in order to analyze scrupulously the different phases of the ventilatory cycle. In this study, evaluation of the hemodynamic effects of both volume-controlled positive-pressure ventilation and various modes of pressure preset ventilation was performed. Apart from the study of the ventricular contractility, pulmonary artery flow and transmitral flow were evaluated.

From a recent mortality study, the usefulness of Pcr-IRV became important compared with extracorporeal oxygenator techniques.3 With Pcr-IRV, the expiratory phase is shortened, creating an alveolar PEEP, which is directly related to the pressure preset on the ventilator; due to altered flow and pressure curves,3 immediate effects on hemodynamics could be expected.

As in clinical practice, we started with volume-controlled PEEP ventilation and compared this mode with pressure-controlled ventilation with the same I-E ratio of 1:1; afterwards, the I-E ratio was increased stepwise until a 4:1 ratio was reached. In order to obtain the same Paw and CO2 elimination, the same ventilatory settings had to be selected changing volume- to pressure-controlled ventilation. Clinically, however, it was impossible to compare volume-controlled ventilation to the pressure-controlled mode by keeping Paw constant, since this parameter decreases per definition with pressure preset ventilation. When lengthening the I-E ratio—especially above 4:1, alveolar pressures rise hyperbolically, resulting in significant augmentation of the risk of barotrauma.29 The 4:1 mode was therefore selected as the most extreme ratio.

Figure 2. Early left ventricular diastolic filling parameters at end-inspiration (top), and at end-expiration (bottom), during CPPV and pressure-controlled ventilation with incrementally increasing I-E ratio in ARDS patients.

Portability. Many authors reported their experience with this technique in the intraoperative as well as in the postoperative period.18,19

Since Laver et al.10 stressed the importance of the right ventricle, the relativity of measurements of pulmonary artery pressures and pulmonary capillary wedge pressure when both extrinsic and intrinsic factors influence right ventricular compliance becomes obvious.31 Volumetric assessment of the right ventricle is therefore essential in conjunction with flow measurements. Real time evaluation of right ventricular function recently became available (right
Pulmonary Artery Flow

The adult respiratory distress syndrome is an acute respiratory failure due to a nonhemodynamic pulmonary permeability edema. Pulmonary hypertension is a common phenomenon of ARDS and results from an increase of pulmonary vascular resistance, due to diffuse thromboembolism, endothelial injury combined with intimal proliferation, and alveolar flooding, resulting in vascular compression. It has been questioned by different authors whether pulmonary vascular resistance is a good measure to describe the functional status of the pulmonary circulation. Pressure and resistance can be better associated and related with volume and flow.

Midpulmonary artery flow did not change, although there was a significant variation of total PEEP (Table 2). Absence of any important change of flow characteristics may be explained by right ventricular compensation capacity, ie, increase of end-diastolic area. On the other hand, the parameters evaluated might be insufficient to detect any significant alteration.

Changes in Left Ventricular Preload

With the advent of TEE and computerized image processing, transmitral flow parameters can be easily obtained, even with high PEEP ventilation. These measures have been proposed as left ventricular diastolic function indices.

End-inspiratory transmitral flow increased significantly with the 2:1 mode (Table 2) in conjunction with an increase of early diastolic filling parameters (Fig 2). Even with the same amount of PEEP, left ventricular preload augmented indeed with a rising I-E ratio; this phenomenon is more pronounced at end-inspiration, even with baseline PEEP ventilation. The reason for this may be an increased degree of pulmonary squeezing during inspiration with PEEP IRV compared with PEEP ventilation due to an altered inspiratory flow pattern, resulting in a pronounced augmentation of the amplitude and TVI of the E wave. These data are consistent with an earlier study, demonstrating augmented cardiac output with the 2:1 mode in conjunction with increased right ventricular preload parameters. Following the results of this study, both increase in right ventricular preload and augmented left ventricular preload contribute to and explain the increase in cardiac output in the PEEP 2:1 mode.

A complex of multiple factors, such as left atrial pressure, relaxation rate and left ventricular systolic pressure, determine the mitral inflow velocity profile; simultaneous variation of different Doppler parameters will not simplify the interpretation of the influence of altering ventilatory patterns on hemodynamics. Reduction of preload disturbs the evaluation of transmitral flow. In the context of ventilatory induced hemodynamic changes with a quite constant peak filling velocity during atrial systole, it means that the early-to-late peak flow velocity ratio is not a good parameter for evaluating left ventricular diastolic function. The Pc-IRV 4:1 mode induced a marked decline of left ventricular preload in comparison with the PEEP 2:1 mode. In contrast, left ventricular filling pressure remained constant. This apparent contradiction can be explained by the fact that TEE presents the unique opportunity to monitor in real time and beat-to-beat the effects of changing intrathoracic pressures, besides the advantages of high resolution imaging.

Biventricular Function

Because of the crescent shape of the right ventricle and the present trabeculations, outlining the endocardium seems more difficult in comparison with the left ventricle. Nevertheless, different authors have asserted the possibility of obtaining adequate right ventricular contouring. Right ventricular end-diastolic area increased significantly following changing ventilation mode, notwithstanding both CPV and PEEP 4:1 create approximately the same degree of total PEEP (Table 1). This suggests an apparently more pronounced inclination of the right ventricular outflow impedance with the 4:1 mode (Table 3). Cardiac output was augmented also, explaining constant pulmonary artery flow (TVI) (Table 2).

Conclusion

Transesophageal echocardiography offers the unique advantage to monitor hemodynamics closely, and especially right ventricular function and outflow impedance during various settings of mechanical ventilation in a beat-to-beat fashion.

Besides lower peak inspiratory pressure and, hence, reduced risk of barotrauma and better outcome, we demonstrated with the PEEP 2:1 mode an important increase in transmitral flow and cardiac output in comparison with positive pressure ventilation. Furthermore, we observed this without altering oxygen transport. In addition, with the 2:1 mode, lower peak inspiratory pressures, and hence reduced risk of barotrauma, were demonstrated. By means of TEE, it was possible to demonstrate change of left ventricular preload parameters, which seems to be of clinical importance concerning the significant augmentation of cardiac index measured with the 2:1 mode.

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