Cyclic changes in right ventricular output impedance during mechanical ventilation

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Vieillard-Baron, Antoine, Yann Loubieres, Jean-Marie Schmitt, Bernard Page, Olivier Dubourg, and François Jardin. Cyclic changes in right ventricular output impedance during mechanical ventilation. J. Appl. Physiol. 87(5): 1644–1650, 1999.—In a context such as acute respiratory distress syndrome, where optimum tidal volume and airway pressure levels are debated, the present study was designed to differentiate the right ventricular (RV) consequences of increasing lung volume from those secondary to increasing airway pressure during tidal ventilation. The study was conducted by combined two-dimensional echocardiographic and Doppler studies in 10 patients requiring mechanical ventilation in the controlled mode because of acute respiratory failure. Continuous monitoring of airway pressure on echocardiographic and Doppler recordings provided accurate timing of each cardiac event during the respiratory cycle, with particular attention being paid to end-expiratory and end-inspiratory atrial diameters, RV dimensions, and pulmonary artery and tricuspid flow estimated by the velocity-time integral (PAVTI and TVTI, respectively). At baseline, lung inflation during the inspiratory phase of mechanical ventilation produced a drop in PAVTI from 14.3 ± 2.6 cm at end expiration to 11.3 ± 2.1 cm at end inspiration. This drop occurred without reduction in right atrial diameter or in RV diastolic dimensions. It was not preceded but was followed by a decrease in TVTI, thus confirming an increase in RV outflow impedance. Manipulation of tidal volume without changing airway pressure and manipulation of airway pressure without changing tidal volume demonstrated that tidal volume, but not airway pressure, was the main determinant factor of RV afterloading during mechanical ventilation.

The effects of mechanical respiratory support on right ventricular (RV) function include reduced preload (6), increased afterload (2), or both, and might be briefly described as an inordinate RV afterload relative to RV preload. Whereas reduced RV preload is mediated through venous return impairment (20), excessive RV outflow impedance might theoretically result from increased airway pressure (21), increased lung volume (32), or both.

Left ventricular impact of RV afterloading secondary to positive end-expiratory pressure (PEEP) and cyclic RV afterloading occurring during the inspiratory phase of mechanically controlled ventilation have been demonstrated in previous clinical studies (12, 13). In a context such as acute respiratory distress syndrome (ARDS), where tidal volume reduction (4) and optimum airway pressure (1) are debated, the present study was designed to differentiate the RV consequences of increasing lung volume from those secondary to increasing airway pressure during tidal ventilation. The relationship between lung volume and airway pressure was allowed to change during the study by introducing an alteration in respiratory mechanics, using a mild thoracic constraint by chest strapping.

METHODS

Between January and May 1998, the 10 patients included in the present study received mechanical respiratory support (controlled mode) for ARDS of various causes, with the arterial P0.9–inspiratory O2 fraction ratio < 0.20 and bilateral chest infiltrates. At the time of the study, all patients were hemodynamically stable, with systolic arterial pressure (invasive) > 105 mmHg and heart rate < 95 beats/min. End-expiratory central venous pressure was 13 ± 2 mmHg at baseline. Patients were sedated with midazolam and sufentanil and paralyzed with vecuronium if necessary to obtain a perfect adaptation to the ventilator.

Hemodynamic measurements were first obtained at baseline, with a tidal volume of 8 ml/kg and zero end-expiratory pressure (baseline period), and were repeated after a change in chest wall elastance. The latter was obtained by producing mild thoracic constraint using the abdominal compartment of a medical antishock trouser placed around the chest and inflated to 30 cmH2O (strapping period). During this second period, tidal volume was decreased to obtain a plateau pressure close to the previous baseline. A third set of measurements was obtained after removal of strapping and restoration of tidal volume to its initial level and addition of an 8-cmH2O end-expiratory pressure (PEEP period). A 100% inspiratory O2 fraction was used during the study. Heart rate, systemic arterial pressure, central venous pressure, and arterial O2 saturation from a nail-bed oxymeter were monitored. The study protocol was approved by the Institutional Review Board for Human Subjects of Paris-Cochin (92/135), and informed consent was obtained from each patient's next of kin.

Respiratory measurements. Tidal volume and airway pressure were obtained from the respirator (Puritan Bennett 7200). During the period of the study, the fixed respiratory rate was unchanged (12 cycles/min), inspiratory flow was constant, and an end-inspiratory pause of 0.6 s was preset. Total quasi-static compliance was calculated as tidal volume divided by the difference between end-inspiratory (“plateau”) and end-expiratory airway pressures.

Doppler echocardiographic measurements. Echo Doppler studies were performed with a Toshiba Corevision (model SSA-350A). By using the signal from the respirator, airway pressure was displayed on the screen of the echo Doppler...
device, allowing accurate timing of cardiac events during the respiratory cycle. Four beats were selected for measurements: an end-expiratory beat, defined as the last beat occurring before mechanical lung inflation (beat 1); a beat occurring during the dynamic phase of lung inflation (beat 2); an end-inspiratory beat defined as the last beat occurring during the end-inspiratory pause (beat 3); and a beat occurring at the onset of exhalation (beat 4).

The multiplane transesophageal echocardiography transducer (5–7 MHz) was first positioned in the esophagus to obtain the long-axis atrial plane, the ultrasonic beam being perpendicular to the interatrial septum at the level of fossa ovalis. From this plane we obtained simultaneous two-dimensional and M-mode recordings to measure left (LAD) and right atrial diameters (RAD) at end systole. Second, the transducer was positioned to obtain a four-chamber view of the cardiac cavities. From this view, RV area was measured at end diastole (RVEDA) and at end systole (RVESA), permitting calculation of RV stroke area as RVEDA – RVESA and RV fractional area contraction as RV stroke area/RVEDA. In the same view, with the ultrasonic beam directed perpendicularly to the tricuspid ring, the Doppler sample volume was placed at the level of the tricuspid orifice to record RV inflow. Third, with the ultrasonic beam parallel to the long axis of the pulmonary artery, the Doppler sample volume was placed beyond the pulmonary valve in the midlumen of the pulmonary artery to record the pulmonary artery flow. From pulsed Doppler spectrum recordings at a high speed of 5 cm/s, we measured velocity-time integrals at tricuspid and pulmonary levels (TVTI and PAVTI, respectively). RV isovolumic contraction time, acceleration time (Ac), peak velocity (Vmax), deceleration time, and flow period were measured from the pulmonary artery Doppler spectrum. Mean acceleration (Acmean) was calculated as Vmax/AcT. Pulmonary artery systolic diameter was measured on the third view, after enhanced contrast by color Doppler. From this diameter, we calculated pulmonary artery cross-sectional area. RV stroke output was calculated by multiplying PAVTI by pulmonary artery cross-sectional area. Stroke output corrected for body surface area was expressed as RV stroke index (RVSI).

A complete set of echo Doppler measurements was obtained at baseline (period 1), whereas only atrial plane and pulmonary artery flow were examined during chest strapping (period 2) and PEEP application (period 3).

Statistical analysis. Statistical calculations were performed by using the Statgraphics version 5 package (Univariate). Data are expressed as means ± SD unless otherwise specified. Doppler echocardiographic measurements at baseline and mechanical and hemodynamic changes within respiratory cycles and between the three periods were analyzed by using a multifactor analysis of variance followed by a Fisher protected least significant difference test when significant changes were individualized. A test giving P < 0.05 was considered as statistically significant.

RESULTS

Heart rate and systemic arterial pressure were unaltered during the whole protocol. Arterial O2 saturation, continuously monitored during the study, remained >90% in each patient.

Respiratory data are presented in Table 1, changes in pulmonary artery flow in Table 2, and simultaneous changes in atrial diameters in Table 3. Intraobserver and interobserver reproducibility of Vmax (2 ± 2.9 and 4 ± 4.8%, respectively), PAVTI (3.4 ± 3.1 and 7 ± 5.6%, respectively), and flow period (3.1 ± 2.6%, respectively) measurements have been published previously (7).

Specific effect of increased lung distension. Chest wall constraint significantly reduced total quasi-static compliance (Table 1). Tidal volume was significantly reduced during strapping so that airway pressure at the end-inspiratory plateau was not different from the baseline value (Table 1).

Specific effect of PEEP. Application of a PEEP level of 8 cmH2O produced a significant increase in end-inspiratory (plateau) airway pressure, whereas tidal volume was unchanged (Table 1).

Cyclic changes in RV inflow and outflow during a whole respiratory cycle. Examples of pulmonary artery and tricuspid flow velocity at low-speed recording are shown in Fig. 1. Average pulmonary artery systolic diameter (2.3 ± 0.2 cm) was unchanged during the

Table 1. Average respiratory data during the 3 periods

<table>
<thead>
<tr>
<th></th>
<th>Period 1 (Baseline)</th>
<th>Period 2 (Chest Strapping)</th>
<th>Period 3 (PEEP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pplateau, cmH2O</td>
<td>23 ± 9</td>
<td>21 ± 9</td>
<td>31 ± 9*</td>
</tr>
<tr>
<td>Vr, ml</td>
<td>637 ± 89</td>
<td>269 ± 56*</td>
<td>636 ± 88</td>
</tr>
<tr>
<td>Cr, ml/cmH2O</td>
<td>28 ± 14</td>
<td>12 ± 8*</td>
<td>28 ± 12</td>
</tr>
</tbody>
</table>

VALUES ARE MEANS ± SD. PEEP, positive end-expiratory pressure; Pplateau, end-inspiratory airway pressure (after an end-inspiratory pause of 0.6 s); Vr, tidal volume; Cr, total compliance. *P < 0.05.

Table 2. Hemodynamic changes produced by lung inflation during the 3 periods

<table>
<thead>
<tr>
<th></th>
<th>Period 1 (Baseline)</th>
<th>Period 2 (Chest Strapping)</th>
<th>Period 3 (PEEP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vmax, m/s</td>
<td>0.85 ± 0.15</td>
<td>0.86 ± 0.24</td>
<td>0.85 ± 0.21</td>
</tr>
<tr>
<td>Exp</td>
<td>0.69 ± 0.16*</td>
<td>0.74 ± 0.25*</td>
<td>0.64 ± 0.19*</td>
</tr>
<tr>
<td>PAVTI, cm</td>
<td>14.3 ± 2.6</td>
<td>13.8 ± 4.9</td>
<td>13.3 ± 3</td>
</tr>
<tr>
<td>Exp</td>
<td>11.3 ± 2.1*</td>
<td>11.9 ± 4.6</td>
<td>10.2 ± 2.6*</td>
</tr>
<tr>
<td>ICT, ms</td>
<td>36 ± 15</td>
<td>34 ± 18</td>
<td>50 ± 26</td>
</tr>
<tr>
<td>Exp</td>
<td>40 ± 12</td>
<td>42 ± 16</td>
<td>53 ± 23</td>
</tr>
<tr>
<td>AcT, ms</td>
<td>89 ± 38</td>
<td>87 ± 37</td>
<td>82 ± 13</td>
</tr>
<tr>
<td>Exp</td>
<td>107 ± 38</td>
<td>97 ± 29</td>
<td>104 ± 31</td>
</tr>
<tr>
<td>DCT, ms</td>
<td>169 ± 31</td>
<td>144 ± 48</td>
<td>152 ± 26</td>
</tr>
<tr>
<td>Exp</td>
<td>137 ± 41</td>
<td>139 ± 56</td>
<td>136 ± 30</td>
</tr>
<tr>
<td>FP, ms</td>
<td>257 ± 32</td>
<td>244 ± 92</td>
<td>234 ± 23</td>
</tr>
<tr>
<td>Exp</td>
<td>244 ± 27</td>
<td>236 ± 51</td>
<td>240 ± 32</td>
</tr>
<tr>
<td>Acmean, m/s^2</td>
<td>9.6 ± 8.5</td>
<td>9.9 ± 6.9</td>
<td>10.4 ± 3.4</td>
</tr>
<tr>
<td>Exp</td>
<td>6.4 ± 2.9*</td>
<td>7.6 ± 6.2</td>
<td>6.2 ± 3.3*</td>
</tr>
<tr>
<td>RVSI, cm^2/m^2</td>
<td>33.0 ± 7.7</td>
<td>31.7 ± 11.1</td>
<td>30.5 ± 6.3</td>
</tr>
<tr>
<td>Exp</td>
<td>26.1 ± 9.2*</td>
<td>27.4 ± 10.3</td>
<td>23.5 ± 5.5*</td>
</tr>
</tbody>
</table>

VALUES ARE MEANS ± SD. Exp, end-expiration (beat 1); Insp, end-inspiration (beat 3); Vmax, peak velocity; PAVTI, velocity-time integral of pulmonary artery flow; TVTI, isovolumic contraction time; AcT, acceleration time; DCT, deceleration time; FP, flow period; Acmean, mean acceleration; RVSI, right ventricular stroke index. Nos. in brackets denote average inspiratory decrease in RVSI at each period. *P < 0.05 end inspiration vs. end expiration. †P < 0.05 period 2 vs. period 1 or 3.
respiratory cycle. Simultaneous changes in TVTI, PAVTI, and RV function occurring during a respiratory cycle are shown in Figs. 2 and 3. At the onset of mechanical lung inflation, the airway pressure increase produced a significant decrease in PAVTI without a change in TVTI (beat 2) compared with end-expiratory values (beat 1). Later, during the static phase of lung inflation (beat 3), both TVTI and PAVTI significantly decreased. At this time, RVEDA was unchanged, but RVESA was significantly enlarged and RV fractional area contraction was reduced (Fig. 3).

Hemodynamic effects of lung inflation. Changes in pulmonary artery Doppler measurements are presented in Table 2. In addition to a significant decrease in PAVTI and RVSI, lung inflation at baseline produced a significant decrease in Vmax and in Acmean. An example of respiratory changes in PAVTI and Acmean at high-speed recording is shown in Fig. 4. Similar changes of the same amplitude were observed during the PEEP period. The strapping period, however, was characterized by a smaller amplitude of these changes, which became nonsignificant for PAVTI, RVSI, and Acmean.

Changes in atrial diameters are presented in Table 3. Whereas RAD was unchanged, LAD significantly increased at the plateau phase of lung inflation. A similar pattern was noted during the three successive periods of the study. An example of respiratory changes in LAD is shown in Fig. 5.

**DISCUSSION**

The first studies devoted to the hemodynamic consequences of mechanical ventilation were performed in the 1950's and 1960's (2, 6, 20, 31) and showed that tidal ventilation by using a positive pressure applied to the airways produced a fall in cardiac output. In the 1970s and 1980s, the number of patients submitted to mechanical ventilation dramatically increased, and the hemodynamic impact of this respiratory support was routinely assessed by invasive pressure monitoring and thermodilution cardiac output measurement (23). The negative impact of mechanical ventilation on systemic arterial pressure and cardiac output was confirmed, and was worsened by PEEP application (16). At this time, the negative influence of increased pleural pressure on cardiac filling (6) was not reexamined. However, pressure and output measurements provided limited hemodynamic information when cardiac cavity dimensions were unknown. Subsequent availability of echocardiography in medical intensive care units has made it possible to combine ventricular pressures, output, and size measurements (13). With this complete hemodynamic evaluation, the negative impact of positive airway pressure on RV output impedance in critically ill patients was demonstrated (11, 13). Further-

![Table 3. Changes in atrial diameters produced by lung inflation during the 3 periods](image)

<table>
<thead>
<tr>
<th></th>
<th>Period 1 (Baseline)</th>
<th>Period 2 (Chest Strapping)</th>
<th>Period 3 (PEEP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAD, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exp</td>
<td>44.1 ± 10.7</td>
<td>48 ± 7</td>
<td>44.4 ± 10.5</td>
</tr>
<tr>
<td>Insp</td>
<td>44.1 ± 10.1</td>
<td>41 ± 11.6</td>
<td>41 ± 11.6</td>
</tr>
<tr>
<td>LAD, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exp</td>
<td>24.6 ± 9.4</td>
<td>26.8 ± 11</td>
<td>26.4 ± 8.6</td>
</tr>
<tr>
<td>Insp</td>
<td>30.6 ± 8.6*</td>
<td>30.1 ± 9.9*</td>
<td>32.4 ± 8.4*</td>
</tr>
<tr>
<td></td>
<td>(+24%)</td>
<td>(+12%†)</td>
<td>(+23%)</td>
</tr>
</tbody>
</table>

Values are means ± SD. RAD, right atrial diameter; LAD, left atrial diameter (measurements of atrial diameters were obtained at the end of ventricular systole). Nos. in brackets denote average inspiratory increase in LAD at each period. *P < 0.05 end inspiration vs. end expiration. †P < 0.05 period 2 vs. period 1 or 3.

![Fig. 1. Examples of simultaneous recording at low speed of pulmonary artery flow velocity and airway pressure (Paw; top) and of tricuspid flow velocity and airway pressure (bottom) with selection of 4 beats (1-4) for measurements.](image)
more, hemodynamic changes during respiratory support also exhibited cyclic variations related to the alternation between inspiratory and expiratory phases (14, 27). The lack of a steady state did not permit assessment of these changes by using cardiac output measurement because it reflected an average value of stroke outputs within the respiratory cycle (9). The recent availability of transesophageal Doppler echocardiography has enabled beat-to-beat evaluation of inflow and outflow of both ventricles in a mechanically ventilated patient. Doppler recording of ventricular inflow velocity at the atrioventricular valve allows assessment of beat-to-beat changes in ventricular filling during respiratory support. Doppler recording of ventricular outflow velocity at the ventriculoarterial valve provides information on ventricular function: VTI directly reflects stroke output, and Acmean (Vmax/Act) is reduced by afterloading (8) and increased by unloading (3), and accurately reflects changes in output impedance.

Cyclic increase in RV output impedance during tidal ventilation was advocated by Andersen and Kuchida (2)
in 1967 and confirmed by our group more recently (10, 12). The significant reduction in PA VTI during lung inflation observed in the present study, which reflected a decrease in RVSI, was in agreement with these previous findings. Reduction in PA VTI occurred with tidal ventilation and before any decrease in RV inflow. This reduction persisted at the end of inflation and was associated with a drop in RV inflow. Moreover, changes in RV dimensions revealed by two-dimensional echocardiography confirmed our previous findings of inspiratory reduction of RV fractional area contraction associated with a significant increase in RV systolic dimensions, a characteristic feature of RV systolic impairment (12). Inspiratory increase in RV output impedance was corroborated by a decreased Acmean at this respiratory time (8).

The present study also failed to detect an absolute decrease in RV preload during tidal ventilation. Two indexes of RV preload, RAD and RVEDA, remained unchanged during lung inflation. However, it is likely that a relative decrease occurred because any increase in afterload would be associated with an increase in preload, which was not observed either. This latter result was somewhat at variance with our previous transthoracic echocardiography data demonstrating an inspiratory increase in RVEDA in mechanically ventilated patients with ARDS (12). This difference might result from the range of tidal volume used (8 ml/kg in the present study, 10 ml/kg in the previous study), a larger range being expected to produce greater afterload. It should also be considered that the abdominal vascular zone condition may modulate the hemodynamic impact of inspiratory diaphragmatic descent on venous return (29, 30). In our well-fluid-resuscitated patients, exhibiting an average central venous pressure of 13 mmHg, a zone 3 condition for abdominal vasculature was very likely.

Reduced lung compliance is a common finding in ARDS patients (15, 18) and may be hemodynamically deleterious by requiring high airway pressure for adequate lung recruitment. High airway pressure, acting as the back pressure for pulmonary venous return when it exceeds pulmonary venous pressure, may increase RV afterload (21). Thus, during lung inflation, RV afterloading depends on airway pressure with respect to pulmonary venous pressure (21, 26). In a steady-state lung and vascular volume condition, pulmonary venous pressure, which reflects left atrial pressure, is directly influenced by pleural pressure, any increase of which during lung inflation would raise pulmonary venous pressure by the same amount. Thus transpulmonary pressure (and related tidal volume), and not airway pressure in its strict sense, may be the main determinant factor of RV afterloading during lung inflation. This hypothesis was supported by our present findings: when tidal volume was reduced without changing airway pressure by chest strapping, the inspiratory decrease in RVSI was abolished, suggesting that RV was unloaded. RV unloading was corroborated by the unaffected Acmean at inspiration during chest strapping. On the other hand, increasing airway pressure without changing tidal volume by applying a moderate level of PEEP was associated with an unchanged inspiratory decrease in RVSI, which suggested that afterload on the RV was the same as baseline. Accordingly, Acmean was still reduced at inspiration during PEEP application.

The contribution of increased RV outflow impedance to the adverse consequences of respiratory support has often been underestimated, because they might be
partly compensated for by an increase in blood volume obtained by fluid challenge (28). In fact, for any given afterload there may be relative preload insufficiency, and, for any given preload, relative inordinate afterload. Thus any therapeutic increase in preload may cancel the simultaneous increase in afterload. However, this therapeutic adjustment is limited by chest wall elastance: elevated airway pressure increases lung volume as well as pleural pressure and thereby reduces the distensibility of cardiac cavities (28). In ARDS patients, elevated wall elastance is a common finding (15), which has recently been reemphasized (19, 25).

Another cyclic event observed during mechanical ventilation was the so-called “reversed pulsus paradoxus” (17). We previously showed that left ventricular filling was improved during mechanical lung inflation and was associated with increased systemic pressure (14). We suggested that, during lung inflation, blood might be squeezed from capillaries, thereby transiently improving left ventricular filling (14). This hypothesis, suggested by Werko (31) as early as 1947, was subsequently corroborated experimentally by Permutt et al. (22). The changes in LAD observed in the present study are in agreement with these studies. Our data confirm that, during mechanical ventilation, tidal ventilation transiently improves left atrial filling and that improvement was mainly related to the tidal volume. According to the opposite effects of lung inflation on the alveolar and extra-alveolar vessels, this finding suggests that pulmonary vasculature in our patients was predominantly in a zone 3 condition at expiration, and that a transition from zone 3 to zone 2 was produced by tidal ventilation (5). This condition appears logical in supine and well-fluid-resuscitated patients. Transient left atrial filling improvement associated with marked RV systolic impairment might explain the cyclic changes in arterial pulse during respiratory support (14).

In conclusion, during mechanical lung inflation, cyclic right ventricular afterloading appeared primarily mediated through the tidal volume. One can speculate that a low-volume strategy in ARDS, recommended as a protective measure for lung parenchyma, might also represent a protective measure for the RV and pulmonary circulation.

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