Mechanism of Paradoxic Pulse in Bronchial Asthma

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SUMMARY To elucidate the mechanism of paradoxic pulse in severe bronchial asthma, we performed hemodynamic studies and measured esophageal pressure in nine patients who had status asthmaticus and clinical paradoxic pulse. Two-dimensional echocardiography allowed simultaneous assessment of cyclic changes in right- and left-heart size throughout the respiratory cycle. Esophageal pressure varied from a markedly negative level during inspiration (−24.4 ± 6.5 cm H2O) to a positive level during expiration (7.6 ± 6.0 cm H2O). Competition between right- and left-heart chambers for pericardial space during inspiration was suggested by the reduced left ventricular cross-sectional area at end-systole (−24%, p < 0.01) and end-diastole (−32%, p < 0.01), the leftward septal shift, and the increased right ventricular internal diameter at end-systole (42%, p < 0.01) and end-diastole (40%, p < 0.001). Competition for filling, however, could not entirely account for the paradoxic pulse, for systemic and pulmonary pulse pressures were almost (within one cardiac cycle) in phase: both were minimal at inspiration and maximal at expiration. The increase in impedance to right ventricular ejection is another major factor reducing left ventricular preload at inspiration. This reduction in preload was shown to be the predominant mechanism for the decrease in left ventricular stroke output at inspiration.

INSPIRATORY DECLINE of the arterial pulse was first described during attacks of bronchial asthma. This inspiratory decrease in systolic arterial pressure was later referred to as "paradoxic pulse" and emphasized as a cardinal manifestation of pericarditis. Pul- sus paradoxus has been recognized in many patients with status asthmaticus, and is now considered an index of the severity of airways obstruction. Paradoxic pulse has been noted in other clinical settings, including acute pulmonary embolism, chronic obstructive pulmonary disease, and tricuspid atresia.

Hemodynamic and echocardiographic studies in patients with cardiac tamponade due to a tense pericardial effusion have improved our understanding of the mechanisms of pul sus paradoxus, emphasizing the severe competition for filling between the right and left ventricle. In other clinical settings, however, the mechanism of paradoxic pulse may differ. In bronchial asthma, pleural pressure is very negative at inspiration, and several mechanisms, all related to these large swings in pleural pressure, have been suggested to explain paradoxic pulse. Most of our knowledge of the pathophysiological mechanisms derives from observations of the hemodynamic alterations induced by a markedly negative pleural pressure during the Müller maneuver in experimental animals and in man. During asthmatic attacks, however, the alveolar volume is markedly increased. Moreover, only a few clinical hemodynamic studies consisting of small numbers of patients have been reported during status asthmaticus.

In this study, we investigated the mechanisms of paradoxic pulse in status asthmaticus using conventional hemodynamics combined with two-dimensional echocardiography to assess right and left ventricular dimensions and configurations.

Materials and Methods

Patients

Nine adults with a clinically detectable (cuff-measured decrease of 10 mm Hg in systolic blood pressure) pulsus paradoxus during a severe attack of asthma were included in the study. There were four men and five women, ages 22–55 years (mean 34 years). Hemodynamic and echocardiographic measurements were performed during the first hour after the patient’s admission to the respiratory intensive care unit. Standard therapy for asthma was started, including nasal administration of humidified oxygen, an i.v. bolus of hydrocortisone, continuous i.v. infusion of theophylline, adequate fluid administration and mild sedation with i.v. diazepam. In two patients who had a major tachycardia (heart rate greater than 160 beats/min), rapid blood volume expansion with 1000 ml of plasma expanders was performed before the study. In three patients, standard therapy was ineffective and persistent respiratory failure necessitated mechanical ventilation; in no patient was mechanical ventilation used at the time of the study. Eight patients recovered; one patient died 18 hours after admission despite mechanical ventilation. In the eight patients who recovered, the paradoxic pulse disappeared, accompanied by clinical improvement and progressive normalization of blood gases. Four patients underwent two-dimensional echocardiography after recovering, and the findings were completely normal.

Hemodynamic Studies

Systemic arterial pressure was measured with a small Teflon catheter inserted percutaneously into the right radial artery. Pulmonary capillary wedge, pulmonary arterial and right atrial pressures were measured with a triple-lumen Swan-Ganz catheter inserted percutaneously into the main pulmonary artery through the right basilic vein. Esophageal pressure was measured with an esophageal balloon advanced through

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the nose into the esophagus, down to 40 cm from the nares. All pressures were measured with Hewlett-Packard transducers positioned at the midaxillary level, with atmospheric pressure as a zero reference level, and recorded on a Honeywell LS 8 multichannel recorder. Transmural pressure was calculated as intravascular pressure minus esophageal pressure. Heart rate was measured from a standard ECG lead. Cardiac output was measured by the thermodilution technique (right atrial injection with temperature recording in the pulmonary artery). Simultaneous sampling of arterial (a) and mixed venous (V) blood permitted determination of oxygen and carbon dioxide tensions (Pao2, Paco2, Pico2) and pH by standard electrode techniques. Base excess was read on a Siggaard-Andersen alignment nomogram. Hemoglobin concentration (Hb) was measured by spectrophotometry and hemoglobin saturation (SaO2, Svo2) was determined using a cooximeter. Oxygen consumption (VO2) was calculated as the product of the arteriovenous oxygen content difference and cardiac index.

Echocardiographic Studies

Echocardiographic studies were performed in the semisupine left lateral position with a phased-array sector scanner and a digital scan converter (Roche RT 400 or Varian V-3400 R). An electrocardiographic lead was recorded during each study. Using a left lateral parasternal or a subcostal approach, a short-axis cross section of the left ventricle was selected at the high papillary muscle level. Two-dimensional echocardiographic images were recorded on a Sanvo VTC 7100 videotape recorder. In three patients, standard M-mode echocardiographic measurements were also obtained simultaneously using the two-dimensional cross-sectional view to direct the ultrasound beam from the right ventricular free wall to the left ventricular posterolateral wall and crossing the middle interventricular septum. Inspiration was signaled by intermittent visualization of an electronic marker on the video screen during two-dimensional echocardiographic study, or by appropriate manipulation of the baseline of the electrocardiographic tracing during M-mode examination.

Two-dimensional echocardiographic studies were taped and played back for subsequent single-frame, stop-motion analysis of left ventricular cavity cross-sectional area, as previously described. The endocardial outlines of the left ventricle were drawn with a grease pen directly from the video screen onto a transparent paper by two trained, independent observers. The end-systolic frame coincided with the end of the T wave of the ECG, and the end-diastolic frame with the onset of the R wave on the ECG. For definition of the cavity outlines, the procedure of tracing the left ventricular lumen to measure short-axis areas was standardized by drawing the inner endocardial margin. Final agreement on delineation of endocardial borders was settled by observing, in slow motion, the preceding as well as the succeeding beats. The end-systolic and end-diastolic left ventricular endocardial outlines were digitized (Hewlett Packard 9871 A digitizer) and processed for the measurement of ventricular areas using a Hewlett Packard 9825 A desktop computer.

Because delineation of the right ventricular outlines in cross-sectional views was often imprecise and difficult to draw accurately, only end-diastolic and end-systolic right ventricular internal diameters were measured. These measurements were made with calipers directly from the two-dimensional echocardiograms synchronized with the ECG. These measurements were validated in three patients by M-mode tracings.

During the echocardiographic analysis, special attention was paid to the spatial changes of the interventricular septal configuration. To evaluate septal shape quantitatively, the radius of curvature of the interventricular septum was determined during inspiration and expiration at both end-diastole and end-systole on cross-sectional views. The radius of curvature was obtained by tracing endocardial borders of the interventricular septum and constructing an arc segment. Two chords, each spanning separate parts of that arc, were drawn and orthogonal lines bisecting each chord were constructed. The intersection of these two orthogonal lines defined the center of the circle described by the arc segment. This technique was described by Brinker et al.13

We also studied the variations in size of the inferior vena cava during the respiratory cycle in four patients. The transducer was placed in a subxiphoid or right subcostal position and rotated so that the two-dimensional sector was parallel to the inferior vena cava. In this manner, the course of the inferior vena cava behind the liver, extending through the diaphragm and anastomosing with the right atrium, was imaged. The transducer was rocked slightly medially and laterally to record the maximal vena cava diameter. Inferior vena caval end-diastolic internal diameters at expiration and inspiration were measured under the junction of the hepatic veins, about 6 cm below the diaphragm. These measurements were made with calipers on still frames. Special attention was also paid to the changes in abdominal vena caval size in its initial part, between the diaphragm and the junction of the hepatic veins.

Statistical Analysis

To compare hemodynamic and echocardiographic data obtained at expiration with those obtained at inspiration, we used the t test for paired values. The results are presented as mean ± SD unless otherwise indicated.

Results

All patients exhibited an inspiratory decline (greater than 20 mm Hg) of systolic blood pressure, marked tachycardia (142 ± 12 beats/min) and increased cardiac index (4.7 ± 0.8 l/min/m2). The stroke index was less than 40 ml/m2 in all patients but one (patient 7) and averaged 33.9 ± 6.2 ml/m2 (table 1). The blood hemoglobin concentration was higher than 15 g/100 ml in seven patients and was normal in the two patients in whom it was measured after blood volume expansion.
TABLE 1.  Hemodynamic and Blood Gas Data

<table>
<thead>
<tr>
<th>Pt</th>
<th>Inspiratory decline of systolic blood pressure (mm Hg)</th>
<th>Heart rate (beats/min)</th>
<th>Cardiac index (l/min/m²)</th>
<th>Stroke index (ml/beat)</th>
<th>Hb (g/100 ml)</th>
<th>Pao₂ (mm Hg)</th>
<th>Paco₂ (mm Hg)</th>
<th>Pao₂/Paco₂</th>
<th>pH</th>
<th>AvDO₂ (ml/100 ml)</th>
<th>VO₂ (ml/m²)</th>
<th>Base excess (mEq/l)</th>
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<tr>
<td>1</td>
<td>40</td>
<td>150</td>
<td>4.5</td>
<td>30</td>
<td>15.5</td>
<td>6.65</td>
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<td>160</td>
<td>-3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>160</td>
<td>5.2</td>
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<td>4.65</td>
<td>10.64</td>
<td>7.13</td>
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<td>-9</td>
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</tr>
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<td>3</td>
<td>55</td>
<td>150</td>
<td>3.7</td>
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<td>15.3</td>
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<td>4</td>
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<td>5.6</td>
<td>39</td>
<td>16.6</td>
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<td>6.11</td>
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<td>130</td>
<td>4.4</td>
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<td>17.2</td>
<td>11.30*</td>
<td>5.05</td>
<td>7.21</td>
<td>3.3</td>
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<td>58</td>
<td>135</td>
<td>4.7</td>
<td>35</td>
<td>17.0</td>
<td>10.51*</td>
<td>10.91</td>
<td>7.17</td>
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<td>122</td>
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</tr>
<tr>
<td>7</td>
<td>46</td>
<td>130</td>
<td>6.1</td>
<td>47†</td>
<td>11.7</td>
<td>12.90*</td>
<td>10.64</td>
<td>7.17</td>
<td>2.5</td>
<td>153</td>
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<td>8</td>
<td>35</td>
<td>126</td>
<td>3.9</td>
<td>31</td>
<td>15.8</td>
<td>12.77*</td>
<td>7.31</td>
<td>7.39</td>
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<td>9</td>
<td>21</td>
<td>148</td>
<td>4.5</td>
<td>31†</td>
<td>12.9</td>
<td>5.88</td>
<td>7.58</td>
<td>7.36</td>
<td>4.4</td>
<td>198</td>
<td>+4</td>
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</tbody>
</table>

Pulsus paradoxus (inspiratory decline of systolic blood pressure) was demonstrated by direct measurement of the radial artery pressure.

*Oxygen, 6 l/min through a nasal tube.
†After blood volume expansion.
Abbreviations: Hb = hemoglobin; Pao₂ = arterial oxygen tension; Paco₂ = arterial carbon dioxide tension; AvDO₂ = arteriovenous oxygen difference; VO₂ = oxygen consumption.

(mean hemoglobin concentration 15.4 ± 1.9 g/100 ml). Characteristic features of severe asthma were shown by blood gas analysis. Hypoxemia was present in all patients except patients 7 and 8, who received oxygen therapy. Eight of the nine patients had hypercapnia. Five patients had mild and two had severe metabolic acidosis. The arteriovenous oxygen content difference was normal in seven patients and narrowed in patients 6 and 7. Calculated oxygen consumption was slightly elevated (157 ± 24.2 ml/min/m²).

Pressure changes from expiration to inspiration are summarized in Table 2. Absolute pressures are given in the top half of the table. At inspiration, pleural (esophageal) pressure decreased dramatically to a markedly negative value (−24.4 ± 5 cm H₂O), and increased at expiration, reaching an average positive value (7.6 ± 6.0 cm H₂O). Systolic and diastolic radial artery pressures both decreased at inspiration; the decrease was greater in systolic than in diastolic pressure, leading to a large and significant decrease in radial artery pulse pressure. Systolic and diastolic pulmonary artery pressure both decreased at inspiration; systolic pres-

TABLE 2.  Pressure Values at Expiration and Inspiration

<table>
<thead>
<tr>
<th></th>
<th>Pleural pressure (esophageal) (mm Hg)</th>
<th>Radial artery pressure (mm Hg)</th>
<th>Pulmonary artery pressure (mm Hg)</th>
<th>Capillary wedge pressure (mm Hg)</th>
<th>Right atrial pressure (mm Hg)</th>
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<tr>
<td></td>
<td>S</td>
<td>D</td>
<td>PP</td>
<td>S</td>
<td>D</td>
</tr>
<tr>
<td>A. Absolute pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exp</td>
<td>7.6 ± 6.0</td>
<td>81.3</td>
<td>65.9</td>
<td>37.0</td>
<td>20.4</td>
</tr>
<tr>
<td>±0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Inspiratory pressure</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exp</td>
<td>139.6</td>
<td>73.7</td>
<td>65.9</td>
<td>29.4</td>
<td>12.8</td>
</tr>
<tr>
<td>±11.6</td>
<td>±15.1</td>
<td>±16.5</td>
<td>±16.5</td>
<td>±8.4</td>
<td>±5.8</td>
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<tr>
<td>Inspiratory pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exp</td>
<td>129.9</td>
<td>87.6</td>
<td>42.3</td>
<td>35.5</td>
<td>21.6</td>
</tr>
<tr>
<td>±14.4</td>
<td>±11.3</td>
<td>±16.2</td>
<td>±16.2</td>
<td>±5.9</td>
<td>±3.5</td>
</tr>
<tr>
<td>±0.001</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
<td>&lt; 0.001</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
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</tbody>
</table>

Values are mean ± sd.
Abbreviations: S = systolic; D = diastolic; PP = pulse pressure (i.e., systolic minus diastolic).
sure decreased more than diastolic pressure, which caused a small but significant decrease in pulmonary artery pulse pressure. Both capillary wedge and right atrial pressures decreased at inspiration, but the inspiratory decrease in capillary wedge pressure was larger than that in right atrial pressure. An example of these large cyclic variations of esophageal and intravascular pressures is shown in figure 1. Both right atrial and pulmonary capillary wedge pressures (left panel) decreased at inspiration along with the decrease in esophageal pressure, but pulmonary wedge pressure decreased more than right atrial pressure, and the pulmonary wedge recording crossed the right atrial recording. Deflation of the Swan-Ganz catheter balloon (right panel) allowed comparison of five successive beats in the same respiratory cycle from simultaneous recordings of pulmonary and radial pulse pressures. The minimal pulmonary pulse pressure (9 mm Hg, beat 2) occurred at the end of inspiration and coincided with the minimal radial pulse pressure (65 mm Hg, beats 2 and 3); conversely, the maximal pulmonary pulse pressure (29 mm Hg, beat 3) occurred at the onset of expiration and was followed after a one-beat delay by the maximal radial pulse pressure (79 mm Hg, beat 4). Transmural pressure values (i.e., absolute values minus esophageal pressure) are given in the bottom half of table 2. At inspiration, systolic radial artery pressure was still significantly decreased (−7%), but diastolic pressure increased significantly (19%). Systolic (29%) and diastolic (70%) pulmonary artery pressures also increased significantly. Both left (capillary wedge) and right (right atrial) ventricular filling pressures increased during inspiration, but the increase in right atrial pressure was three times greater than the increase in pulmonary capillary wedge pressure. Consequently, right atrial pressure was lower than pulmonary wedge pressure at expiration and much higher at inspiration.

Two-dimensional echocardiographic data are summarized in figure 2. Compared with the expiratory values, the end-systolic and end-diastolic left ventricular cross-sectional areas were reduced by 24% and 32%, respectively, during inspiration (p < 0.01). A smaller decrease in areas between end-diastole and end-systole (−3.3 ± 1.2 cm² at inspiration vs −6.0 ± 2.9 cm² at expiration, p < 0.01) was also evidenced, leading to the assumption that left ventricular stroke output was decreased during inspiration. In sharp contrast to the changes in the left ventricle, right ventricular end-systolic and end-diastolic internal diameters were increased by 42% (p < 0.01) and 40% (p < 0.001), respectively, during inspiration. These phasic alterations in left and right ventricular cavity dimensions were associated with septal flattening, as demonstrated by a significant increase in the end-systolic and end-diastolic radii of septal curvature (by 31% and 38%, respectively p < 0.001). Figure 3 shows the respiratory variations in left ventricular cavity cross-sectional area that were demonstrated by two-dimensional echocardiograms. In figure 4, phasic changes in left and right ventricular internal diameters are demonstrated by M-mode examination. At inspiration, the left ventricular internal diameter decreased and the right ventricular internal diameter increased; at expiration, opposite changes occurred.

Two-dimensional echocardiographic measurements of abdominal vena cava internal diameter obtained about 6 cm under the diaphragm in four patients are given in table 3. The vena caval diameter decreased (−60 ± 13%) during inspiration in each patient. This decrease was associated in each case with an end-inspiratory collapse of the inferior vena cava in its initial abdominal portion (fig. 5).

**Discussion**

Our patients with status asthmaticus had a high cardiac output state presumably caused by elevated oxy-

![Figure 1](image_url)  
**Figure 1.** Respiratory changes in intrathoracic and intravascular pressures. From top: ECG, systemic arterial pressure (SAP), pulmonary capillary wedge pressure (PCWP) and pulmonary artery pressure (PAP), right atrial pressure (RAP), and esophageal pressure (EP). All pressures are expressed in mm Hg. \( \nabla \) = balloon deflation of the Swan-Ganz catheter. \( \uparrow \) = onset of inspiration; \( \downarrow \) = onset of expiration. Arabic numbers indicate five successive cardiac beats during a respiratory cycle.
gen demand due to the increased effort of breathing.\textsuperscript{16} Stroke volume was lower than normal, but marked tachycardia resulted in increased cardiac output. This finding, and the fact that seven patients had metabolic acidosis, suggested inadequate cardiovascular adaptation.\textsuperscript{17} Paradoxic pulse\textsuperscript{6} may result from one or several of the following: impairment to left ventricular ejection;\textsuperscript{12,15} mechanical impairment of left ventricular filling caused by increased transpulmonary pressure (i.e., alveolar pressure minus pleural pressure); and hypovolemia, as suggested in our study by hemoconcentration.\textsuperscript{18}

Clinically detectable paradoxic pulse corresponding to an inspiratory decrease of 10 mm Hg or more in systolic blood pressure\textsuperscript{7} was a prerequisite for including patients in our study, and was further documented by invasive measurements of the radial artery pressure relative to atmospheric pressure. However, a significant decline was still noted when arterial pressure was measured relative to pleural pressure. Therefore, direct transmission of intrathoracic pressure changes to the left ventricle and subsequently into the arterial system does not totally account for the observed decrease in arterial pressure. This finding, as well as a substan-
Table 3. Diameter of Inferior Vena Cava at End-diastole in Four Patients

<table>
<thead>
<tr>
<th>Pt</th>
<th>Exp (cm)</th>
<th>Insp (cm)</th>
<th>Inspiratory decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>16.7</td>
<td>6.7</td>
<td>-60%</td>
</tr>
<tr>
<td>7</td>
<td>23.3</td>
<td>13.0</td>
<td>-44%</td>
</tr>
<tr>
<td>8</td>
<td>20.0</td>
<td>5.0</td>
<td>-75%</td>
</tr>
<tr>
<td>9</td>
<td>11.4</td>
<td>4.3</td>
<td>-62%</td>
</tr>
</tbody>
</table>

Abbreviations: Insp = inspiration; Exp = expiration.

Partial inspiratory decrease in systemic pulse pressure, clearly suggest that the inspiratory decrease in left ventricular stroke volume plays an important role in the mechanism of paradoxical pulse. A reduced left ventricular stroke output during inspiration was also indirectly evidenced by a smaller reduction in left ventricular area between diastole and systole.

Theoretically, the lower the pleural pressure during inspiration, the larger the pressure gradient between the intra- and extravascular compartments against which the left ventricle must eject a given stroke volume. Our data, in which an increased inspiratory impedance for left ventricular ejection was suggested by an increased inspiratory transmural diastolic aortic pressure, are consistent with those of Robotham et al. Accordingly, it has been argued that the inspiratory increase in left ventricular afterload resulted in decreased left ventricular stroke output, which in turn was reflected by the decrease in aortic pressure. Recent studies using implanted markers suggest that left ventricular end-diastolic and end-systolic dimensions are increased during sustained decrease in pleural pressure in man and in experimental animals.

In contrast, our study tends to demonstrate an inspiratory decrease in left ventricular size at both end-diastole and end-systole. These seemingly paradoxical observations can be explained by the fact that none of the studies mentioned above took into account the free wall to interventricular septum dimension. Our results are consistent with those of Brinker et al. during the Müller maneuver and Settle et al. in patients with chronic obstructive lung disease, who reported a reduction in left ventricular two-dimensional echocardiographic cross-sectional area, and those of Sharf et al., who found in dogs that both systolic and diastolic dimensions decreased in the early phase of an obstructive inspiratory effort. One might object to these studies and also to our work because possible compensatory changes in the left ventricular long axis may be undetected by two-dimensional echocardiography because these measurements are based on short-axis views; but it is unlikely that a 25% reduction in left ventricular cross-sectional areas could be totally compensated for by an increase in the left ventricular long axis. In other clinical settings, important modifications in left ventricular volumes without significant changes in the left ventricular long axis have been evidenced, which suggests that acute modifications in left ventricular volume result from changes in short-axis dimensions.

In our patients, echocardiographic left ventricular dimensions were smaller during inspiration and left ventricular transmural filling pressure (estimated by the pulmonary capillary wedge pressure minus esophageal pressure) was significantly higher. Although pulmonary capillary wedge pressure might not reflect the true left ventricular filling pressure in patients with increased alveolar volume, increased left atrial and left ventricular end-diastolic pressures during deep inspiration or during the Müller maneuver have been reported. Increased left ventricular filling pressure in the presence of decreased left ventricular dimension indicates a reduction of the apparent compliance of the left ventricle. Such a reduction is consistent with a displacement of the interventricular septum toward the left ventricular cavity, and has also been noted in other clinical settings in which lung volume was increased or pleural pressure decreased. We attempted to quantify variations of septal curvature suggested by obvious changes in ventricular size.

Figure 5. Two-dimensional echocardiographic subcostal view of the abdominal portion of the inferior vena cava in the long-axis view at expiration (left panel) and inspiration (right panel). Legends are given on a retouched photocopy of the glossy print; IVC = inferior vena cava; HV = hepatic vein; RA = right atrium; D = diaphragm. The arrow indicates the end-inspiratory collapse of the vessel in its initial abdominal part.
changes in ventricular shape noted during real-time viewing and playback analysis. We used the technique described by Brinker et al.,\textsuperscript{15} which may be sensitive to noise and somewhat subjective because it uses two chords of septal arc segment drawn in a somewhat arbitrary fashion. However, this technique has been helpful in the study of pathophysiologic consequences of right ventricular loading.\textsuperscript{15, 23} In the present study, two-dimensional echocardiograms clearly demonstrated an inspiratory increase in the septal radius of curvature associated with a reduced left ventricular cross-sectional area. Leftward displacement and flattening of the interventricular septum during diastole is consistent with an inverse transseptal pressure gradient. In fact, during inspiration right-heart filling pressure decreased less than left-heart filling pressure, although both chambers were exposed to the same negative external pressure. During expiration, opposite pressure changes were noted and the septum returned to its normal circular configuration. Respiratory variations of the transseptal pressure gradient may be explained by respiratory changes in systemic venous return and increased impedance to ejection of the right ventricle during inspiration.

Facilitation of venous return to the right-heart chambers with subsequent increase in right ventricular volume by inspiratory negative pleural pressure is well known\textsuperscript{26} and was further documented in our study. The inspiratory reduction of the abdominal vena cava diameter in our patients (fig. 5) illustrated the boosting effect of increased subatmospheric pressure at inspiration. These two-dimensional echocardiographic findings do not differ from those in normal subjects.\textsuperscript{24} But in our patients, the initial part of the abdominal vena cava collapsed at the end of inspiration (fig. 5). Venous collapse is usually considered the result of the inability of collapsible vessels to transmit negative pressures.\textsuperscript{25} However, reduction of venous diameter in high-velocity flow secondary to a decreased lateral pressure could also play a role. However, positive intrathoracic pressure during expiration has been noted in severe asthma\textsuperscript{11} and was present in our patients. An expiratory increase of the abdominal vena caval size and a reduction of right ventricular diameter are consistent with diminished right ventricular filling during expiration. In fact, distention of the jugular veins during expiration and venous collapse during inspiration are common findings in patients with status asthmaticus. Accordingly, in severe asthmatic attacks, a markedly negative pleural pressure during inspiration accelerates venous return, whereas a suddenly positive pleural pressure during expiration severely impedes venous return. The contribution of respiratory variations of systemic venous return to the development of paradoxical pulse in patients with cardiac tamponade has been emphasized. In an experimental study by Shabetai et al.,\textsuperscript{26} maintenance of constant systemic venous return prevented paradoxical pulse from developing. Indeed, increased venous return to the right heart during inspiration in patients with cardiac tamponade is associated with a substantial increase in pulmonary arterial blood flow.\textsuperscript{26} In contrast, in status asthmaticus, despite markedly enhanced venous return to the right-heart chambers during inspiration, pulmonary arterial blood flow does not increase, as suggested by the decreased pulmonary pulse pressure. Thus, in cardiac tamponade, right and left ventricular pulse pressures have been shown to be approximately (by one or two beats) 180° out of phase,\textsuperscript{26} whereas in status asthmaticus they were almost in phase (i.e., both minimal during inspiration and maximal during expiration). Therefore, the mechanism of pulsus paradoxus in severe asthma is not merely caused by a competition between the two ventricles for intrapericardial space, as in cardiac tamponade; an additional contributing factor must be considered, namely, increased impedance to right ventricular ejection.

A marked inspiratory decrease in pleural pressure results in an increased transpulmonary pressure and, in turn, in increased alveolar volume. Raising the alveolar volume increases resistance to flow through the alveolar vessels (capillaries) and therefore the afterload upon the right ventricle. In addition, this effect would combine with any eventual increase in pulmonary vascular resistance due to hypoxia, hypercapnia and acidosis. During inspiration, the finding of a larger increase in diastolic than in systolic pulmonary arterial transmural pressure suggested increased pulmonary vascular resistance in our patients. Hence, marked subatmospheric intrathoracic pressure tends to impede right ventricular ejection, which is consonant with an inspiratory increase in diastolic and systolic right ventricular dimensions observed in the present study and in others.\textsuperscript{6, 15} This finding may also explain why pulmonary and systemic pulse pressures were approximately in phase in status asthmaticus. Thus, acute right ventricular overloading appears to be the major hemodynamic alteration induced by markedly negative intrathoracic pressure during inspiration. Reduced pulmonary venous return and decreased apparent left ventricular compliance, both secondary to right ventricular overload, result in decreased left ventricular volume. Furthermore, lung distention may compress the heart chambers, and thereby enhance the normal ventricular interaction.

A rationale for the mechanisms of paradoxical pulse must take into account all the above factors throughout a respiratory cycle. At the onset of inspiration, pleural pressure abruptly drops from the supraatmospheric level at end-expiration to a markedly negative level. This sudden fall of pleural pressure increases lung volume and vascular resistance (increased afterload) and boosts extrathoracic blood into the right ventricle (increased preload). The net result, however, is a decrease in right ventricular stroke volume. Reduced right ventricular output combined with exaggerated input results in overdistention and a subsequent leftward shift of the interventricular septum. Concomitantly, left ventricular stroke volume decreases, because of reduced filling due to diminished pulmonary venous return and increased stiffness, when left ventricular afterload is also increased. At the onset of
expiration, pleural pressure suddenly increases to a suprathermospheric level, which leads to a decrease in lung volume and in turn unloads the right ventricle. The unloaded and overfilled right ventricle ejects a larger stroke volume and thereby allows the septum to return to its normal shape and the left ventricle to be more compliant. As soon as the next beat, systemic arterial pulse pressure increases. However, as expiration continues, pleural pressure remains positive and an adverse pressure gradient for filling is created between the right heart and extrathoracic vessels. Consequently, right ventricular stroke volume decreases gradually, as shown by the progressive decline in pulmonary pressure, and systemic pulse pressure declines after the same lag of one beat. This short transit time (one beat) between right and left ventricular events may be due to the hyperkinetic state and presumably reduced capacitance of the pulmonary vascular bed in the presence of increased alveolar volume.

In conclusion, direct transmission of intrapleural pressure changes to the left ventricle and subsequently into the arterial system does not totally account for the respiratory variations of systemic blood pressure in patients with severe asthma. Paradoxic pulse also appears to result from the interplay of respiratory variations in both systemic venous return and impedance to right ventricular ejection and of an exaggerated ventricular interdependence due to lung distension.

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