Inspiratory Impairment in Right Ventricular Performance during Acute Asthma*

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Right ventricular function was investigated in seven asthmatic patients during an acute attack, using simultaneous bedside right heart catheterization and two-dimensional echocardiography (2DE). Hemodynamic and echocardiographic data were compared during four successive periods of the respiratory cycle: inspiration, early expiration, mid-expiration, and late expiration. During inspiration, 2DE showed a significant increase in right ventricular area at both end-systole and end-diastole. This inspiratory right ventricular enlargement coexisted with a significant reduction in 2DE stroke area and pulmonary artery pulse pressure suggesting an inspiratory reduction in right ventricular stroke output. A transient depression of right ventricular function during deep inspiratory effort in asthma was thus strongly suggested. The negative pressure surrounding the right ventricle at inspiration is advocated as the causative factor enabling reduction in the hydraulic force effecting right ventricular ejection. The highly negative pleural pressure probably holds the right ventricular free wall and restrains its systolic inward motion, as suggested by the finding of a concomitant inspiratory reduction in right ventricular developed pressure and 2DE fractional area contraction.

The influence of respiration on cardiac performance has been investigated extensively in the past.1,4 Numerous experimental and clinical studies have proposed several explanations for the inspiratory decline in arterial pulse observed in dyspneic patients5,6 or during cardiac tamponade.7 Pulmonary venous pooling;1 ventricular interdependence,2 phasic changes in right ventricular input,1 and left ventricular afterloading9 have successively been advocated. In a previous clinical study devoted to bronchial asthma, we have noticed a profound inspiratory decrease in pulmonary artery pulse pressure.8 Occurring despite simultaneous enhancement of right ventricular filling, this decrease suggests an impairment in right ventricular pumping ability during inspiratory efforts. The present study was designed to assess right ventricular function in a group of patients during a severe attack of asthma. This clinical setting is associated with large negative swings in pleural pressure9,9-11 and markedly increased functional residual capacity.10

**Patients and Methods**

**Patients**

Seven asthmatic patients (mean age: 39 years, ranging from 21 to 55 years) were investigated during a severe attack requiring management in our intensive care unit. Informed consent was obtained from each patient, and the protocol was consistent with the ethical regulations of our hospital. Simultaneous hemodynamic and echocardiographic measurements, performed in the semisupine position, were obtained during the first hour in the ICU while patients were breathing spontaneously. All patients recovered from their attack and were discharged after three to five days.

Additional data from two previous studies9,11 were also included to provide reference values concerning pleural pressure in acute asthma, and respiratory changes in right ventricular function in normal subjects. The first previous study9 concerned nine asthmatic patients with comparable age range, in whom pleural pressure was measured during an acute attack by means of an esophageal balloon, together with right heart pressure measurements. Using these data, we plotted the relationship between pleural pressure and pulmonary capillary wedge pressure throughout the respiratory cycle (Fig 1). In the second study, right ventricular dimensions were evaluated in 12 healthy volunteers by two-dimensional echocardiography throughout a quiet respiratory cycle, and used as reference values to assess the changes induced by continuous positive airway pressure breathing.9 From this second study, we obtained echocardiographic data to illustrate the respiratory changes in right ventricular size occurring in normal subjects (Table I).

**Hemodynamic Study**

Bedside right heart catheterization was performed using a triple

**Table I—2DE Measurements of Right Ventricle (Short Axis View)**

<table>
<thead>
<tr>
<th></th>
<th>Inspiration</th>
<th>Expiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVEDA cm³/m²</td>
<td>9.1 (2.7)</td>
<td>8.5 (2.3)</td>
</tr>
<tr>
<td>RVESA cm³/m²</td>
<td>7.4 (2.5)</td>
<td>6.9 (2.1)</td>
</tr>
<tr>
<td>RVSA cm³/m²</td>
<td>1.7 (0.8)</td>
<td>1.6 (0.6)</td>
</tr>
<tr>
<td>RVFAC %</td>
<td>18.7 (8)</td>
<td>18.8 (5.3)</td>
</tr>
</tbody>
</table>

*Obtained in a previous study conducted in young adult volunteers during quiet breathing. Values are mean ± (SD). RVEDA, right ventricular end-diastolic area; RVESA, right ventricular end-systolic area; RVSA, right ventricular stroke area; and RVFAC, right ventricular fractional area contraction. The slight changes observed between inspiration and expiration were not statistically significant.
lumen balloon catheter permitting simultaneous recording of pulmonary artery (or pulmonary capillary wedge) and right ventricular pressures. Pressures were measured with Hewlett-Packard quartz transducers positioned at the midaxillary line, and atmospheric pressure was used as the zero reference level. Pressure measurements were recorded on a multichannel photographic recorder together with an ECG lead and exhaled volume, obtained by means of a disposable pneumotachograph while patients were breathing spontaneously through a mouthpiece with the nose occluded. The pneumotachograph was previously calibrated with a 500 ml syringe and was connected to a differential transducer and a Hewlett-Packard respiratory integrator. From pressure recordings, we directly measured pulmonary artery pulse pressure (\(Pp\), pulmonary artery systolic minus succeeding diastolic pressure) and right ventricular developed pressure (\(Pd\), right ventricular peak systolic minus preceding end-diastolic pressure). Right ventricular end-diastolic pressure was read as the prejection diastolic plateau, and if a plateau was not clear, the pressure at the onset of the Q wave of the ECG was used. Cardiac output was measured by the thermodilution method. To avoid additional discomfort to the patients, we did not measure pleural pressure with an esophageal balloon, as we had previously done. Since respiratory changes in esophageal pressure and pulmonary capillary wedge pressure have previously been found parallel, the latter was used to approximate the magnitude of respiratory changes in pleural pressure.

**Echocardiographic Study**

Echocardiographic studies were performed using a phased-array sector scanner. In asthmatic patients, echocardiographic examination is often difficult due to the markedly increased lung volume. During the period of the study, four other patients were not included because satisfactory echocardiograms could not be obtained. Even if parasternal short axis views were occasionally recorded in some cases, satisfactory examination permitting visualization and measurement of the right ventricular size during the whole respiratory cycle was obtained only from the subcostal short axis view. This subcostal short axis view was taken using the papillary muscles of the left ventricle as reference points. We also studied the variations in size of the inferior vena cava. The transducer was placed in a subcostal position and rotated so that the two-dimensional sector was parallel to the inferior vena cava, and the vessel was carefully observed in its initial abdominal portion.

Two-dimensional echocardiographic examinations were recorded on a JVC video-tape recorder, together with an ECG lead and respiratory flow. Two-dimensional echocardiographic recordings were played back for subsequent single frame stop-motion analysis of right ventricular cavity cross-sectional area at end-diastole and end-systole, using a previously described technique. End-diastole was defined by the onset of the QRS, and end-systole was defined as the smallest cross-sectional cavity area throughout the cardiac cycle. From these measurements, we calculated stroke area (ie, end-diastolic area minus end-systolic area) and fractional area contraction (ie, stroke area/end-diastolic area).

**Protocol**

During the study, simultaneously recorded respiratory flow permitted individualizing of four different cardiac beats in a whole respiratory cycle: (1) an inspiratory beat, defined as a diastole followed by a systole, both occurring during inspiration; (2) an early expiratory beat, defined as a diastole occurring at the end of inspiration followed by a systole occurring at the onset of the expiration; (3) a midexpiratory beat, defined as a diastole followed by a systole, both occurring in midexpiration; (4) a late expiratory beat, defined as an expiratory diastole followed by a systole occurring just before the onset of the next inspiration. The value for each subject represents the average calculated from three consecutive respiratory cycles. Percentage of expiratory volume achieved at each expiratory beat was also calculated as the actual expiratory volume divided by the total expiratory volume.

**Statistical Analysis**

Statistical analysis was performed using a two-way analysis of variance followed by Scheffe’s test. A value of \(p<0.025\) was required to exclude the null hypothesis.

**RESULTS**

All asthmatic patients had a clinically detectable paradoxical pulse. They also exhibited a respiratory rate of \(21 \pm 10\) (mean [SD]) breaths per minute, with an I/E ratio at 0.41 \(\pm\) 0.16. Mean tidal volume was \(541 \pm 185\) ml. Nine \(\pm\) 7 percent of this tidal volume was exhaled during an early expiratory beat, whereas \(51 \pm 4\) percent and \(85 \pm 6\) percent was exhaled during a mid and a late expiratory beat, respectively. Heart rate was \(125 \pm 12\) beats per minute, and cardiac index \(4.15 \pm 0.79\) \(\text{L/min/m}^2\). Respiratory swings in pulmonary capillary wedge pressure ranged between \(24\) and \(33\) mm Hg, with an average of \(30 \pm 4\) mm Hg. Pulmonary capillary wedge pressure averaged \(15.4 \pm 4.5\) mm Hg at expiration, at a time when pleural pressure is usually supraatmospheric in acute asthma and \(-14.4 \pm 5.8\) mm Hg at inspiration, when pleural pressure is markedly subatmospheric. Similar values have been found in our previous study\(^6\) at both expiration (\(16 \pm 7.9\) mm Hg) and inspiration (\(-12.4 \pm 8.3\)). As shown in Figure 1, there was a strong linear correlation between pulmonary capillary wedge pressure and pleural pressure either at inspiration or expiration. Moreover, the respiratory time did not significantly affect the slope of this relationship.
Table 2—2DE and Hemodynamic Measurements in Asthmatic Patients

<table>
<thead>
<tr>
<th></th>
<th>Inspiration†</th>
<th>Early Exp</th>
<th>Mid Exp</th>
<th>Late Exp</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVEDA cm²/m²</td>
<td>11.7(3.3)</td>
<td>10.1(3)</td>
<td>7.1(2.5)</td>
<td>6.1(1)</td>
</tr>
<tr>
<td>RVESA cm²/m²</td>
<td>9.6(2.4)</td>
<td>6.2(3.1)</td>
<td>4.5(2)</td>
<td>4.1(0.7)</td>
</tr>
<tr>
<td>RVSA cm²/m²</td>
<td>2.1(1.3)</td>
<td>3.9(1.4)</td>
<td>2.7(1.6)</td>
<td>2.0(0.8)</td>
</tr>
<tr>
<td>RVFAC %</td>
<td>17.4(9)</td>
<td>40.1(14.9)</td>
<td>36.9(16.3)</td>
<td>31.9(9.9)</td>
</tr>
<tr>
<td>PAPP mm Hg</td>
<td>6.3(5.4)</td>
<td>19.3(7)</td>
<td>13.2(4)</td>
<td>8.8(4.1)</td>
</tr>
<tr>
<td>RVDP mm Hg</td>
<td>14(7.5)</td>
<td>36.2(8.1)</td>
<td>26.7(6.9)</td>
<td>22.3(5.1)</td>
</tr>
</tbody>
</table>

*Mean (SD). RVEDA, right ventricular end-diastolic area; RVESA, right ventricular end-systolic area; RVSA, right ventricular stroke area; RVFAC, right ventricular fractional area contraction; PAPP, pulmonary artery pulse pressure; RVDE, right ventricular developed pressure. †p<0.025 inspiration versus expiration.

Right ventricular measurements using 2DE examination in the short axis view and obtained in a previous study conducted in young adult volunteers, during quiet breathing are given in Table 1. In normal breathing conditions, respiratory changes in right ventricular size and function were minimal and not statistically significant. Right ventricular measurements obtained by 2DE examination and cardiac catheterization in asthmatic patients are presented in Table 2. An example of 2DE examination (subcostal short axis view) is given in Figure 2. A significant increase in right ventricular size at both end-diastole and end-systole was observed at inspiration when compared with expiratory values. Right ventricular stroke area and pulmonary artery pulse pressure were also significantly reduced at this respiratory time. Asthmatic patients also exhibited a significant reduction in right ventricular fractional area contraction and right ventricular developed pressure at inspiration, comparatively to expiratory values. Furthermore, both parameters exhibited parallel changes during the whole respiratory cycle. Illustrative examples of pressure changes recorded in asthmatic patients are shown in Figure 3.

An inspiratory collapse of the inferior vena cava was observed at 2DE examination in all patients, and a representative example is given in Figure 4.

**DISCUSSION**

In the present study, right ventricular performance was assessed by correlating bedside right heart catheterization data with two-dimensional echocardiographic measurements of the right ventricle. Both techniques deserve special comments, particularly concerning their use in a group of acutely dyspneic patients.
patients. During acute asthma, the inspiratory fall in right heart pressures merely represents the concurrent fall in intrapleural pressure. Thus, it would appear more appropriate for our purpose to use transmural pressures. Pleural pressure was not measured in the present study. However, in a previous study, we demonstrated that pulmonary capillary wedge pressure could be used instead of pleural pressure to calculate transmural pressure. Although this mode of calculation may affect the absolute value of transmural pressures, it does not alter the validity of the comparison between inspiratory and expiratory values for three reasons, as follow: (1) both absolute values are affected to the same extent; (2) our subsequent reasoning is based upon measurements of instantaneous changes in pressure and not upon absolute pressure values; and (3) pressure changes measured in the present study occurred almost instantaneously so that they could not be influenced by pleural pressure, which did not change during this short lapse of time.

Concomitantly, two-dimensional echocardiography was used to measure right ventricular dimensions in the short axis view, at the midpapillary muscle level of the left ventricle. Papillary muscles were used as reference points to insure reproducibility of the echocardiographic views. The reliability of 2DE for assessing right ventricular volumes and performance has been previously demonstrated. The usefulness of 2DE in distinguishing normal patients from those with ventricular volume overload has also been reported, and in a recent study, we found that measurements of right ventricular size using thermodilution compared favorably with similar determinations by 2DE. In our asthmatic patients, respiratory changes in right ventricular size were determined in the short axis view. One may argue that this approach could not

**Figure 3.** Two illustrative examples of pressure recordings. PA, pulmonary artery pressure; RV, right ventricular pressure. 1 is inspiratory beat; 2 is early expiratory beat; 3 is mid-expiratory beat; and 4, late expiratory beat.

**Figure 4.** An illustrative example of vena caval collapse at inspiration. Top, four end-diastolic views of the inferior vena cava (IVC), receiving hepatic veins (hv) and anastomosing with the right atrium (ra). 1, inspiration; 2, early expiration; 3, midexpiration; 4, late expiration. Bottom, frame-by-frame view at endexpiration (A, B) and onset of inspiration (C, D) illustrating the rapidity of IVC collapse.
provide an accurate estimate of right ventricular volumes if the right ventricle configuration changed in an eccentric manner during respiration. However, in normal volunteers, Brinker et al found parallel changes in right ventricular long axis and short axis dimensions during a loaded inspiratory effort. We thus assumed that changes in right ventricular short-axis area reflected similar changes in right ventricular volume.

The results of the present study suggest that right ventricular function is impaired at inspiration during acute asthma. On two-dimensional echocardiograms, an inspiratory enlargement of the right ventricular cavity was noted at both end-diastole and end-systole. It is a well recognized fact that venous return to the right heart is augmented during inspiration with a concurrent increase in right ventricular stroke volume.10-12 The increase in right ventricular diastolic size at inspiration observed in asthma might thus be related to an increased venous return due to the negative pleural pressure.6,9 In fact, in our asthmatic patients, the initial part of the abdominal vena cava exhibited an inspiratory collapse, as already reported.4 A 50 percent inspiratory decrease in inferior vena cava diameter due to compression from the inspiratory increase in intraabdominal pressure has been reported in normal subjects.13 The inspiratory collapse of the abdominal vena cava observed in asthmatic patients might also be explained by the inability of collapsible vessels to transmit a negative pressure, a classic20 but still debated concept.21 In any case, abdominal vena caval collapse is expected to limit the effect of deep negative pleural pressure in promoting venous return and protect the right ventricular cavity against excessive enlargement.

A second possible explanation for the observed inspiratory increase in right ventricular end-diastolic size is that it resulted from an inspiratory impairment in right ventricular ejection. The inspiratory reduction in the pulmonary arterial pulse observed in asthmatic patients, and previously noticed,4 indirectly suggested a reduction in right ventricular output at the same respiratory time. Indeed, an inspiratory reduction in pulmonary arterial pulse does not necessarily imply a reduction in right ventricular stroke output. Pulmonary arterial pulse also depends on the distensibility (compliance) of the pulmonary vascular bed. Thus, the observed decrease in pulse pressure at inspiration could also have been caused by an inspiratory increase in pulmonary vascular distensibility. The effects of lung inflation on pulmonary vascular distensibility has previously been addressed in several reports.22,23 The vascular bed of the lung was divided into two compartments that responded opposite to inflation.22 However, when the lungs were highly distended, the net effect of inflation was a major reduction in vascular distensibility.25 Thus, when functional residual capacity is markedly increased as in acute asthma,26 additional lung inflation by inspiration is expected to reduce pulmonary vascular compliance. Accordingly, the inspiratory reduction in the pulmonary arterial pulse likely reflected a reduction in right ventricular stroke output. This is consonant with the finding by 2DE of an inspiratory reduction in right ventricular stroke area and fractional area contraction.

In a previous study, we postulated that impairment in right ventricular ejection at inspiration in asthma could result from an inspiratory increase in right ventricular afterload.6 Experimentally, the relationship between vascular resistance and lung volume is U-shaped,22 and therefore, in normal respiratory conditions, lung inflation is expected to have little or no effect on vascular resistance.24 Just the opposite, in asthma where functional residual capacity is markedly increased,26 any increase in lung volume by a tidal breath would sharply increase pulmonary vascular resistance which, in turn, raises right ventricular afterload. However, the highest values for right ventricular developed pressure and 2DE fractional area contraction were observed at early expiration, before any substantial exhalation had occurred. Thus, it is likely that a rise of pulmonary vascular resistance mediated through changes in lung volume cannot account for the inspiratory decrease in right ventricular ejection.

The hydraulic force affecting left ventricular ejection is decreased during inspiration by an amount equal to the decline in intrapleural pressure.4,25-27 As a result, left ventricular stroke volume falls at inspiration. On the opposite, right ventricular ejection is thought not to be affected by this mechanism, since the right ventricle ejects blood into the pulmonary circulation which is presumably subjected to the same inspiratory fall in pleural pressure. However, if the pleural pressure actually reflects the external pressure for the right ventricle, it does not reflect the external pressure for the whole pulmonary vascular bed. Changes in pleural pressure or lung volume can modify the size of the intraparenchymal vessels and the amount of blood present in these vessels in opposite ways.22 Moreover, the intraalveolar vessels, which represent about 60 percent of the total vascular resistance of the pulmonary circulation, are not directly exposed to the pleural pressure but are actually exposed to the alveolar distending pressure.28 When the airways are open to the atmosphere, as in acute asthma, the alveolar distending pressure should be calculated as atmospheric pressure minus pleural pressure. With the markedly negative levels of pleural pressure achieved during inspiratory efforts, the alveolar distending pressure can indeed reach a very positive value. Accordingly, we believe that right ventricular ejection
can no longer be considered as strictly independent from pleural pressure.

As often emphasized by the physiologists, the right ventricle acts as a bellows. The inward motion of the right ventricular free wall is responsible for an increase in intracavitary pressure during systole, and in turn, for the ejection of a given stroke volume. Experimentally, there is a direct relation between the magnitude of the free wall motion and the level of right ventricular developed pressure. Thus, changes in right ventricular developed pressure noted in the present study presumably reflected changes in amplitude of the inward motion of the right ventricular free wall. This amplitude was also directly assessed by 2DE fractional area contraction. Both parameters changed in a parallel manner during the whole respiratory cycle and indicated a marked reduction in the systolic inward motion of the right ventricular free wall during inspiration. This finding can best be explained by the presence of a negative force surrounding the right ventricle at inspiration, which holds the right ventricular free wall and impedes its systolic inward motion.

Our data seem at variance with previous reports dealing with the effects of inspiration on cardiac performance, and especially, right ventricular function. A well-established concept is that inspiration, by promoting venous return, increases right ventricular filling and ejection. Scharf et al demonstrated experimentally that an average 8 mm Hg increase in negative pleural swings caused by loaded inspiration produced an inspiratory increase in pulmonary artery flow. More recently, similar findings were reported by Olsen et al in dogs in whom inspiratory pleural pressure reached an average negative level of 12 mm Hg. However, the levels of negative pleural pressure achieved in these experimental protocols are far less pronounced than those observed in acute asthma. In this clinical setting, negative pleural pressure currently overtakes a negative value of 25 mm Hg, and this can account for the apparent discrepancy between our data and those reported in other studies. One can object that similar levels of negative pleural pressure could be reached in man during the Mueller maneuver, without any noticeable right ventricular systolic dysfunction. However, during the Mueller maneuver, Brinker et al and Guzman et al produced evidence of a systolic flattening of the interventricular septum leading to suspect a significant right ventricular systolic dysfunction, even if the Mueller maneuver, which is a forced inspiration against a closed airway, does not induce a large pressure gradient between the alveolar distending pressure and the pleural pressure. On the other hand, an inspiratory effort performed with an open airway, as in acute asthma, results in a significant increase in alveolar distending pressure.

In conclusion, our present data suggest that a markedly negative pleural pressure, when it is associated with an increased lung volume, can significantly impair right ventricular contraction. Such findings could be expected since the thin compliant wall and the weak contractile power of the right ventricle make it more vulnerable than the left ventricle to the effect of an external pressure, either negative as in asthma, or positive as in cardiac tamponade.

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Neural and Endocrine System of the Lung

This one-day program will be held January 28, 1988 sponsored by and at the Royal Postgraduate Medical School, Hammersmith Hospital, London, England. For information, contact Professor J. M. Polak or Professor S. R. Bloom, Departments of Histochemistry and Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 OHS, England.

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