Assessment of Right Atrial Pressure-Volume Relations in Patients With and Without an Atrial Septal Defect

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Assessment of the complex relations between pressure and volume in the right atrium has been hampered in the past by difficulties in the measurement of atrial volume. Accordingly, in the present study the dynamics of right atrial pressure-volume relations were examined (with the use of an impedance catheter to measure right atrial volume) in patients with and without an atrial septal defect. Right atrial pressure and impedance volume were measured in 16 patients at the time of cardiac catheterization with the use of a multi-electrode impedance catheter to provide continuous, on-line, pressure-volume data. Eleven patients without evidence of an interatrial shunt were examined during normal respiration and during the Valsalva maneuver and contrasted with five patients with an atrial septal defect documented by oxygen saturation step-up and echocardiographic studies.

Right atrial pressure-volume diagrams in patients without an atrial septal defect exhibited the normal figure eight pattern, with a 'A' loop (atrial contraction) and a 'V' loop (passive filling), corresponding to the A wave and V wave of right atrial pressure, respectively. During inspiration, mean right atrial pressure decreased and mean right atrial volume increased, consistent with augmented venous return. With the Valsalva maneuver, right atrial pressure increased and both right atrial stroke volume and mean right atrial volume decreased compared with baseline.

Patients with an atrial septal defect demonstrated baseline pressure-volume diagrams similar to those of patients without an interatrial shunt. However, no change in mean right atrial volume occurred with either respiration or the Valsalva maneuver despite changes in right atrial pressure similar to those seen in patients without an atrial septal defect.

It is concluded that the impedance catheter provides a useful method of assessing dynamic changes in human right atrial pressure-volume relations. Patients with an atrial septal defect show a lack of variation in right atrial volume during respiration and the Valsalva maneuver.

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The assessment of right atrial pressure-volume relations in humans has been extremely difficult because of technical limitations of the currently available methods for volume measurement. Standard methods for examining the right atrium include angiographic (1-3), echocardiographic (4-8) and radionuclide techniques. All of these techniques have drawbacks when applied to the assessment of atrial volume. Each method has its own unique problems arising from an overriding right ventricle or the lack of any consistent geometric shape to the right atrium, obviating the application of a standardized volume formula. Moreover, the pressure-volume relation within the right atrium is a complex, dynamic function (9-11) and requires the use of techniques for the continuous measurement of atrial pressure and volume throughout the cardiac cycle.

The continuous on-line measurement of intraventricular electrical impedance has been documented in previous reports (12-18) as an accurate and reproducible method for the instantaneous determination of relative chamber volume. We (10,18) and others (15,17) have shown that this technique can be used for continuous assessment of left and right ventricular chamber volume (15-17), as well as right atrial volume (18). In an earlier study (18) of an experimental model of tricuspid regurgitation, we validated the use of an
impedance catheter in the right atrium with ultrasonic crystals and echocardiography. To date, however, this technique has not been applied to the measurement of relative right atrial volume in humans.

The purpose of the present study was to examine the dynamics of right atrial pressure-volume relations (with the use of an impedance catheter to measure right atrial volume) in patients with and without an atrial septal defect. In patients with an interatrial shunt, there are a number of potential mechanisms (1,2,5-8,19-28) whereby the effects of provocative maneuvers on right atrial pressure-volume relations may be altered. We sought to compare right atrial pressure-volume relations during normal respiration and the Valsalva maneuver in patients without evidence of an intracardiac shunt with right atrial pressure-volume relations in patients with a hemodynamically significant atrial septal defect.

**Methods**

**Study group.** Measurements of right atrial electrical impedance and pressures were made at the time of cardiac catheterization in 16 patients. The group comprised 10 men and 6 women with an average age of 55 years (range 26 to 73). All patients were referred for diagnostic evaluation and had been previously scheduled for cardiac catheterization. Five of the patients were referred because of the suspicion of an atrial septal defect. After approval of the project by Beth Israel Hospital’s Committee on Clinical Investigation, all patients gave written informed consent. There were no complications as a result of the study.

**Cardiac catheterization.** Cardiac catheterization and coronary angiography were performed in all patients from the femoral approach with use of standard techniques. Left ventriculography was performed with a pigtail catheter with use of simultaneous biplane cineangiographic recordings in the right and left anterior oblique projections. Right heart catheterization was performed in all patients with a flow-directed thermocatheter that was inserted percutaneously through a sheath into the right femoral vein and advanced to the pulmonary artery. In the five patients suspected of having an atrial septal defect, a diagnostic oxygen saturation study was also obtained.

**Measurement of right atrial electrical impedance.** After completion of the routine diagnostic study and withdrawal of the flow-directed right heart catheter, a no. 8F end-hole multi-electrode impedance catheter (Cardiac Pacemakers Inc.) was inserted percutaneously through the sheath in the right femoral vein and advanced over a guidewire (under fluoroscopy) from the right femoral vein to the right atrium. This catheter has a 0.046 in. (11.7 cm) lumen and 12 platinum ring electrodes (1 mm in width) mounted at 1 cm intervals along the distal end of the catheter. Under fluoroscopic guidance, the distal tip of the catheter was placed in the superior portion of the right atrium with the tip directed toward the superior vena cava, and the axis of the catheter aligned along a pathway between the inferior and the superior vena cava.

Once the catheter was in position, a constant alternating 1.3 kHz current of 4 μA was applied between driving electrodes that spanned the right atrial cavity. Electrical impedance was measured with the use of a pair of sensing electrodes located between the driving electrodes within the right atrium. Right atrial pressure was monitored through the fluid-filled lumen of the catheter with use of a Gould Statham P50 pressure transducer attached directly to a manifold that was connected to the proximal hub of the catheter without intervening tubing. The frequency response characteristics of this type of system have been previously reported (29). Luminal pressure was balanced against mid-chest as a zero reference. Impedance measurements from the sensing electrodes and luminal pressure were recorded on a multichannel recorder (Honeywell, Electronics for Medicine VR16).

**Maneuvers.** After the impedance catheter had been properly positioned along the long axis of the right atrium, baseline right atrial pressures and impedance volume signals were obtained in all patients. Each patient was subsequently asked to breathe deeply and then to perform a Valsalva maneuver (by closing the mouth and bearing down), while continuous measurements of right atrial impedance volume and pressure were recorded.

**Data analysis.** Right atrial pressure and volume data were initially recorded on a multichannel recorder (Honeywell, Electronics for Medicine) in the catheterization laboratory. These hard-copy recordings were subsequently digitized with use of a graphics tablet (Tektronix 4956) and microcomputer (Tektronix 4052). The digitized data were then used to construct pressure-time, volume-time and pressure-volume curves for visual analysis.

The impedance volume signal generated in the right atrium was not calibrated to absolute atrial volume. An arbitrary volume scale from 0 to 100 was used for each patient with each patient serving as his or her own control for subsequent measurements or comparisons.

**Results**

**Study group characteristics.** Of the 16 patients studied, 2 were found to have normal coronary arteries and no evidence of shunting at the atrial level. Nine patients were found to have coronary artery disease and no evidence of an atrial septal defect; none of these nine had any hemodynamic evidence of right ventricular dysfunction.

Five patients were found to have normal coronary arteries with evidence of a significant atrial septal defect; their clinical and hemodynamic data are summarized in Table 1. One of the patients was documented to have an ostium primum atrial septal defect by echocardiography. The shunt
Table 1. Clinical and Hemodynamic Data in Five Patients With an Atrial Septal Defect

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Gender</th>
<th>Type of Defect</th>
<th>RAP (mm Hg)</th>
<th>PAP (mm Hg)</th>
<th>Art P (mm Hg)</th>
<th>$Q_p/Q_s$</th>
<th>Art Sat (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>53F</td>
<td>F</td>
<td>Primum</td>
<td>13</td>
<td>67/25</td>
<td>107/70</td>
<td>5.9</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>62F</td>
<td>F</td>
<td>Secundum</td>
<td>6</td>
<td>26/12</td>
<td>144/70</td>
<td>1.4</td>
<td>92</td>
</tr>
<tr>
<td>3</td>
<td>41F*</td>
<td>F</td>
<td>Secundum</td>
<td>2</td>
<td>20/8</td>
<td>128/91</td>
<td>1.5</td>
<td>94</td>
</tr>
<tr>
<td>4</td>
<td>27M</td>
<td>M</td>
<td>Secundum</td>
<td>6</td>
<td>22/8</td>
<td>108/65</td>
<td>1.3</td>
<td>96</td>
</tr>
<tr>
<td>5</td>
<td>59F*</td>
<td>F</td>
<td>Secundum</td>
<td>5</td>
<td>65/25</td>
<td>130/70</td>
<td>2.2</td>
<td>91</td>
</tr>
</tbody>
</table>

*Small right to left shunt as calculated with the bidirection shunt formula. Art P = arterial pressure; Art Sat = arterial saturation; $PAP = pulmonary artery pressure$; $Q_p/Q_s = pulmonary/systemic flow ratio$; RAP = mean right atrial pressure.

across these defects ranged from a pulmonary ($Q_p$) to systemic ($Q_s$) blood flow ratio of 1.3 to 5.9 with a mean $Q_p/Q_s$ ratio of 2.5. The four patients with an ostium secundum atrial septal defect had a mean $Q_p/Q_s$ ratio of 1.6. Two patients had pulmonary hypertension and one patient had evidence of a right to left shunt and slight arterial oxygen desaturation. No patient with an atrial septal defect had evidence of either mitral or tricuspid regurgitation. All patients who had evidence of an atrial septal defect had these findings corroborated with two-dimensional echocardiographic contrast studies.

**Normal right atrial pressure-volume relations.** In the 11 patients who had no evidence of an intracardiac shunt, right atrial pressure-volume loops exhibited a normal figure eight pattern. Figure 1 shows baseline simultaneous pressure and volume signals obtained from a patient with normal coronary arteries and no atrial septal defect. When right atrial pressure is plotted against simultaneous right atrial impedance volume, the result is a figure eight curve (Fig. 2). This curve consists of a counterclockwise A-loop (atrial contraction) and a clockwise V-loop (passive filling) corresponding to the $A$ wave and $V$ wave of right atrial pressure, respectively.

Respiration produced characteristic changes in patients with an intact interatrial septum with a decrease in right atrial pressure and an increase in right atrial volume during inspiration consistent with augmented venous return (Fig. 3). In contrast, during expiration, mean right atrial pressure increased while right atrial volume declined. With the Valsalva maneuver in patients with an intact interatrial septum, right atrial pressure increased and both right atrial stroke volume and mean right atrial volume decreased in comparison with previous baseline measurements (Fig. 4).

**Right atrial pressure-volume relations in patients with an atrial septal defect.** In the five patients with an atrial septal defect, baseline right atrial pressure-volume loops also exhibited a normal figure eight pattern. When right atrial pressure is plotted against simultaneous right atrial impedance volume in a patient with a secundum atrial septal defect
Figure 3. The effect of respiration on right atrial pressure and volume in a patient without an atrial septal defect. With inspiration (INSP), there is a decline in right atrial pressure and an increase in right atrial volume. During expiration, right atrial pressure increases as right atrial volume declines. ECG = electrocardiogram.

(Patient 2, Table I), the result is the pressure-volume loop shown in Figure 5. The overall configuration of the curve is still figure eight, with a large counterclockwise A loop and a smaller clockwise V loop.

There were significant differences between patients with and without an atrial septal defect, particularly with reference to respiratory variation in atrial volume and the response of atrial volume to Valsalva maneuver. Figure 6 shows right atrial pressure and volume relations in the same patient as in Figure 5. In this patient, there was no change in mean right atrial volume with either respiration or the Valsalva maneuver despite changes in right atrial pressure that were similar to those seen during these maneuvers in patients without an atrial septal defect. Figure 7 shows right atrial pressure and volume relations in the same patient during the initiation of a Valsalva maneuver. There was an increase in right atrial pressure, but no corresponding change in right atrial volume. On subsequent release of the Valsalva maneuver, right atrial pressure decreased promptly, but there was again no change in right atrial volume. These tracings contrast markedly with the earlier findings in patients without an atrial septal defect.

Discussion

In the present study, we have attempted to define right atrial pressure-volume relations by means of an impedance catheter in patients without evidence of interatrial shunts. We have extended this work to examine right atrial pressure-volume relations in patients with atrial septal defects.

Impedance volume measurements. The theoretic basis for the use of impedance volume measurements in the cardiovascular system has been well described previously (17,18). The volume of blood that is measured between any two
sensing electrodes can be visualized as a cylinder with boundaries defined by the endothelial surface of the vessel wall and equipotential surfaces through the two sensing electrodes. During the cardiac cycle, the measured change in impedance in this cylinder is caused by a change in resistance between the two sensing electrodes as a result of a change in the cross-sectional area of the cylinder. The relations between instantaneous resistance \( R(t) \) and instantaneous cross-sectional area \( A(t) \) is given by

\[
R(t) = \rho \times \frac{L}{A(t)},
\]

where \( \rho \) = resistivity of blood and \( L \) = distance between sensing electrodes. For a cylindrical volume where volume \( V \) is equal to cross-sectional area multiplied by length \( A \times L \), equation (2) may be substituted for instantaneous resistance:

\[
R(t) = \rho \times \frac{L^2}{V(t)}.
\]

Thus, for a given cylinder of blood between any two sensing electrodes, the instantaneous volume is inversely proportional to the instantaneous resistance of the blood.

The use of impedance volume techniques have been reported (15-17) in documenting instantaneous relative volume changes in both the left and right ventricles. We have also recently reported (18) the use of this catheter in the right atrium in the assessment of tricuspid regurgitation in an experimental animal model. The present study represents an extension of our previous work in animals to the study of dynamic right atrial pressure-volume relations in humans. It is worth noting that we have not made any attempt to determine the absolute right atrial volume with this technique. Relative volume signals, however, were obtained with each patient serving as his or her own control.

Limitations of impedance volume techniques. There are several inherent limitations in the application of impedance catheter techniques to volume measurements in the right atrium. Among the issues that future work will have to address are the effects of catheter position and stability, the contribution of parallel conductance from adjacent structures, the issue of relative versus absolute volume, the effects of hematocrit, temperature and blood electrolyte composition on blood resistivity, the effects of blood flow on the impedance measurement and the lack of generally accepted standards for validation of right atrial volume.

One theoretic drawback to impedance catheter techniques is the issue of parallel conductance. Previous studies (30) have shown that the contribution of tissue impedance diminishes as the frequency of the measuring current decreases. Thus, our studies used a driving current of 1.3 kHz to minimize the contribution of the atrial wall and adjacent structures. In addition, our previous work with this catheter in the right atrium has shown that it can provide reliable relative volume signals.

The resistivity of blood is not uniformly constant but has
been shown to vary with hematocrit (31), temperature (32) and velocity (33). Our experiments were conducted at uniform temperatures with minimal loss of blood. Finally, there remains a lack of absolute standards for measuring the volume of the right atrium in vivo. The volume measurements obtained in our study are of relative volume, and the changes we report are qualitative and not quantitative.

**Respiratory effects on shunt dynamics in atrial septal defect.** One potential explanation of our results is that maneuvers such as respiration and Valsalva may provoke changes in the dynamics of interatrial shunting in patients with an atrial septal defect. To date, there has been little work on the effect of spontaneous respiration on the dynamics of interatrial shunting. Levin et al. (1) reported that the left to right pressure gradient in children with an atrial septal defect was accentuated during periods of increasing intrathoracic pressure and was diminished (or the right to left gradient became more prominent) during decreased intrathoracic pressure. With sustained increased intrathoracic pressure, the left to right gradient, though persistent, was reduced.

Berry and Austen (27) measured the flow of blood through an experimentally created interatrial shunt in dogs. In all cases and at all times during the respiratory cycle, the flow of blood was left to right. However, there was a consistent inspiratory depression in the magnitude of the left to right shunt that was most prominent at the peak of inspiration.

Alexander et al. (24) documented the bidirectional nature of flow across a surgically created atrial septal defect in dogs. Atrial contraction augmented left to right flow, whereas right to left flow was associated with the onset of ventricular contraction. Flow again became left to right during the latter part of ventricular contraction, the maximal left to right shunting occurring in early diastole. They also reported that inspiration was accompanied by either a decrease in the left to right shunt or an augmentation of the right to left shunt, depending where respiration occurred in the cardiac cycle. Both spontaneous and positive pressure respiration decreased overall net left to right shunting.

**Effects of respiration and the Valsalva maneuver in patients without an atrial septal defect.** Our results suggest that in patients without atrial septal defects inspiration results in a decrease in right atrial pressure and an increase in venous return to the right atrium, with a subsequent increase in right atrial volume. As expected, expiration results in an increase in right atrial pressure and a decline in venous return to the right atrium with a subsequent decrease in right atrial volume.

Normal respiratory variation in venous return and the duration of right ventricular systole is one mechanism for the physiologic splitting of the second heart sound (34). Other more complex mechanisms, including changes in the hang-out time may also be involved (35). One previous study in an experimental model of interatrial shunting has suggested that respiratory variations in the amount of shunting may play a role as well (27).

In patients without intracardiac shunts at the atrial level, the Valsalva maneuver produced changes similar to those with expiration, with a marked decrease in overall right atrial volume and right atrial stroke volume. These changes resolved promptly with release of Valsalva.

**Effects of respiration and the Valsalva maneuver in patients with atrial septal defect.** The Valsalva maneuver is a technique that, paradoxically, has been suggested as one way of improving the sensitivity of contrast echocardiography in detecting right to left shunts in patients with an atrial septal defect (6,7,27). However, the maximal yield from this maneuver comes during phase III, the release phase, and not during the initial (phase I) or strain (phase II) phases of the maneuver (6,7,27). Theoretically, the lower portion of phase II (the strain phase, when the effects on right ventricular filling no longer predominate) would be another time when it might be possible to provoke a right to left shunt.

Our findings in patients with an atrial septal defect contrast sharply with our findings in normal subjects. There was no change in right atrial volume with respiration, Valsalva maneuver and release of Valsalva in patients with an atrial septal defect. Our findings are consistent with a change in the magnitude of intracardiac shunting of blood during respiration and the Valsalva maneuver, and support this as one explanation for the fixed splitting of the second heart sound typically seen in patients with an atrial septal defect.

An alternate explanation would be that the right atrium is at the limits of its pressure-volume relation and that small immeasurable changes result in large changes in pressure. Thus, in patients with an atrial septal defect, with inspiration or release of a Valsalva maneuver, the increase in venous return that would ordinarily elevate right atrial volume may not have as much effect in an enlarged, noncompliant right atrium.

To distinguish these two potential mechanisms, future work will need to directly examine in the catheterization laboratory the dynamics of atrial shunting in patients with an atrial septal defect. The only feasible technique for detecting such beat to beat changes at present is Doppler echocardiography, but further refinements of impedance volume techniques may play an additional role. The previously cited experimental reports would suggest that at least one component of the lack of variation in right atrial volume in patients with atrial septal defect may relate to changes in the magnitude of the interatrial shunting of blood.

**Conclusions.** We have demonstrated that an impedance catheter device provides a useful method of assessing dynamic changes in human right atrial pressure-volume relations. Patients with an atrial septal defect show none of the normal response of right atrial volume to respiration or the
Valsalva maneuver. The lack of variation in right atrial volume during normal inspiration and expiration and during the Valsalva maneuver in patients with an atrial septal defect is consistent with a change in the magnitude of interatrial shunting of blood.

References

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