Right atrial pressure-volume relationships in tricuspid regurgitation

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ABSTRACT Pressure-volume relationships in the right atrium were examined before and after the creation of acute experimental tricuspid regurgitation in pigs. A 1.3 kHz multielectrode impedance catheter with a measuring current of 4 mA was used to determine instantaneous right atrial pressure and relative blood volume; right atrial dimension was assessed simultaneously with ultrasonic crystals attached to the atrial walls. Impedance volume waveforms and ultrasonic crystal dimensions closely paralleled each other at baseline and after the induction of tricuspid regurgitation. The normal right atrial pressure-volume plot exhibited a figure-of-eight configuration, with an “a-loop” and a “v-loop” corresponding to the a-wave and v-wave of the right atrial pressure tracing. With severe tricuspid regurgitation, atrial pump function was abolished, and the pressure-volume plot exhibited a single clockwise loop, consistent with complete ventricularization of the right atrium. Intermediate degrees of tricuspid regurgitation preserved the figure-of-eight loop, but the size of both the a-loop and the v-loop were increased, consistent with a Starling-type load imposed on the atrium by the regurgitant blood volume. Increased right ventricular afterload mediated by constriction of the pulmonary artery and infusion of methoxamine reversibly converted the right atrial pressure-volume loop from that of mild to that of severe tricuspid regurgitation. Alternatively, constriction of the inferior vena cava and infusion of nitroprusside changed the right atrial pressure-volume loop from that of a severe pattern of tricuspid regurgitation to a less severe type of pattern. Infusion of dobutamine increased the size of the a-loop relative to the v-loop both at baseline and after induction of tricuspid regurgitation. We conclude that tricuspid regurgitation induces changes in right atrial mechanics that can be detected and quantified with an impedance catheter.


TRICUSPID REGURGITATION remains a difficult condition to evaluate for severity and effects on circulatory dynamics.1,2 Angiographic assessment may be unreliable when the tricuspid valve is crossed with an angiographic catheter. Noninvasive techniques, including contrast echocardiography and Doppler ultrasound, have been shown to be relatively sensitive and specific in the diagnosis of tricuspid regurgitation but have not been fully validated for quantifying the degree of regurgitation.3 In addition, noninvasive quantification of right atrial volume has been difficult because of the anatomic relationships and complex geometry of the chamber.

Even if the degree of regurgitation is determined, the clinical significance and optimal therapeutic intervention (medical management vs surgical correction) remain difficult to determine,4,5 primarily because tricuspid regurgitation is most often secondary to, or accompanied by, another disease process.6,7 The relative contribution of the regurgitant blood flow to the clinical situation may be difficult to assess in the face of right ventricular failure or elevated pulmonary arterial pressure.

Normal right atrial function in man and the changes in function induced by tricuspid regurgitation have not been adequately described. This is due in part to the difficulties associated with determining atrial volumes and beat-to-beat changes in volume.10 Previous reports
by us\cite{11} and others\cite{12} have described the use of an impedance catheter to evaluate volume changes in the right and left ventricles of experimental animals and human subjects. This new catheter device provides a method of determining relative volume changes on a beat-to-beat basis. Accordingly, we examined the utility of this device in determining right atrial pressure-volume relationships in acute, experimental tricuspid regurgitation.

**Methods**

**Surgical preparation.** Fourteen juvenile pigs (weight 28 to 55 kg) were premedicated with ketamine (10 mg/kg) and general anesthesia was induced with intravenous thiamylal (10 mg/kg body weight). Periodic injections of thiamylal (100 to 200 mg) were given intravenously as necessary to maintain anesthesia. Respiration was maintained by a mechanical respirator with a cuffed endotracheal tube placed via tracheostomy. Supplemental oxygen at 4 liters/min was administered. Surgical exposure of the heart was accomplished through a median sternotomy; the animal was then turned on its left side, and the right atrium, right ventricle, and vena cavae were exposed with a wide pericardial incision and cradle.

**Impedance measurements.** The impedance catheter system used in this study had been described previously.\cite{11} Briefly, it consists of a woven dacron No. 8F end-hole catheter with 12 platinum-ring electrodes spaced at 1 cm intervals along the distal end of the catheter (Cardiac Pacemakers Inc., St. Paul, MN). The catheter was introduced via a femoral vein sheath, and under direct palpation was guided into the right atrium so that the tip of the catheter was in the superior vena cava (figure 1). In this position, the catheter was stable throughout the experiment, and the sensing and driving electrodes could be selected to detect changes in right atrial blood volume. Position of the sensing electrode was determined by estimating the distance from the palpated catheter tip to the junction of the right atrium with both the superior and the inferior vena cavae and by selecting the electrode positions corresponding to those distances from the catheter tip. A 1.3 kHz alternating driving current of 4 mA was applied to the electrode pair immediately outside of the sensing pair.

Impedance measurements throughout the experiment used the same electrode combinations and recording settings as at baseline. The impedance catheter device used in this study generates a signal that can be recorded and displayed on standard laboratory recording equipment. Impedance measurements were recorded in real time on either a Honeywell Electronics-For-Medicine OR 8 or a Gould ES 1000 recorder. The signal generated was not calibrated to the absolute volume of the right atrium, so that all measurements in this study reflect the instantaneous relative electrical impedance in the chamber.

The theoretical basis of volume determinations from impedance measurements has been described previously.\cite{11, 12} As a first approximation, the volume of blood through which current passes between any two sensing electrodes (figure 1) can be considered to be a cylinder, with boundaries defined by the endothelial surfaces of the cardiac walls and by the equipotential surfaces through the electrodes. The change in impedance sensed during atrial contraction in any one of these cylinders 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 relationship between resistance and cross-sectional area is given by:

\[ R = \rho \frac{L}{A} \]  
(1)

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

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

Resistance at end-diastole and end-systole can now be defined as:

\[ R_{ed} = \rho \frac{L^2}{V_{ed}} \]  
(3)

and

\[ R_{es} = \rho \frac{L^2}{V_{es}} \]  
(4)

where \( ed \) = end-diastole and \( es \) = end-systole. By combining these two equations and subtracting we get:

\[ V_{ed} - V_{es} = \rho \frac{L^2}{R_{es} - R_{ed}} \]  
(5)

Thus, for a given cylinder of blood between any two sensing electrodes, the change in volume that occurs with atrial contraction can be determined from difference in impedance at end-systole and end-diastole.

**Other measurements.** Right atrial and right ventricular pressures were measured with high-fidelity micromanometer-tipped catheters (Mikro-tip; Millar Corporation, Houston) inserted through incisions in the right atrial appendage and right ventricular apex, respectively. These catheters were calibrated against a simultaneously obtained fluid pressure (Statham-Gould P23ID). No catheter was placed across the tricuspid valve. Aortic pressure was monitored by a fluid-filled catheter placed in the aortic root. In six animals, right atrial dimension was assessed by ultrasonic crystals sewn in place directly across from one another on the right atrial appendage. The crystals were on a fabric backing and were sewn into place as close as
possible to the attachment of the appendage to the main body of the right atrium. The crystals were activated with an ultrasonic signal generator (sonomicrometer model 120; Triton Technology, Inc.; San Diego) that was calibrated electronically during each experiment. A continuous electrocardiogram (ECG) was also obtained.

**Induction of tricuspid regurgitation.** Tricuspid regurgitation was induced by sectioning of the tricuspid chordae or right ventricular papillary muscles with a nerve hook. Before induction of tricuspid regurgitation the animal received heparin for anticoagulation (4800 U iv bolus, followed by 1000 U/hr iv boluses). The nerve hook was introduced into the right ventricle via a purse-string incision at the ventricular apex. The hook was advanced along the free wall—septal wall margin to about the mid-ventricular level. It was then swept across the septal wall until tricuspid valve supporting structures were engaged by the hook of the instrument. These were then easily severed with a quick tug on the instrument’s handle. Sectioning of these structures was accompanied by the development of a systolic thrill palpable on the right atrial surface. The nerve hook was then removed and the purse-string suture was tightened but not tied to allow reintroduction of the hook as needed. Valvular damage was confirmed at necroscopy in all animals (table 1).

**Echocardiographic study.** Two-dimensional echocardiograms were obtained in six of the 14 pigs, by means of a Hoffrel 201A/514 echocardiograph coupled with a 5.5 MHz transducer. The transducer was placed gently on the anterior wall of the right ventricle and angled to obtain a four-chamber view, a long-axis view of the right heart (figure 2), and a short-axis view of the base of the heart. Images were recorded both before and after creation of tricuspid regurgitation and were stored on videotape for later analysis. Contrast echocardiographic studies, designed to confirm the presence or absence of tricuspid regurgitation, were performed with the injection of 5 ml of agitated blood and saline into the right ventricular cavity through the lumen of the Millar catheter. The two visualized tricuspid leaflets were evaluated for patterns of flail leaflet movement, and the two-dimensional end-systolic area of the right atrium in each animal before and after the creation of tricuspid regurgitation was measured by planimetry in the two-dimensional view allowing the best determination of the borders of the right atrium.

**Special interventions.** Right atrial pressure and volume were examined during several maneuvers: constriction of the inferior vena cava (n = 9) and the pulmonary artery (n = 3) and infusion of methoxamine (n = 8), nitroprusside (n = 8), and dobutamine (n = 3). These studies were undertaken to assess the effects of manipulations of right ventricular preload and afterload and variations in the inotropic state of the myocardium on right atrial dynamics.

Constriction of the inferior vena cava and pulmonary artery was accomplished by passing a length of umbilical tape around the appropriate vessels. The tape was then passed through a length of stiff tubing, creating a snare. For those experiments in which these interventions were undertaken, the maneuvers were performed at baseline and after the induction of tricuspid regurgitation.

Methoxamine (20 μg/ml) was infused at a rate sufficient to produce a rise in right ventricular peak systolic pressure of 10 to 15 mm Hg. Infusion of nitroprusside (50 μg/ml in normal saline) was titrated to produce a decrease in right ventricular peak systolic pressure of 5 to 10 mm Hg. These drugs were administered at baseline and after induction of tricuspid regurgitation, with sufficient time between infusions to allow a return to pre-drug pressure values. Dobutamine was administered as a steady-state infusion at a rate of 5 μg/kg/min before and after induction of tricuspid regurgitation.

In two animals, the contribution of left atrial volume to the impedance signal detected in the right atrium was examined.

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**TABLE 1**

Necroscopy findings after induction of tricuspid regurgitation

<table>
<thead>
<tr>
<th>Animal</th>
<th>Anterior leaflet</th>
<th>Posterior leaflet</th>
<th>Septal leaflet</th>
<th>Other findings</th>
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</table>

M = transection of a major tricuspid valve chorda (two or more attachment sites on valve leaflet); m = transection of a minor chorda (single attachment from papillary muscle or ventricular wall to valve leaflet).
This was done by placing a separate impedance catheter system in the left atrium through an incision in the left atrial appendage, and setting the electrode to sense left atrial volume. A micromanometer-tipped catheter was also passed into the left atrium via the left atrial appendage to measure left atrial pressure. In these animals, constriction of the inferior vena cava and pulmonary artery was performed before the induction of tricuspid regurgitation. Left and right atrial pressure, left and right atrial impedance volume, right atrial dimension (ultrasonics crystals), and an ECG were recorded continuously during these interventions. The constrictions were performed and the recordings were made immediately after stopping the respirator at end-expiration to eliminate respiratory-induced variations.

Data analysis. The data for pressure and impedance were analyzed with a Tektronix model 4052 computer, which was interfaced with a Tektronix model 4956 graphics tablet. Each measurement represents the average of at least 5 beats unless otherwise indicated. Pressure vs impedance volume plots for the baseline state and for each intervention were generated. The maximum impedance volume recorded was arbitrarily designated as 100% for the purpose of graphing volume signals and pressure-volume diagrams. In addition, the relative areas of these loops were compared by circumscribing the areas of the right atrial pressure-volume loops derived by the impedance catheter; in each case, the a-loop and v-loop were digitized on the Tektronix graphics tablet, and the area within each loop was determined by integrating the area under the top half of each loop and subtracting the integrated area under the bottom half of the loop. The baseline a-loop was arbitrarily designated with a relative area of 100%. The baseline v-loop and total loop area (a-loop area plus v-loop area) and the a-loop, v-loop, and total loop area after induction of tricuspid regurgitation were compared with the baseline a-loop.

Statistical methods. Analysis of variance was used to compare values obtained at baseline and with each intervention. A p value of less than .05 was considered statistically significant.

Results

Figure 3 is a graph of right atrial size as assessed by two different methods, the impedance "volume" signal and the right atrial ultrasonic crystal dimension. These two methods of determining right atrial chamber size exhibited a similar contour on a beat-to-beat basis and, in addition, changed in a similar fashion with the interventions undertaken.

Illustrated in figure 4, A, is the baseline right atrial pressure (RAP) and impedance catheter-derived right atrial relative volume (RAV) plotted against time. Beginning with the P wave of the ECG at time zero, RAP increases with the onset of active atrial contraction and RAV moves in the opposite direction, indicating that as the atrium empties with active force generation, pressure is generated as the chamber decreases in size. In atrial diastole, both pressure and volume fall as the atrial musculature relaxes and the atrium fills passively with blood returning from the venae cavae. This is marked by the rise in both pressure and volume shortly after the R wave of the ECG, the right atrial V wave. With the T wave of the ECG, presumably marking the opening of the tricuspid valve, RAP and RAV plateau and then decline, consistent with passive emptying of the atrium into the ventricle during right ventricular diastole.

The right atrial pressure-volume plot (figure 4, B) also illustrates these aspects of right atrial mechanics. The electrocardiographic and hemodynamic markers of the cardiac cycle are included to indicate the timing of the pressure-volume relationships. The normal right atrial pressure-volume plot has a figure-of-eight configuration composed of two loops, which we have designated the a-loop and the v-loop of right atrial mechanics. These loops correspond to the a-wave and the v-wave of right atrial pressure.

Effect of tricuspid regurgitation. Figure 5, A, illustrates a typical response of the RAV and RAP to the induction of severe tricuspid regurgitation. In comparison with the normal RAP and RAV vs time relationships, the most striking difference is the large v-wave of RAP, which occurs during right ventricular systole. In this example, the v-wave pressure has increased from 5 to 21 mm Hg as compared with the baseline recording, and no a-wave of RAP is seen on this pressure tracing. Immediately after the P wave of the ECG, RAV and RAP track together rather than move in opposite directions, as was the case for the normal right atrium. The RAV curve for the remainder of the cardiac cycle (atrial diastole) tracks along with the RAP, as was the case for the baseline recording during atrial diastole. The impedance volume excursion (maximum RAV − minimum RAV) is increased.
compared with baseline, and both the maximum and minimum atrial volumes are greater with severe tricuspid regurgitation compared with the control values.

Figure 5, B, is a plot of RAP vs RAV during acute, severe tricuspid regurgitation, illustrating the changes in right atrial mechanics that occur with severe regurgitation. The pressure-volume loop consists of a single v-loop, which moves in a clockwise direction. The right atrial filling curve (ascending pressure and volume) becomes very steep, possibly indicating decreased distensibility of the atrium at higher right atrial pressures. As in the passive filling and emptying phase of normal right atrial mechanics (the v-loop), the pressure-volume curves for right atrial filling and emptying do not fall along precisely the same pressure-volume curve. This may represent hysteresis from the viscoelastic properties of the atrial wall or possibly load-dependent active relaxation of the atrial myocardium.

Grades of tricuspid regurgitation. Figure 6 illustrates right atrial pressure-volume plots obtained from a single animal with different grades of tricuspid regurgitation. The severity of regurgitation was defined from the pressure recordings; in mild tricuspid regurgitation v-wave pressure was equivalent to or greater than a-wave pressure but less than 20 mm Hg, whereas in severe tricuspid regurgitation, the peak atrial pressure exceeded 20 mm Hg. More severe regurgitation was created by reinserting the nerve hook into the right ventricle to section additional tricuspid valve chordae. The superimposed broken line designates a hypotheti-

**FIGURE 4.** Baseline RAP and RAV. A, RAP and RAV vs time. B, RAP (ordinate) vs RAV (abscissa) for a single cardiac cycle, averaged from 5 beats. Note figure-of-eight configuration of the normal atrial pressure volume loop. Point 1 corresponds to onset of the P wave on the ECG, point 2 corresponds to onset of the QRS complex, and point 3 corresponds to onset of the T wave.

**FIGURE 5.** RAP and RAV after the induction of severe tricuspid regurgitation. A, RAP and RAV vs time. B, RAP (ordinate) vs RAV (abscissa). Right atrial pressure-volume relationship demonstrates a single v-loop typical of severe tricuspid regurgitation. Points 1, 2, and 3 are defined in legend to figure 4.
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FIGURE 6. RAP (ordinate) vs RAV (abscissa) from a single experiment illustrating the effect of progressively severe tricuspid regurgitation. Regurgitation was induced by chordal rupture and confirmed with two-dimensional contrast echocardiography. Superimposed dotted line shows hypothetical filling curve of atrial diastole derived by connecting portions of the pressure-volume line that occurred during ventricular systole (rightward and upward arrows).

CAL right atrial filling curve derived by connecting the pressure-volume curve between atrial end-systole to tricuspid valve opening (onset of the y-descent) for each grade of regurgitation. Note how steep this curve becomes at higher pressures, consistent with decreased distensibility. With milder degrees of tricuspid regurgitation, both the a-loop and the v-loop are increased in relative area as compared with the baseline. A similar finding was noted if the ultrasonic crystal dimension across the root of the right atrial appendage was used instead of the impedance catheter signal on the RAV axis.

The areas of the a-loop and the v-loop and the total loop area were compared in the baseline state and after the induction of tricuspid regurgitation in all animals. The baseline a-loop pressure-volume area was defined as 100% in comparison with the baseline v-loop and total-loop and the a-loop, v-loop, and total-loop areas after induction of tricuspid regurgitation. If no a-loop was present after induction of tricuspid regurgitation, the area was defined as zero. This analysis confirmed that with mild tricuspid regurgitation the mean relative areas of each loop increased (a-loop 317%, v-loop 211%, and total-loop 285% as compared with respective baseline values), whereas with severe tricuspid regurgitation, the a-loop was much diminished and the v-loop and total-loop areas increased (a-loop 7%, v-loop 2594%, total-loop 784% as compared with the baseline values).

Necroscopy findings. The findings at necropsy are summarized in table 1 and confirmed that damage was done to the tricuspid valve apparatus in all animals. Transection of one or more major tricuspid valve chordae was present in all animals; other damage included tears in the leaflets in three animals, perforated leaflets in two, and a nearly transected septal wall papillary muscle in one animal. Of course, these findings represent the maximum extent of induced damage; the valvular structure after preliminary attempts at chordal sectioning is not known.

CONTRIBUTION OF LEFT ATRIAL VOLUME CHANGES. The contribution of changes in left atrial volume to the changes we detected in the right atrium was examined by noting the differential effects of constriction of the pulmonary artery and inferior vena cava on simultaneously recorded right and left atrial impedance signals (figure 7). These maneuvers reproducibly produced the findings observed in multiple attempts on the two animals studied in this way. With constriction of the inferior vena cava, RAP, LAP, and impedance-derived RAV and LAV all declined, consistent with a reduced load in these chambers. During constriction of the pulmonary artery, the RAV and RAP both rose, while LAV and LAP both declined. The fall in RAV with constriction of the inferior vena cava and the rise in RAV with constriction of the pulmonary artery were confirmed by similar changes in right atrial dimension, as determined by the ultrasonic crystals placed on the right atrial appendage.

Drug actions. The drugs methoxamine, nitroprusside, and dobutamine were administered in the baseline state and after the induction of tricuspid regurgitation to assess the effects of changes in preload, afterload, and contractility on normal atrial function and on the regurgitation-induced right atrial pressure and volume changes.

For the baseline state (figure 8, A), representative RAP and RAV vs time curves and the RAP vs RAV loop are shown with the superimposed curves generated after the infusion of methoxamine and dobutamine.

After the induction of mild tricuspid regurgitation (figure 8, B), nitroprusside reduced the peak v-wave pressure and altered the form of the RAP vs RAV loop from that seen with more severe regurgitation to that seen with milder regurgitation. Methoxamine produced the opposite effect: the v-loop increased in relative area and peak v-wave pressure was increased as compared with those before drug infusion. Dobutamine shifted the entire RAV vs RAV loop leftward and upward; the area of the a-loop increased as compared with that before infusion of dobutamine. These changes were reversible upon the withdrawal of the drugs.

ECHOCARDIOGRAPHIC STUDY. Contrast echocardiography demonstrated appreciable reflux of microbubbles from
the right ventricle to the right atrium in all six pigs after
knife injury, confirming the presence of tricuspid re-
gurgitation. In five of the six animals, a two-di-
men-
sional pattern of flail tricuspid leaflet movement was
observed, involving both of the two visualized tricus-
pid leaflets in three pigs and one leaflet in the two
others. Right atrial area at the end of ventricular sy-
tole increased significantly from 6.8 ± 1.4 cm² before
tricuspid regurgitation to 8.3 ± 2.1 cm² after induction
of tricuspid regurgitation (p < .05). The nerve hook
was able to be visualized in proximity to the tricuspid
valve during attempts at disruption of the tricuspid
valve apparatus. Two-dimensional echocardiographic
guidance may therefore facilitate the creation of ex-
perimental valvular regurgitation.

Discussion

In the present study, we attempted to define normal
right atrial pressure-volume relationships and the
changes in those relationships induced by acute, ex-
perimental tricuspid regurgitation by means of an im-
pedance catheter to monitor the instantaneous volume
in the right atrium. The impedance catheter has been
used by us and others to determine relative and abso-
lute ventricular volumes.11-12 This study represents an
extension of this technique to include determination of
atrial volume. We were not able to determine absolute
right atrial volume with this technique and therefore
cannot compare our measurements with those obtained
by angiography or other methods. However, we were
able to record a continuous signal that reflected right
atrial dimension as determined by ultrasonic crystals
attached to the right atrium. This method of determin-
ing atrial dimension has been used by others on the left
atrium.13, 14

The configuration of the normal right atrial pres-
sure-volume loop found in the present study is similar
to that found by others for the left atrium.14-16 Three
distinct phases of atrial mechanics were observed:
atrial systole (volume falls as pressure rises), passive
atrial filling during ventricular systole (pressure and
volume both rise), and passive atrial emptying (both
pressure and volume fall).

FIGURE 7. Simultaneously recorded right and left
atrial impedance volumes (RAV and LAV), right
atrial crystal dimension (RACD), and right and left
atrial pressures (RAP and LAP) during constriction
of the inferior vena cava (A) and constriction of the
pulmonary artery (B). During constriction of the in-
ferior vena cava, RAP, RAV, RACD, LAP, and
LAV all decrease. With constriction of the pulmo-
nary artery, LAP and LAV decline, but RAP, RAV,
and RACD all increase. RAV and LAV relate to the
same relative volume scale.
FIGURE 8. Drug effects on right atrial pressure-volume relations at baseline (A) and after the induction of tricuspid regurgitation (TR) (B).

In acute, experimental regurgitation of the mitral valve, Sasayama et al. observed an initial increase in atrial function with moderate regurgitation, which they attributed to the operation of Frank-Starling forces resulting from the increased atrial size. With severe regurgitation of the mitral valve, they noted the disappearance of effective atrial contraction, possibly caused by the action of the atrium on the descending limb of contraction. Our results in the right atrium validate and extend their observations, insofar as mitral regurgitation and left atrial function are analogous to tricuspid regurgitation and right mechanics, respectively.

The method of induction of tricuspid regurgitation used in this experiment is similar to other experimental methods of generating valvular insufficiency of the tricuspid and mitral valves. No directly comparable clinical lesion exists, although our preparation might most closely resemble acute chordal or papillary muscle rupture or papillary muscle dysfunction of various origins. Our experiments were short-term in nature and the comparability of our results to long-standing tricuspid regurgitation in human subjects, in whom hypertrophic, biochemical, and anatomic adaptations take place in response to volume overload, is not known.

As depicted in figure 6, there appears to exist a filling curve of atrial diastolic function analogous to that known to exist for the ventricle. We did not attempt to determine a curve of atrial systolic function in these experiments, but one might speculate that such a curve would intersect the steeper portion of the diastolic filling curve, thereby determining the point at which atrial function was abolished by the acute regurgitant volume overload. Other authors have noted a loss of atrial pump function with a greatly increased atrial end-diastolic pressure load. The loss of effective atrial contraction noted with severe tricuspid regurgitation could result from an increase in right ventricular diastolic pressure producing increased atrial afterload. Also, as noted by Neill et al., atrial coronary blood flow declines in pressure overload, possibly resulting in decreased function from diminished nutrient supply.

The inotropic intervention of dobutamine demonstrated the salutary effect of this drug in modifying right atrial mechanics in acute tricuspid regurgitation. This beneficial effect could take place through several mechanisms. The direct effects of positive inotropic stimulation of the atrial muscle would increase atrial contractility and allow effective contraction to take place despite the increased atrial afterload. An alternative explanation for the effect of dobutamine is that by decreasing right ventricular size and the diameter of the tricuspid anulus, the valvular apparatus would be brought into closer apposition, thereby decreasing the regurgitant volume. The displacement of the passive filling portion of the pressure-volume curve upward and to the left could represent a true change in the passive atrial stiffness or could be secondary to interatrial interaction.

Methoxamine and nitroprusside are known to increase and decrease right ventricular afterload, respectively, probably by their effects on the pulmonary circulation. With methoxamine infusion, the right atrial pressure-volume loop could be seen to deteriorate from
the pattern found in mild regurgitation to the predominant v-loop pattern seen in severe regurgitation. Infusion of nitroprusside after induction of tricuspid regurgitation had the opposite effect from that of methoxamine; that is, the area of the a-loop increased and the area of the v-loop decreased as compared with those before nitroprusside. Increasing right ventricular afterload by constriction of the pulmonary artery produced an effect similar to that of methoxamine, whereas reduction of right ventricular afterload (and preload) constriction of the inferior vena cava duplicated the effects of nitroprusside right atrial pressure-volume loops. These findings are similar to the observations on experimental mitral regurgitation by Sasayama et al.\textsuperscript{13, 14} and are consistent with the known clinical effects of changes in loading conditions and inotropic state on tricuspid regurgitation.

Certain limitations of this study should be emphasized. One problem that must be considered in impedance volume measurement in vivo is the problem of parallel conductance, i.e., current leakage through tissues other than blood. This is a critical problem in absolute volume determinations, in which the amount of current leaking through tissues other than blood must be accounted for. In our study, we did not attempt to determine absolute volumes of the right atrium. Our assumption was that the parallel conductance current was constant throughout any experiment, allowing the determination of relative volumes in the volume-varying blood of the right atrium. Two factors make this assumption reasonable. First, with the alternating-current frequency used in our device (1.3 kHz), the electrical resistance of myocardium is much greater than that of blood, thereby decreasing the contribution of parallel conductance by myocardium. Second, the wall of the right atrium is much thinner than either the right or left ventricular walls; thus the amount of current conducted by the atrial wall would presumably be less than that conducted by the ventricular walls. It should be noted, however, that one major potential source of parallel conductance in the atrium is the interatrial septum and the blood pool of the left atrium. Although we did not attempt to quantitate this current and did demonstrate the gross differential effects of constriction of the pulmonary artery and the inferior vena cava on simultaneously determined right and left atrial impedance volumes (figure 7, B). Initially, right atrial stroke volume appears to decrease mildly when it should have increased; the real increase may have been negated by a decrease in left atrial volume. Further experiments to determine the contribution of parallel conductance to the signal observed and to determine absolute atrial volume by means of an impedance catheter should be performed.

Our study also does not address the issue of atrial contribution to ventricular filling or the changes in atrial stroke volume that take place with tricuspid regurgitation. This is because changes in atrial volume detectable with the system used in this study do not necessarily reflect atrial flow dynamics. During at least part of the cardiac cycle, the atrium is a conduit for venous return, and hence the volume changes in the atrium might not accurately reflect blood flow. One possible experiment that might be conducted to assess the role of the active atria transport system would involve studying the effect of crushing the sinoatrial node on the impedance signal before and after the production of tricuspid regurgitation.

The applicability of these results to the clinical situation remain to be determined. As discussed above, our preparation of acute tricuspid regurgitation does not have an exact clinical counterpart, and caution must therefore be exercised in extrapolating to human disease states. However, our results lend support to the approach of treating acute tricuspid regurgitation with maneuvers to decrease right ventricular afterload and suggest that negative inotropic agents should be avoided in this situation. Interesting speculation would center on the applicability of our findings to the decision regarding the operative repair of a regurgitant tricuspid valve. We have noted that in mild, acute experimental tricuspid regurgitation the apparent systolic function of the right atrium is acutely enhanced as compared with the baseline state. Patients exhibiting this degree of regurgitation might require only medical therapy and monitoring. However, a right atrium exhibiting the pressure-volume pattern of complete ventricularization that we noted with severe tricuspid regurgitation may not be contributing to the forward flow of blood in the circulation. Such an atrium might be returned to a functioning state with the elimination of the regurgitant blood burden with replacement or repair of the tricuspid valve.

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Circulation. 1986;73:799-808
doi: 10.1161/01.CIR.73.4.799
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1986 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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