Right Ventricular Volumes in Patients with and without Heart Failure

By Elliot Rapaport, M.D., Maylene Wong, M.D., Richard E. Ferguson, M.D., Philip Bernstein, M.D., and Bernard D. Wiegand, M.D.

Since Starling first related the force of myocardial contraction to end-diastolic fiber length,1 most studies have evaluated ventricular performance in terms of end-diastolic pressure. End-diastolic volume (EDV), a closer approximation to fiber length, has been generally neglected because satisfactory methods for measuring it in vivo were not available. Angiocardiographic technics, recently applied by several investigators for estimating ventricular volumes,2-7 seemingly give reasonable approximations. However, the calculated volumes are measured when the heart (and coronary circulation) are filled with the hypertonic contrast media, which produce immediate, profound circulatory effects.8, 9 Consequently, the volumes and tensions (which can be estimated from knowledge of simultaneous shape, pressure, and volume) obtained may not be those in the steady state prior to injection of the media. Furthermore, because of the shape of the right ventricle, angiocardiographic estimations of ventricular volumes in man have been limited to the left ventricle. Reedy and Chapman10 recently estimated total ventricular volume and subtracted that of the left ventricle to estimate right ventricular volume in the dog.

The indicator-dilution technic may be used to estimate ventricular volumes if the injection is made quickly into the ventricle, adequate mixing takes place, and the resultant time-concentration curve in the vessel leading from the ventricle can be recorded faithfully. Although Bing's early attempts3 to measure a right ventricular volume in man by injecting Evans-blue dye into the ventricle and recording a dye curve from the pulmonary artery were complicated by catheter distortion of the dye curves, Freis12 has recently successfully accomplished this in six normal subjects. Left ventricular volume in the dog was similarly measured by Jacob and his associates,13 using Cardio-green. Folsé and Braunwald14 used precordial scanning after left ventricular injection of radioisotope to estimate left ventricular volumes in man. Luthy and colleagues15-16 recently reported the use of thermal dilution curves for a variety of circulatory measurements including estimating right ventricular volumes. In their more detailed report on the results of studies on right ventricular volumes, however, it appears that injections of cold fluids were made sometimes into the right atrium and sometimes into the right ventricle; consequently, their calculations may be valid only part of the time, since, theoretically, the downstroke slope will represent ventricular wash-out after atrial injection only if right ventricular volume is significantly greater than right atrial volume.17 Right atrial volume, however, frequently exceeds right ventricular volume.18 Cournand, Donato, and their colleagues19-22 used the slope of a wash-out curve, obtained by precordial scanning after right atrial injection of radioactive krypton, to measure right ventricular volumes in man. The same theoretical objection applies, and the chamber whose volume is being estimated is questionable. Finally, Holt and his...

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colleagues made numerous measurements of both right and left ventricular volumes in a host of different species (but not man) by ventricular injections of hypertonic saline and recording the resultant wash-out curves as changes in the electrical conductivity of the blood.

We have previously used and described the technic of thermodilution for measuring ventricular volumes in the dog. The method involves the rapid introduction of negative heat into the ventricle, usually in the form of the animal's own cooled blood or as cold saline. As the resultant cooled ventricular blood is washed out of the ventricle, a step function or staircase temperature curve, which is exponential in respect to time, can be recorded by a fast-responding thermistor-tipped catheter in the artery leading from the ventricle. The present report is a study of right ventricular volumes of human subjects with and without heart failure by the technic of thermodilution. Volumes were measured at rest and, in some, during mild to moderate exercise in the recumbent position.

Methods

All subjects were unsedated and had had a light breakfast. A no.-8 or 9 double-lumen cardiac catheter was inserted in the usual manner into the main pulmonary artery. The distal lumen was sealed with a fast-response time thermistor bead to record the pulmonary arterial thermodilution curve. Details of the response of the system and other aspects of the method are reported elsewhere. The catheter was adjusted so that the proximal lumen lay in the right ventricle close to the tricuspid valve. During a 3-minute collection of expired air, and immediately after arterial and mixed venous blood samples were drawn for determination of a direct Fick cardiac output, repeated injections of approximately 5 ml of chilled saline were made into the right ventricle and recordings were taken of the thermodilution curves in the pulmonary artery. A compressed air-driven syringe device, actuated by an electrocardiographic signal and containing a variable electronic delay circuit, permitted injection to be accomplished generally in one diastole.

Forty-seven thermodilution recordings were made at rest in 15 patients who had no evidence of heart disease (table 1), and 37 recordings were made in 10 patients with congestive heart failure of diverse etiology (table 2). Although all the patients with heart disease had had some treatment, all had some degree of dependent edema at the time of study. Only subjects who had a normal sinus rhythm were studied. All of these patients had primary diseases involving the left ventricle and it was thought that the congestive heart failure had developed secondary to left ventricular decompensation. Eleven of the control subjects and six of the patients with congestive heart failure were also studied during mild to moderate exercise performed for 5 minutes in the recumbent position on an Elema bicycle. A direct Fick cardiac output was obtained during minute 3 to 4 of exercise and repeated thermodilution curves were taken immediately thereafter as described above.

The ratio of right ventricular end-systolic volume (ESV) to end-diastolic volume (EDV) was obtained from the thermodilution curve by the following formula:

$$\frac{\text{ESV}}{\text{EDV}} = \frac{\Delta T_{n+1}}{\Delta T_n}$$

where $\Delta T_n$ and $\Delta T_{n+1}$ are differences between baseline pulmonary arterial temperature and that at beats n and n + 1, respectively, measured at end-diastole from the exponential step-function of the pulmonary arterial thermodilution curve. Since the calibration of thermistor resistance against temperature is essentially linear over the small temperature range involved in these thermodilution curves, the ratio $\frac{\Delta T_{n+1}}{\Delta T_n}$ was obtained directly from the measured distance of the record from the baseline at beats n and n + 1, and conversion into absolute temperature was unnecessary. In actual practice the ESV/EDV ratio for any curve was obtained by averaging the ratios $D_2/D_3$, $D_3/D_4$, $D_4/D_5$, and so forth, where D is the distance in mm. from the baseline to the exponential wash-out plateau for that beat.

Occasionally in the patients with congestive heart failure, the gradual decay in the wash-out curve made it impossible to see a series of steps. In these cases, the downstroke was simply assumed to be an exponential and the following formula applied:

$$\frac{\text{ESV}}{\text{EDV}} = \left( \frac{Y_n}{Y_o} \right)^{\frac{1}{n}}$$

where $Y_o =$ distance from the baseline of a point on the record near the beginning of the exponential downstroke, in mm.

$Y_n =$ distance from the baseline of a point in

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Table 1

Right Ventricular Volumes and Pressures in Subjects without Heart Disease

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Age, yr.</th>
<th>BSA, M²</th>
<th>Activity</th>
<th>Right ventricular pressure, mm. Hg</th>
<th>ESV/EDV, %</th>
<th>Rate, beats/min.</th>
<th>SV, ml./M²</th>
<th>ESV, ml./M³</th>
<th>EDV, ml./M³</th>
<th>O₂ consumption, ml./min./M³</th>
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Mean (Rest) ± S.D.

53.4 ± 10.9

103 ± 24.4

*Sinus tachycardia, presumably secondary to anxiety.
SV, stroke volume; ESV, end-systolic volume; EDV, end-diastolic volume.
Table 2

Right Ventricular Volumes and Pressures in Patients with Congestive Heart Failure

<table>
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<tr>
<th>Subject no.</th>
<th>Age, yr.</th>
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<th>Diagnosis</th>
<th>Activity</th>
<th>Right ventricular pressure, mm Hg</th>
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<th>Rate, beats/min.</th>
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Mean (Rest) ± S.D.  

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<th>RHD</th>
<th>HCVD</th>
<th>ESV / EDV, %</th>
<th>Rate, beats/min.</th>
<th>SV, ml./M.²</th>
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<td>71.9 ± 12.3</td>
<td>123 ± 67.7</td>
<td>534</td>
<td>RAPAPORT ET AL.</td>
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PMD, primary myocardial disease; RHD, rheumatic heart disease; HCVD, hypertensive cardiovascular disease; ASHD, arteriosclerotic heart disease; AS, aortic stenosis; AI, aortic insufficiency; SV, stroke volume; ESV, end-systolic volume; EDV, end-diastolic volume.
an identical part of the cardiac cycle (judged from the ECG) \( n \) beats later, in mm.

\( n = \) number of heart beats from point \( Y_0 \) to arbitrarily selected point \( Y_n \).

The ratio ESV/EDV is independent of the volume and temperature of the injected material; it is dependent only on the emptying characteristics of the ventricle and represents the fraction of the EDV remaining in the ventricle at end-systole.

Since repeated injections were made during the same experimental period in each subject, the reproducibility of this measurement was assessed in the following manner: Each determination was expressed as a percentage difference from the average for each subject. One standard deviation of the variations from the average ESV/EDV for all subjects was 4.2 per cent; in only those subjects with congestive heart failure it was 4.1 per cent. This is in close agreement with our previous observations in the dog on the reproducibility of the method.27, 28

Stroke volume (SV) was obtained by dividing the cardiac output by the heart rate.

ESV and EDV were obtained by the following formula:

\[
\text{EDV} = \frac{SV}{1 - \text{ESV/EDV}}
\]

\[
\text{ESV} = \text{EDV} - \text{SV}
\]

**Figure 1**

A pulmonary arterial thermodilution curve is recorded after right ventricular injection of 3 ml. of cold saline in a subject without heart disease. The right ventricular residual fraction is obtained by dividing the distance from the baseline of a step at end-diastole by the distance of the comparable point of the beat before.

**Figure 2**

The residual fraction is plotted against the absolute end-diastolic volumes for all subjects. The boxes represent one standard deviation from the mean on both axes.

**Results**

Figure 1 illustrates a typical thermodilution curve from the pulmonary artery of a subject without heart disease following right ventricular injection of cold saline. The ratios of the temperature change at the end of a beat to the beat before averaged 47.5 per cent. Therefore, the residual or end-systolic volume (ESV) was 47.5 per cent of the end-diastolic volume (EDV). Since stroke volume (SV) by the direct Fick method was 61 ml./M.2 in this subject, ESV was 51 ml./M.2 and EDV 112 ml./M.2.

The resting values for SV, ESV, EDV, and ESV/EDV or residual fraction for all subjects without heart disease are summarized in table 1. The ESV/EDV ratio in the control group ranged from 30 to 67 per cent and averaged 53.4 per cent; EDV averaged 103 ml./M.2 ± 24.4 (table 1, fig. 2).

Figure 3 illustrates a pulmonary arterial thermodilution curve in a patient with congestive heart failure. The prolonged down-stroke from poor emptying requires four beats to produce two-thirds disappearance. The resultant ESV/EDV ratio or residual fraction in this case was 75.6 per cent. ESV/EDV in patients with congestive heart failure ranged from 52 to 95 per cent with a mean of 71.9 per cent. The EDV among these patients averaged 123 ml./M.2 ± 67.7 (table 2, fig. 2).

The values during exercise are summarized in tables 1 and 2. Seven of 11 control subjects
decreased their residual fraction (ESV/EDV) during mild to moderate exercise. In contrast, five of six patients in congestive heart failure increased their ESV/EDV while exercising (fig. 4).

Figure 5 illustrates the effects of exercise on absolute end-diastolic volumes.

Discussion

A major concern in these studies is the adequacy of ventricular mixing of the injected thermal indicator. We have previously dealt with this extensively in our original description and uses of the method. The adaptation of the thermodilution method to the patient with congestive heart failure, however, introduces the additional question as to whether a hypodynamic ventricle or one in which there might be an increased EDV would have poorer mixing than a normal ventricle. Presumably, random mixing problems would lead to less reproducibility and greater variability. The fact that reproducibility was the same for the subjects with heart failure as for those without heart disease suggests that this is not a practical problem. Furthermore, with injection close to the tricuspid valve, inadequate mixing might be expected to have produced a peak temperature change after two or more beats rather than one. It should also be pointed out that the validity of the method does not require perfect ventricular mixing. It is only necessary that the plateaus of systolic indicator concentrations in the pulmonary artery correspond to the average ventricular end-diastolic concentrations of the corresponding beats, regardless of whether or not the indicator is well mixed.

Apprehension over the problem of inadequate ventricular mixing led Donato, Courand, and their colleagues to attempt to measure right ventricular volume in man by injecting indicator into the right atrium close to the tricuspid valve rather than directly injecting into the right ventricle. However, if one assumes significant right atrial mixing after injection, it follows that the wash-out slope of indicator appearing in the pulmonary artery will be a function of the atrial rather than the ventricular volume when maximum right atrial volume exceeds right ventricular EDV. This has been shown in analysis of indicator-dilution curves in mathematical circulatory models, not only where there is con-
RIGHT VENTRICULAR VOLUME

It is more reasonable to assume that a variable degree of mixing with the atrial volume would result. Should the volume of distribution in the atrium exceed right ventricular end-diastolic volume, the resultant pulmonary artery radioactive washout curve would reflect the atrial rather than the ventricular volume. Even if the atrial volume of distribution of injected radioactivity is less than the ventricular volume, it is reasonable to assume that several beats will be necessary for all of the indicator to wash from the atrium into the ventricle. This results in a situation analogous to separate injections over several beats of variable amounts of indicator into the ventricle, and the resultant wash-out curve in the pulmonary artery would not be a single exponential susceptible to the mathematical treatment necessary to arrive at the residual fraction, and, therefore, the absolute ventricular volumes.

The mixing advantages that Courand, Donato, and their colleagues hoped to gain by injecting into the low atrium rather than into the ventricle directly, furthermore, hold only for the first beat. With ventricular injection, poor initial mixing would result in an artificial pulmonary artery concentration with the first beat. Thereafter, the concentration curve is independent of how the initial injection was carried out and depends solely on how well right atrial stroke volume normally mixes with the ventricular residual volume. Since the wash-out slope is an exponential, the downslope ratio can be calculated from later beats, excluding the first beat, as we have done in these experiments. The problem of whether initial mixing of the indicator introduced into the ventricle occurred or not then becomes irrelevant.

**Rest**

Our data indicate that approximately one half of the right ventricular volume of a resting subject without heart disease is expelled with each heart beat. The mean value of 53.4 per cent calculated by Courand and his colleagues lies between the 47.8 per cent obtained by Freis as an average of six normal subjects using Evans-blue dye and the 57.5 per cent for the ratio ESV/EDV or residual volume from radiocardiograms after right atrial injection of tracer in 18 subjects without heart disease. As noted earlier, however, some doubt exists in the latter study as to whether the emptying rate being observed is that of the right atrium or right ventricle.

The EDV, calculated from the SV obtained by the direct Fick method and the ESV/EDV ratio, averaged 103 ml./M.² in the subjects without heart disease. This average volume also lies between the value of 79 ml./M.² reported by Freis and associates and the average of 126 ml./M.² calculated by Courand and his associates. It is of interest that our values for end-diastolic volume of the right ventricle in subjects without heart disease correspond very closely to those obtained by other workers for the left ventricle using the thermodilution technic. In preliminary communications, Bristow and his colleagues reported an average EDV of 97 ml./M.² in six patients with normal left ventricular function,
and Elliott, Lane, and Gorlin have found an average left ventricular EDV of 103 ml./M.² in 18 subjects without left ventricular disease.

The most unexpected observation to us in this study was the frequent finding of a normal EDV among subjects in heart failure. Average EDV for the subjects with heart failure was 123 ml./M.², i.e., a value not significantly higher than the control group. Thus, although two patients (nos. 16 and 25) with severe congestive heart failure had volumes that were obviously greatly increased, most of the patients with congestive failure had an EDV within the normal range (fig. 2). These two cases had the highest ventricular end-diastolic pressures. However, an increased EDV was observed with a normal filling pressure (no. 19) and a normal EDV was observed with an elevated EDP (no. 17).

The ESV/EDV or residual fraction was significantly greater in patients with heart failure. Whereas the subjects without heart disease expelled approximately one half their EDV as SV at rest, the patients with congestive heart failure expelled less than one third. Thus a characteristic functional abnormality of the right ventricle in congestive heart failure appears to be an inability to empty itself whether EDV or EDP are normal or greater than normal. Since the EDV was comparable in both groups as a whole, it follows that SV was less in the heart failure group.

It is difficult at first glance to reconcile the common finding of an enlarged cardiac shadow by x-ray in heart failure with a right ventricular EDV frequently in the normal range. Part of the explanation may be that the marked cardiac enlargements on x-ray reflect, to a large extent, enlarged atria rather than ventricles. Thus, in patients with severe mitral insufficiency, well over 500 ml. of blood may reside within the left atrium alone. Furthermore, given any rise in common transmural diastolic filling pressure, the less compliant ventricle would be expected to enlarge less than its atrium. In addition, we have recently studied the effects of tilting into the upright position on a separate group of subjects without heart disease and patients with heart failure. The recumbent right ventricular volumes in the normal and heart failure subjects were comparable to the values reported in this study. On upright tilting, however, the EDV fell in the normal subjects and remained unchanged in the patients with heart failure. Since chest x-rays are taken in the standing position, the finding of a larger cardiac shadow in heart failure is not inconsistent with the observations at rest reported in this study, which were made with the subjects in the recumbent position.

It should also be noted that our heart failure cases involved primarily left ventricular disease, with resultant heart failure. Left ventricular volumes were not measured in our study. If left ventricular EDV were in fact increased, the pericardium might limit overall enlargement with the result that the interventricular septum could impinge upon the cavity of the right ventricle and prevent any significant increase in its volume. It is possible that the results would have been different had the heart failure resulted from primary right ventricular disease.

Several patients exhibited significant right ventricular systolic hypertension that reflected pulmonary artery hypertension. Resultant right ventricular hypertrophy may have acted to prevent appreciable increases in intracavitary volume at the pressures of diastolic filling observed at rest in this study. This concept is supported by the observations of Bristow and his collaborators, who found that left ventricular end-diastolic volumes in patients with pure aortic stenosis were in the normal range regardless of end-diastolic pressures.

Functional tricuspid insufficiency accompanying right ventricular failure might have introduced an error in the measurement. Theoretically, significant amounts of regurgitation would lead to a change in slope or break in the exponential downstroke. We failed to observe this in any case. Presumably, this reflected the fact that none of our patients had massive or intractable heart failure. Luthy and associates placed a thermistor in

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the right atrium and demonstrated that injection of cold saline into the right ventricle could not be detected from tricuspid regurgitation unless failure was very severe and right ventricular volume exceeded 340 mL/M\(^2\), a value not reached in any of our cases.

The possible influence of heart rate must also be considered in evaluating our findings. The group with heart failure had a faster heart rate. Although tachycardia impairs ventricular emptying and decreases EDV, it would not be expected to produce a significant effect when differences were as small as our study.\(^{20}\)

The observation that EDV may be increased in some patients but others have a normal EDV in the presence of an elevated EDP implies that some patients in heart failure have a decrease in the diastolic compliance of their right ventricle. Such factors as myocardial edema, changes in cardiac shape with rearrangement of muscle bundles, local biochemical factors such as change in catechol content, and anatomic changes such as scarring may play a role. Our experiments were not designed to investigate the nature of this change. Until the mechanism is understood, however, the finding of an elevated diastolic pressure in the presence of a normal volume suggests that caution should be used in interpreting studies relating ventricular performance in terms of end-diastolic pressure.

Exercise

During exercise, the slight average increase in SV of 12.5 per cent (table 1) in the subjects without heart disease was in the range observed by others.\(^{35}\) EDV did not change significantly; consequently, the residual fraction generally decreased (fig. 4). The fall in ESV/EDV in seven of the 11 subjects, despite the opposite effect to be expected in the presence of an increase in their heart rate,\(^ {29}\) indicates that an improvement in myocardial performance occurred with exercise.

In contrast, five of six subjects with congestive heart failure, in whom resting end-diastolic volumes were within the normal range, increased their EDV greatly with exercise. This was associated with a large increase in filling pressure in all patients (table 2). Despite the large abnormal increment in EDV, SV increased as little as it did in the control subjects. Consequently, the ratio of ESV/EDV, although increased at rest in patients with heart failure, rose even further with exercise (fig. 4). It should be noted that the increase in EDV, although accompanied by little change in SV, occurred at a time when stroke work materially increased, since significant right ventricular systolic hypertension reflecting pulmonary artery hypertension resulted during exercise.

Figure 6 illustrates the relationship between ESV and EDV observed for all periods in all subjects. The linear correlation confirms for the right ventricle in man the same relationship we previously observed in the left ventricle of dogs under a variety of circumstances\(^ {28}, {29}\) and which Holt observed in the dog and several other mammals.\(^ {29}\) The linear correlation is seen in patients with and without heart disease, although the slope is displaced upwards in the former. Since the SV represents the difference between EDV and

\[ \text{EDV} = \text{ESV} + \text{SV} \]

\[ \text{ESV} = \text{EDV} \times \text{ESV/EDV} \]

\[ \text{SV} = \text{EDV} - \text{ESV} \]

The end-systolic volume is plotted against the end-diastolic volume for all values. A linear correlation is seen. The slope is displaced upwards in the subjects with heart failure, reflecting a smaller SV at any given EDV.

\[ \text{SV} = \frac{\text{EDV} \times \text{ESV/EDV}}{1 + \text{ESV/EDV}} \]
ESV and, since the slope of the regression line for these points is under unity, the SV must also be increasing as the EDV increases in both the patients with failure and the controls. This is a reaffirmation of the Starling principle as applied to the right ventricle of intact man.

Conclusion
We measured right ventricular volumes in 15 subjects without heart disease and in 10 patients with congestive heart failure secondary to left ventricular disease. The residual fractions were determined from pulmonary artery thermodilution curves following injections of cold saline into the right ventricle. Stroke output was measured simultaneously from a direct Fick cardiac output, permitting calculation of absolute end-systolic and end-diastolic volumes. The ratio ESV/EDV averaged 53.4 per cent in subjects without heart disease and was significantly higher, averaging 71.9 per cent, in the patients with congestive heart failure. Although absolute right ventricular end-diastolic volume was occasionally increased, most patients with congestive heart failure had end-diastolic volumes in the normal range at rest. Moderate exercise in the recumbent position generally decreased the residual fraction in subjects without heart disease without a significant change in end-diastolic volume; in contrast, patients with congestive heart failure increased both residual fraction and absolute end-diastolic volumes with exercise.

References

Earliest Measurement of Cardiac Minute Volume Output

The volume of the ventricle was determined by casting with wax.

"So that this Piece of Wax thus formed, may reasonably be taken to be nearly commensurate to the Quantity of Blood received into this Ventricle at each Diastole, and is thence propelled into the Aorta at the subsequent Systoles."

Right Ventricular Volumes in Patients with and without Heart Failure

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