A Method for the Estimation of Right Ventricular Volume by Equilibrium Radionuclide Angiography

Robert Slutsky, M.D.; William Ashburn, M.D.; and Joel Karliner, M.D.

To develop a method for estimating right ventricular volume and to assess right ventricular volume at rest, we studied 45 persons with equilibrium radionuclide angiography. The study group comprised 15 normal control subjects (5 with atypical chest pain and normal coronary angiograms) and 30 patients with coronary heart disease (CHD). Each coronary patient and 5/15 control subjects had both right and left heart catheterization studies with intracardiac pressure measurements within 24 hours of the radionuclide study. Using a previously described method for generating right ventricular volume curves, we used the counts at end-diastole, corrected for frame time, the total number of processed heart beats, and blood radioactivity to derive right ventricular end-diastolic volume units. All normal controls (group 1) had a right ventricular ejection fraction ≥ 0.40, with a right ventricular volume index ≤ 5.8. The CHD patients consisted of two subgroups: group 2 (N = 20) and group 3 (N = 10), with right ventricular end-diastolic pressures < 10 mm Hg and ≥ 10 mm Hg, respectively. In group 2, 19/20 had a normal right ventricular ejection fraction, and 18 had a normal end-diastolic volume. In group 3, 4/10 patients had a depressed ejection fraction (< .40) and 9/10 an increased end-diastolic volume. We conclude that right ventricular volume can be estimated with radionuclide angiography, and that dilatation may precede depression of the right ventricular ejection fraction in some patients with CHD.

Because of the irregular anatomic configuration of the right ventricle, relatively few investigators have attempted to develop simple methods for calculation of right ventricular volume. These studies have used contrast ventriculography, and the invasive nature of the technique made serial determinations impractical.

Recently we have developed a method for calculating right ventricular ejection fraction. In related work we have found an excellent correlation between left ventricular volumes and counts calculated at the end-diastolic and end-systolic data points, respectively, from standard left ventricular time-activity curves when counts are corrected for blood radioactivity, frame time, and the number of cycles processed. Using the right ventricular volume curve and applying the methodology from the previously mentioned studies, relative right ventricular end-diastolic volume can be obtained and cases compared. To assess the usefulness of this technique and its potential value, we used equilibrium radionuclide angiography to study 45 subjects, of whom 15 were normal controls and 30 were patients with coronary artery disease.

METHODS AND MATERIALS

Patient Populations

Group 1 consisted of 15 normal control subjects. Five had atypical chest pain and underwent contrast ventriculography and coronary angiography. In all five, coronary angiograms, contrast ventriculograms and both right and left ventricular hemodynamics were normal. Ten subjects were normal volunteers without any history of cardiac disease. All 15 had a normal resting and stress ECG, a normal increase in left ventricular ejection fraction with exercise (≥ .05 ejection fraction unit increase), were not taking any medication, had a normal physical examination result and a normal chest roentgenogram. This group was composed of 11 men and one woman, with a mean age 49 ± 6 years and a range of 26 to 63 years.

Group 2 was composed of 20 patients with coronary arterial stenoses (at least one significant obstruction, defined as ≥ 70 percent intraluminal occlusion of a major coronary artery). Each patient in this group was examined for possible coronary artery bypass surgery. No patient had ingested long-acting nitrate preparations, propranolol, or antihypertensive medications within 48 hours of the radionuclide or contrast study. All patients in this study had a right ventricular end-diastolic pressure during right heart catheterization of < 10 mm Hg. No subject had clinical evidence of tricuspid regurgitation, a raised mean right atrial pressure, or prominent V waves on the right atrial pressure tracing. There were 10 men and four women in this group, with a mean age of 49 ± 5 years. Two patients had suffered previous transmural...
myocardial infarctions (both inferior as defined by cineventriculograms and ECG).

Group 3 was composed of ten subjects with significant coronary artery disease as defined in group 2. None had clinical or hemodynamic evidence of tricuspid regurgitation and all had right ventricular end-diastolic pressures $\geq$ 10 mm Hg. Eight had suffered previous transmural myocardial infarctions (four anterior and four inferior), and three were taking oral digoxin (mean level $\pm$ SD of 1.34 $\pm$ .30 ng/ml) and furosemide. There were eight men and two women, with a mean age of 47 years. Five patients in group 1 and all patients in groups 2 and 3 underwent right and left heart catheterization using standard techniques. All patients had right-sided catheters that measured pressures using standard fluid-filled techniques, with a reference level at the mid- chest level. All patients were studied in the postabsorptive state after the intramuscular injection of 100 mg of pentobarbital. All patients had thermodilution cardiac outputs performed in triplicate, and the three values averaged. Stroke volume was then determined using the simultaneous heart rate.

Data Acquisition and Analysis

All subjects underwent first pass radionuclide angiograms for the evaluation of right ventricular ejection fraction as previously noted. In brief, two intravenous (IV) catheters were placed, one in each antecubital fossa. Fifteen to 20 mCi of human serum albumin labeled with $^{99}$Tc was given as a bolus injection, followed by a flush of 15 ml of normal saline solution. The second catheter was used for periodic blood sampling to assess serial blood radioactivity. The patients were supine, and the injection followed the positioning of a single crystal, mobile scintillation gamma camera, which was placed over the thorax in the 30$^\circ$ right anterior oblique position. The camera was equipped with a general purpose, low-energy parallel-hole collimator. The data were stored on videotape and then transferred in real time to a dedicated minicomputer system (General Electric Med II Computer System). A previously described light pen program was used for calculation of right ventricular ejection fraction from the first-transit scintigraphic data. Two or three beats of the high-frequency background corrected time-activity curve were manually evaluated, using the peak of the curve as the end-diastolic data point and the nadir of the curve as the end-systolic data point.

All patients underwent an equilibrium study after the IV injection and mixing of the radiopharmaceutical. All studies were performed with the scintillation camera detector located in the 45$^\circ$ left anterior oblique position, which included a 5 to 10$^\circ$ caudal tilt to achieve maximal separation of the left ventricle from the left atrium. A modified $V_e$ ECG lead was used to gate the scintigraphic data. Data were stored on video tape as digital pulses and transferred to a minicomputer for calculation of left and right ventricular ejection fractions (Medical Data Systems-PAD). Both the left and right ventricular ejection fractions were calculated by dividing each R-R interval into 28 equal frames of variable duration depending on heart rate and then by summing scintigraphic data from multiple cardiac cycles at each corresponding frame to assemble a composite cardiac cycle. Each image frame had a spatial resolution of $64 \times 64$ channel elements.

The left ventricular time-activity (volume) curve was generated with the aid of semiautomatic computer algorithm (MUGO) as previously described. The right ventricular ejection fraction was determined from a fixed region of interest assigned at the end-diastolic frame. The operator, with the aid of a light pen, outlined the right ventricle, taking care to avoid the pulmonary outflow tract and, when visible, the edge of the right atrium (Fig. 1). Background was assigned around the right ventricle and included the pulmonary outflow tract but not the interventricular septum. If the right atrium was visible, it was also included in the background. Background was normalized to the end-diastolic area, and the activity in the fixed background region-of-interest subtracted from each frame to form a corrected time-activity curve. Ejection fraction was calculated from the peak and valley of the curve, where ejection fraction $= (EDC_{e}-ESC_{e})/EDC_e$, where $EDC_e =$ background corrected end-diastolic counts and $ESC_e =$ background corrected end-systolic counts. We have previously shown this to be a reproducible and accurate method for calculating right ventricular ejection fraction.

Right ventricular end-diastolic volume was derived from the following equation:

$$\text{Volume (units)} = \frac{EDC_e \times \text{No. Cardiac cycles} \times \text{Actual frame time} \times 10^4}{\text{Plasma radioactivity}}$$

where end-diastolic counts were corrected for the number (No.) of cardiac cycles processed, the acquisition time (frame time) and the radioactivity of 0.1 ml of plasma counted in a well counter (photopeak 140 KEV with a 20 percent win-

![Table 1—Hemodynamic Results from All Three Study Populations](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21251/)
Reproducibility

The reproducibility of right ventricular ejection fraction calculation by this technique has been previously evaluated and reported. In general interobserver and intraobserver variability was ≤ 0.04 ejection fraction units. Serial reproducibility (two studies performed at least ten days apart) was also ≤ 0.04 ejection fraction units. When 2, 5, or 10 minutes' scintigraphic data were evaluated, variability was also small. Because the primary interest in this study was in the number of counts at the end-diastolic data point, we repeated the previous reproducibility study, examining the variability in the background corrected counts at end-diastole. The analyses included interobserver and intraobserver variability in 15 cases, serial (two separate studies) variability in ten cases, and the effect of acquisition duration in ten cases (2, 5, and 10 minutes of data).

Statistical Analyses

All data were analyzed using standard analysis of variance. Correlations were performed using a least squares linear fit. All data are given as the group mean ± 1 SD.

RESULTS

Hemodynamic Data

There was no significant difference among the three groups in heart rate or blood pressure. Those
in group 3 had a greater mean right atrial pressure (10.9 ± 3.6 vs 4.8 ± 2.1 mm Hg; P < .05), right ventricular end-diastolic pressure (12.9 ± 2.9 mm Hg vs 6.4 ± 1.8; P < .01), pulmonary artery mean pressure (28.7 ± 11.1 vs 14.6 ± 4.2 mm Hg; P < .01), and mean pulmonary artery wedge pressure (20.2 ± 10.6 vs 9.0 ± 2.9 mm Hg; P < 0.1) compared with the subjects in group 2. All five control subjects had a normal mean right atrial pressure (≤ 6 mm Hg), right ventricular end-diastolic pressure (≤ 5 mm Hg), mean pulmonary artery pressure (≤ 15 mm Hg), and mean pulmonary artery wedge pressure (≤ 10 mm Hg).

The contrast ventriculographic left ventricular ejection fractions were significantly lower in group 3 (0.50 ± 0.24) compared with the results in group 2 (0.64 ± 0.15, P < .01). Five patients in group 3 and five patients in group 2 had a depressed resting left ventricular ejection fraction (defined as the lower limit of left ventricular ejection fraction determined from 35 patients with atypical chest pain and normal angiographic studies). The left ventricular end-diastolic volume was also significantly larger in the subjects in group 3 compared with the results from group 2 (192.1 ± 116.4 ml vs 131.5 ± 52 ml, P < .01).

Correlation with First-pass Radionuclide Angiography

The correlation of the equilibrium technique for calculating right ventricular ejection fraction with the virtually simultaneous first-pass study was good in all 45 subjects (r = .80). The mean difference between the first-transit and equilibrium technique was 0.03 ± 0.02 ejection fraction units. The mean difference between the first-pass and equilibrium techniques did not change significantly in the presence of an increased right ventricular or right atrial pressure; these values were 0.032 ± .025 ejection fraction units in the patients with a right ventricular end-diastolic pressure ≥ 10 mm Hg, and 0.029 ± .02 ejection fraction units in the subjects with a right ventricular end-diastolic pressure < 10 mm Hg. Similarly, elevations in right atrial pressure and presumably right atrial volume did not produce significantly higher mean differences between the two techniques or poorer linear fit correlation coefficients, though the trend was toward somewhat larger differences with high pressures, as previously suggested.

Reproducibility

The reproducibility, including interobserver and intraobserver variability and serial (two studies per-formed 10 to 14 days apart) variability, of the right ventricular ejection fraction calculations has been found to be good (mean observer variability < 0.04 ejection fraction units and a mean serial reproducibility of < 0.04 ejection fraction units).

The effect of acquisition time (2, 5, or 10 minutes) on background corrected end-diastolic counts, when corrected for the number of processed cycles and frame time, was 4.1 ± 2.1 percent, with a range of 1.4 to 9.2 percent. Intraobserver variability was 3.9 ± 2.4 percent in 15 cases (five-minute duration, with a range of 1.3 to 8.7 percent). Interobserver variability was 4.2 ± 2.4 percent in ten cases (range, 1.5 to 9.1). Ten studies performed two weeks varied by 4.2 ± 2.6 percent (range, 0.9 to 9.6 percent).

Right Ventricular Volume

Right ventricular stroke volume by radionuclide angiography (ml/m²) correlated well with thermodilution estimates of stroke volume (r = .83) as well as with ventriculographic estimates derived from the left ventricular cineangiograms (r = .84).

The results for the right ventricular ejection fractions and volumes are given for all groups in Figures 2 and 3.

The right ventricular end-diastolic volume (units/m² BSA) in the normal control patients

![Table](image.png)

**Figure 2.** Right ventricular ejection fractions in all three groups. Lower right ventricular ejection fractions in coronary patients with elevated right ventricular end-diastolic pressures.
The patients without right coronary disease (five isolated left anterior descending involvement, and four double-vessel disease). The pulmonary arterial wedge pressure (7.44 ± 2.8 vs 8.44 ± 3.8 mm Hg) was somewhat smaller in the patients with right coronary lesions, although again this difference was not statistically significant.

Ten patients had right ventricular end-diastolic pressures of 10 mm Hg or more. As a group, their right ventricular ejection fraction was significantly lower than the subjects in group 1 or group 2 (0.40 ± .18 vs 0.50 ± .06 and 0.53 ± .12, respectively; both P < .01). Additionally their right ventricular end-diastolic volumes were significantly larger than the end-diastolic volumes of the subjects in either group 1 or group 2 (8.72 ± 1.99 vs 5.10 ± 0.68 and 5.27 ± 1.03, respectively, both P < .01). Similarly, the patients with elevated right ventricular end-diastolic pressures also had greater mean pulmonary artery wedge pressures compared with the other two groups (20.2 ± 10.6 mm Hg vs 9.02 ± 2.93 mm Hg in group 2; P < .005) and a greater mean pulmonary artery pressure (28.7 ± 11.1 mm Hg vs 14.6 ± 4.2 mm Hg; P < .01). Nine patients in this group had an increase in right ventricular end-diastolic volume (> 5.8 units/m²), while only four had a depressed right ventricular ejection fraction (< 0.40). In this group, six of ten subjects had an elevated pulmonary artery wedge pressure (> 12 mm Hg). All of these six subjects had suffered previous myocardial infarctions (two inferior and six anterior by ECG criteria). Four of these had depressed right ventricular ejection fractions, and all six had enlarged right ventricles. The relationship between wedge pressure and either right ventricular ejection fraction (r = -.14) or end-diastolic volume (r = .44) were both poor in these six individuals. Four subjects had normal wedge pressures (≤ 12 mm Hg) three of whom had increased right ventricular volumes, but all four had normal right ventricular ejection fractions. Two of these subjects had suffered previous inferior (and possibly right ventricular) myocardial infarctions. Thus, abnormalities in right ventricular size were more commonly seen in association with left ventricular dysfunction (six of nine abnormal subjects).

**DISCUSSION**

It has been suggested that left ventricular dysfunction during exercise contributes to and may exacerbate right ventricular dysfunction, although it would also seem that right ventricular dysfunction may occur in the absence of any overt left ventricular dysfunction. It was shown by Ferlinz et al. that patients with significant right coronary ar-

---

**Figure 3.** Right ventricular volume indices (units of volume/m² BSA) shown in all three groups. Note larger ventricular volumes in coronary patients with elevated right ventricular end-diastolic pressures.

(group 1) was 5.1 ± 0.68 units (range 3.1 to 5.8). This was not significantly different from those in group 2 (patients with an end-diastolic pressure less than 10 mm Hg), who, as a group, had a mean right ventricular volume of 5.27 ± 1.03 (range, 3.1 to 7.67). Two subjects in this group had enlarged right ventricles (defined as an end-diastolic volume index greater than 5.8). One of these had a normal right ventricular ejection fraction, and one was clearly depressed (0.35). Both patients had significant right coronary artery intraluminal occlusions (greater than 90 percent in both), and both had suffered previously well-documented inferior infarctions (an elevated serum creatine phosphokinase MB band with new Q waves in the inferior leads of a 12-lead surface ECG). Both patients had normal left ventricular ejection fractions and volumes with inferoposterior hypokinesis. Both had normal pulmonary artery wedge and pulmonary artery mean pressures. Of the remaining 18 patients in this group, 9 had significant stenosis in the right coronary artery, 5 had triple-vessel disease, and 2 had double-vessel disease. The end-diastolic volume in these nine patients with right coronary disease was not significantly different (4.9 ± 0.8 vs 5.1 ± .65) from
terial lesions had right ventricular ejection fractions and right ventricular volumes similar to those of normal controls. None of their subjects had previous infarctions or elevations of right ventricular end-diastolic pressure. In a preliminary report Bless et al., using biplane contrast ventriculograms of the right ventricle, found that right ventricular dilation most commonly occurred when left ventricular dysfunction and anterior asynergy was present. On the other hand, inferior asynergy was associated with normal right ventricular global function and size, though right ventricular inferior shortening was abnormal.

The use of gated equilibrium scintigraphy for the evaluation of right ventricular performance and size has been recently proposed by Maddahi et al., Horn et al., as well as our own group. Extrapolating methods previously validated for assessment of left ventricular volume, we have used the counts at end-diastole obtained from right ventricular time-activity (volume) curves to obtain measurements of relative right ventricular size.

In this study we have found that right ventricular function and size are generally normal when right ventricular end-diastolic pressure is normal. When end-diastolic pressure increases to 10 mm Hg or more, right ventricular dilation occurred in nine of ten patients, while right ventricular ejection fraction was depressed in only four of ten cases. Interestingly, six of the nine patients with right ventricular dilation had significantly elevated pulmonary artery mean and wedge pressures, suggesting the possible adverse influence of elevated outflow impedance on right ventricular performance in these individuals. The other three patients with right ventricular dilation had suffered previous inferior and quite probably right ventricular infarctions. In general, right ventricular dysfunction or dilation at rest was not seen in the absence of left ventricular dysfunction or previous myocardial infarction regardless of the coronary anatomy.

The limitations of end-diastolic fixed right ventricular regions of interest have been emphasized previously by Slutsky et al., Gandsman and coworkers, and Maddahi et al. and are due in part to the overlap of the right atrium with the right ventricle. This approach would be particularly likely to increase the end-systolic counts, reduce the stroke counts, and decrease the ejection fraction. In this study, from which patients with tricuspid regurgitation were excluded, we found the difference between the right ventricular ejection fraction calculated from the first-transit (right superior oblique projection) and the equilibrium method relatively constant in the presence of both normal and depressed ejection fractions. This observation suggests that either the right atrium played little role in distorting ejection fraction calculations, or, more likely, that the atrium was not sufficiently enlarged to create substantial artifacts. Thus subjects with tricuspid regurgitation or stenosis would provide unusual difficulties for this technique. An additional concern is that the right ventricle may be subject to greater soft-tissue attenuation than the left ventricle (particularly in men with large thoracic cages and in women) because of its anterior position in the left anterior oblique projection. This would tend to exaggerate the variability in results in diverse patient populations. Because of these potential pitfalls we have limited our data to determinations of right ventricular ejection fraction and relative right ventricular end-diastolic volume.

In summary, then, it is conceivable that patients with marked right atrial enlargement, large chest walls, pulmonary hyperinflation, and women with large breasts may have different attenuation effects than a man with a typical masculine body habitus. Variable right ventricular regions of interest defined at end-diastole and end-systole may prove to be more useful in the evaluation of right ventricular size and function, though this has been shown only with a left paraventricular background to date. The position of the right atrium, being somewhat posterior to the right ventricle in the 45° left anterior oblique projection, will invariably limit fixed right ventricular assignments at end-diastole. The background chosen in this study will also prove faulty when the right ventricular stroke volume is substantially greater than the left (ie, any substantial left-to-right shunt) and when the right atrium cannot be visualized well enough to be included, at least in part, in the background. In a preliminary study of nine patients with coronary heart disease, we correlated this radionuclide technique with biplane contrast right ventriculograms. The radionuclide study was performed just before the contrast study. The correlation for ejection fraction (r = .78) and right ventricular end-diastolic volume (r = .85) was good using this method.

We conclude that right ventricular dilatation in patients with coronary heart disease is more common than reductions in global indices of right ventricular function. Additionally, dilatation occurs in the presence of left ventricular disease and elevated pulmonary pressures, or in the presence of inferior and presumably old right ventricular infarctions. Within certain methodologic limitations, right ventricular ejection fraction and relative end-diastolic volume may be assessed by this method from radionuclide time-activity curves.
REFERENCES