Peak Rate of Left-Ventricular Ejection by a Gated Radionuclide Technique: Correlation with Contrast Angiography

Valmik Bhargava, Robert Slutsky, and Dennis Costello

Veterans Administration Medical Center, San Diego, and University of California, San Diego School of Medicine, La Jolla, California

Gated radionuclide cardiac blood-pool imaging can produce reliable estimates of left-ventricular (LV) volume and ejection fraction. The ventricular volume curve can be used to develop normalized ejection rates, since count volumes and framing times are known. To test the accuracy of the peak ejection rate (maximum dv/dt), as derived by a standard computer algorithm, we studied 15 patients with coronary artery disease by both contrast ventriculography and radionuclide angiography. Max dv/dt by the radionuclide technique correlated well with the angiographic result: $r = 0.92$, $p < 0.01$. The mean intraobserver variation was ± 0.3 end-diastolic volumes per sec ($\pm 12\%$) and the mean interobserver variation ± 0.33 end-diastolic volumes per sec ($\pm 13\%$). We conclude that maximum dv/dt may be derived from gated blood images, with reasonable accuracy and modest variability.

J Nucl Med 22: 506–509, 1981

Ejection-phase indices have proven to be the most clinically effective way to characterize global left-ventricular performance (*1*). It has been suggested that global, holosystolic velocity-dependent indices may be more sensitive than ejection fraction alone in detecting subtle left-ventricular dysfunction (*2*). Ejection fraction depends on both preload and afterload (*3–5*), whereas velocity phase indices seem relatively independent of preload (*3,4*). Thus, velocity indices may prove more suitable for clinical situations where preload is altered, such as during atrial pacing, active diuresis, or volume infusions (*5,6*).

Gated radionuclide imaging of the heart has been shown to be a reliable and reproducible technique for evaluating left-ventricular function, size, and regional performance (*7–18*). Nonetheless, little data are available on the accuracy of the peak value of the first derivative of the gated time-activity (volume) curves, an easily derived velocity index of the cardiac ejection period. To determine this, we studied 15 patients with coronary heart disease by both contrast ventriculography and radionuclide angiography.

METHODS

The 15 patients consisted of 12 men and three women with a mean age of 56 ± 6 yr (range 31–78 yr). All radionuclide studies were performed within 48 hr of the contrast ventriculograms.

Contrast ventriculography. Biplane left ventriculography was performed after completion of hemodynamic studies but before coronary arteriography. A 3-sec injection of 76% sodium and meglumine diatrizoate (12–18 ml/sec) was delivered through either a No. 8 Pigtail or NIH catheter opening in front of the mitral valve. Thirty-degree right anterior oblique and 60° left anterior oblique projections were routinely used. The opacified ventricle was filmed at 58–62 frames/sec, and exposed on 35 mm film. To identify the exposure of each cine

Received Aug. 27, 1980; revision accepted Jan. 22, 1981.

For reprints contact: V. Bhargava, PhD (111A), Veterans Administration Medical Center, 3350 La Jolla Village Dr., San Diego, CA 92161.

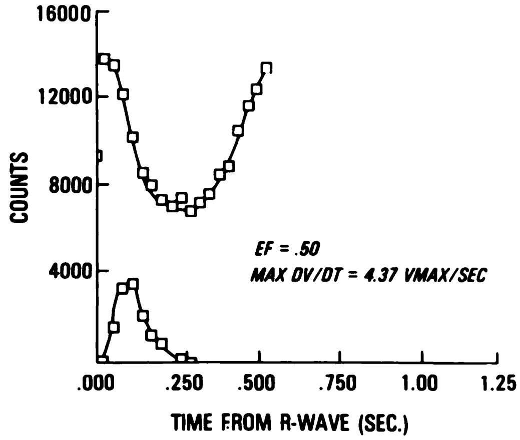

FIG. 1. Computer-generated time-activity curves. Because of difficulty in photographing the computer image, the time-activity curve and its first derivative were redrawn from the original. For convenience, the dV/dt curve is inverted.

frame the surface ECG and a cine-pulse marker were recorded on a strip chart at 200–400 mm/sec. Ventriculograms were made at held peak-inspiration. The magnification grid located at the tip of the catheter was exposed in each plane. Sinus beats removed from ectopic beats by at least two cardiac cycles were analyzed. Left-ventricular silhouettes for both projections, along with the magnification grid, were drawn on paper and digitized using a digitizer* interfaced to a table-top calculator. The area-length method was used to calculate ventricular volumes (*19*). Frame-by-frame left-ventricular volume-time data were then smoothed using a digital 5th-order Butterworth low-pass filter with a cutoff frequency of 7.5 Hz. The slope of this curve was derived using a Lagrange polynomial (*20*) (Fig. 1). The peak negative value was normalized to the end-diastolic volume to give the peak rate of emptying in end-diastolic volumes/sec.

Radionuclide data analysis. After equilibration of Tc-99m-labeled human serum albumin in the vascular space, multiple-gated acquisition studies were performed using a portable gamma camera with a low-energy, general-purpose parallel-hole collimator. Energy selection was set at 140 keV with a 20% window.

In order to provide good separation between the left and right ventricles, the detector was positioned in the 40–50° left anterior oblique position with a 5–10° caudal tilt.

A nuclear medicine digital computer system was used to integrate several hundred heart beats (R-R intervals) and to construct multiple, identically phased composite images. Each heart beat was divided into 28 frames of 20–40 msec duration (R-R interval/28), each depending on heart rate. In a 5-min acquisition, usually an average of 10,000 counts (range 8,000–18,000) could be accumulated within the left ventricular region of interest at end-diastole in one 40-msec frame. Counts were corrected for background activity.

To generate a time-activity curve and to calculate ejection fraction and ejection rate, a rectangle was placed around the left ventricle at end diastole. A computer algorithm was used to locate the edge of the left ventricle, using as guidelines a combination of (a) the second derivative of the count profile of the image within the rectangle and (b) a minimum count-rate decline of 5% per element. The threshold of edge detection was then lowered by inspection to the point at which the entire left-ventricular outline was incorporated by the "second derivative" function. Each subsequent frame was processed at the same threshold level so that throughout all 28 frames a "variable" region of interest closely approximating the ventricular silhouette was used to determine the changing count rate within the left ventricle. A computer-assigned region of interest adjacent to the left lower border of the left-ventricular ROI was used to correct for noncardiac activity. A typical curve is shown in Fig. 2. This computer algorithm has been previously shown to develop, reproducibly, left-ventricular ejection fractions and volumes that correlate well with contrast angiographic results (*9–11*).

A first-derivative curve of the ventricular activity curve was computed using the difference between each two consecutive points divided by the time interval between them (R-R interval/28). The peak negative value of this curve, which indicates the maximum emptying rate, was normalized to the end-diastolic counts to permit comparisons of hearts of varying sizes and to allow the characterization of meaningful emptying rates, in lieu of converting relative count volumes to absolute milliliter. No subject had more than three extrasystolic beats during the radionuclide study, and no attempt was made to exclude sinus beats of varying R-R duration.

Correlations were performed using a least-squares linear curve fit. All data are given as the group mean ± standard deviation.

Reproducibility. Intraobserver reproducibility was

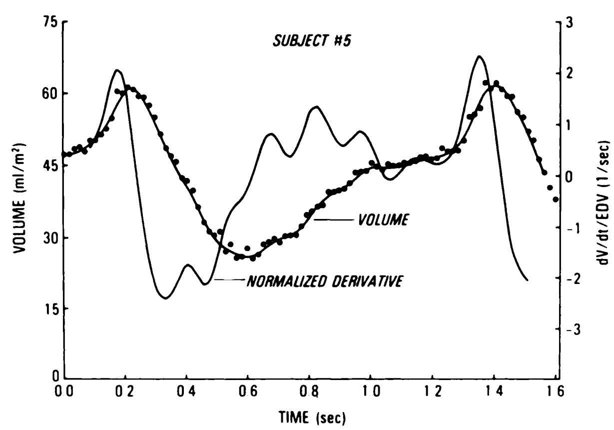

FIG. 2. Volume and normalized derivative, as calculated from contrast ventriculograms, are plotted against time. Dots are real data points; smoothed volumes are shown by curve. Volumes are normalized by body surface area.

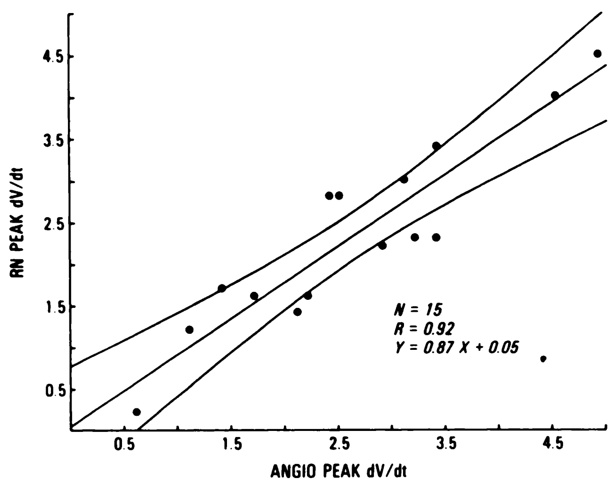

FIG. 3. Correlation between peak rate of left-ventricular ejection, as calculated from contrast angiographic and radionuclide data is shown.

assessed by having the observer make the radionuclide studies on two different occasions separated by at least 1 mo. Interobserver reproducibility was investigated by having the second observer analyze the scintigraphic data without knowledge of the results of the first observer, usually within 1 mo (but not less than 2 wk) of the original data collection and processing.

RESULTS

In 15 patients the peak rate of ejection, as measured by angiographic techniques (x), correlated well with the radionuclide method (y) ($r = 0.92$). The regression equation was found to be $y = 0.87x + 0.05$ (Fig. 3). Peak emptying rates are given in Table 1.

When the radionuclide data were reprocessed by the first observer, the mean variation in the peak emptying rate was 0.3 ± 0.1 end-diastolic volumes/sec (±12%). When the data from two different observers were compared, in all 15 cases, again little variation in peak ejection was found (0.33 ± 0.1 end-diastolic volumes/sec, ±13% variation).

TABLE 1. COMPARISON OF RATES OF LEFT-VENTRICULAR EJECTION, AS ASSESSED BY THE RADIOTRACER (y) AND CONTRAST (x) METHODS

Subject no.	Maximum negative (Angio)	$\left[\frac{1}{EDV} \cdot \frac{dV}{dt}\right]$ (Radionuclide)
1	2.5	2.8
2	3.1	3.0
3	2.2	1.6
4	4.5	4.0
5	2.4	2.8
6	0.6	0.2
7	2.1	1.4
8	3.4	3.4
9	4.9	4.5
10	1.4	1.7
11	2.9	2.2
12	3.2	2.3
13	1.1	1.2
14	3.4	2.3
15	1.7	1.6
Mean ± s.d.	2.63 ± 1.9	2.33 ± 1.2

CONCLUSIONS

Standard gated radionuclide techniques can produce accurate cardiac time-activity (volume) curves, though there is some controversy over the absolute accuracy of the timing and shape of the curve during early systolic ejection (*21,22*). Nonetheless, peak normalized ejection rates can be determined by merely calculating the change in counts between two frames of known duration, and determining the highest value during ventricular empyting. In our study of 15 patients with coronary heart disease, the correlation between peak emptying rates determined from biplane contrast ventriculograms and those obtained by means of a standard, commercial nuclear computer and gated blood images was excellent ($r = 0.92$, $p < 0.01$). The variability of the techniques was modest for the same observer (±12%) or a second one (±13%).

Validation of the radionuclide peak ejection rate had not been examined previously. Bacharach and coworkers (*23*) have demonstrated that 40-msec frame durations provide reproducible and reliable measurements of peak ejection rate. They examined frame durations from 10–50 msec, and found that even 50-msec frame durations are reliable at rest. This explains why the shorter framing time of the contrast study (16–17 msec) did not distort the results, and thus correlated with the radionuclide study (frame time 30–40 msec). The slope of the regression equation can be expected to be less than unity, because the sample time for the radionuclide studies is higher.

Thus we conclude that a velocity-dependent, ejection-phase index can be satisfactorily derived from gated blood-pool images. This index may be of particular use when alterations of preload are expected, with the expectation that the data will be accurate and reproducible.

FOOTNOTE

* Talos.

ACKNOWLEDGMENTS

This work was supported by the Medical Research Service of the San Diego Veterans Administration Center and NIH Research Grant

No. HL 17682, Awarded by the National Heart, Lung and Blood Institute.

REFERENCES

1. Peterson KL, Skloven D, Ludbrook P, et al: Comparison of isovolumic and ejection phase indices of myocardial performance in man. *Circulation* 49:1088-1101, 1974
2. Slutsky R, Karliner JS, Battler A, et al: Comparison of early systolic and holosystolic ejection phase indexes by contrast ventriculography in patients with coronary artery disease. *Circulation* 61:1083-1090, 1980
3. Karliner J, Peterson K, Ross J, Jr: Myocardial mechanics: Assessment of isovolumic and ejection phase indices of left ventricular performance. In *Cardiac Catheterization and Angiography*. Grossman W, Ed. Philadelphia, Lea and Febiger, 1974, pp 188-206
4. Mahler F, Ross J, Jr, O'Rourke R, et al: Effects of changes in preload, afterload and inotropic state on ejection and isovolumic phase measures of contractility in conscious dogs. *Am J Cardiol* 35:626-634, 1975
5. Slutsky R, Watkins J, Peterson K, et al: The response of left ventricular function and size to atrial pacing, volume loading and afterload stress in patients with coronary artery disease. *Circulation*, in press
6. DeMaria AN, Neumann A, Schubart PJ, et al: Systematic correlation of cardiac chamber size and ventricular performance determined with echocardiography and alterations in heart rate in normal persons. *Am J Cardiol* 43:1-9, 1979
7. Burow RD, Strauss HW, Singleton R, et al: Analysis of left ventricular function from multiple gated acquisition cardiac blood pool imaging. *Circulation* 56:1024-1028, 1977
8. Sorenson SG, Hamilton GW, Williams DL, et al: R-wave synchronized blood pool imaging: A comparison of the accuracy and reproducibility of fixed and computer-automated varying regions-of-interest for determining the left ventricular ejection fraction. *Radiology* 131:473-478, 1979
9. Slutsky R, Karliner J, Ricci D, et al: Left ventricular volumes by gated equilibrium radionuclide angiography: A new method. *Circulation* 60:556-564, 1979
10. Slutsky R, Karliner J, Battler A, et al: Reproducibility of ejection fraction and ventricular volume by gated radionuclide angiography after myocardial infarction. *Radiology* 132:155-159, 1979
11. Slutsky R, Pfisterer M, Verba J, et al: Influence of different background and left ventricular assignments on ejection fraction in equilibrium radionuclide angiography. *Radiology* 135:725-730, 1980
12. Slutsky R, Karliner J, Gerber K, et al: Peak systolic blood pressure end-systolic volume: Assessment at rest and during exercise in normal subjects and patients with coronary heart disease. *Am J Cardiol* 46:813-820, 1980
13. Ashburn WL, Schelbert HR, Verba JW: Left ventricular ejection fraction—A review of several radionuclide angiographic approaches using the scintillation camera. *Prog Cardiovasc Dis* 20:267-284, 1978
14. Strauss HW, McKusick KA, Boucher C, et al: Of linens and laces—the eighth anniversary of the gated blood pool scan. *Semin Nucl Med* 9:296-309, 1979
15. Brady TJ, Lo K, Trall JH, et al: Exercise radionuclide ejection fraction: Correlation with exercise contrast ventriculography. *Radiology* 132:703-705, 1979
16. Alderson PO, Bernier DR, Ludbrook PA, et al: Serial radionuclide determinations of ejection fraction with ^{99m}Tc-labelled red blood cells. *Radiology* 119:729-730, 1976
17. Maddox DE, Wynne J, Vien R, et al: Regional ejection fraction: A quantitative radionuclide index of regional left ventricular performance. *Circulation* 59:1001-1009, 1979
18. Okada RD, Kirshenbaum HD, Kushner F, et al: Observer variance in the qualitative evaluation of left ventricular wall motion and the quantitation of left ventricular ejection fraction using rest and exercise multigated blood pool imaging. *Circulation* 61:128-136, 1980
19. Dodge HT, Sandler H, Ballew DW, et al: The use of biplane angiocardiography for the measurement of left ventricular volume in man. *Am Heart J* 60:762-776, 1960
20. Ralston A: *A First Course in Numerical Analysis*. New York, McGraw Hill, 1965, pp 78-79
21. Slutsky R, Gordon D, Karliner J, et al: Assessment of early ventricular systole by first pass radionuclide angiography: Useful method for detection of left ventricular dysfunction at rest in patients with coronary artery disease. *Am J Cardiol* 44:459-465, 1979
22. Green MV, Ostrow HG, Scott RN, et al: A comparison of simultaneous measurements of systolic function in the baboon by electromagnetic flowmeter and high frame rate ECG-gated blood pool scintigraphy. *Circulation* 60:312-319, 1979
23. Bacharach SL, Green MV, Borer J, et al: Left ventricular peak ejection rate, filling rate and ejection fraction-frame rate requirements at rest and exercise: Concise communication. *J Nucl Med* 20:189-193, 1979