# Left-ventricular Peak Ejection Rate, Filling Rate, and Ejection FractionFrame Rate Requirements at Rest and Exercise: Concise Communication 

Stephen L. Bacharach, Michael V. Green, Jeffrey S. Borer, John E. Hyde, Susan P. Farkas, and Gerald S. Johnston<br>National Institutes of Health, Bethesda, Maryland


#### Abstract

The effect of framing rate on the measurement of left-ventricular (LV) ejection fraction (EF), peak ejection rate (PER), and peak filling rate (PFR) was evaluated at rest and during exercise in 11 normal subjects and 21 patients who underwent gated equilibrium blood-pool imaging. Left-ventricular time-activity curves were obtained in each subject, at rest and during stress, at temporal resolutions of $\mathbf{1 0}, \mathbf{2 0}, \mathbf{3 0}, \mathbf{4 0}$, and 50 msec per frame. Ejection fraction, PER, and PFR were determined for each frame duration. By observing changes in the measured values of these quantities with framing rate we conclude that: a) for the measurement of $E F, 50$ msec per frame at rest and 40 msec per frame at exercise is sufficient; b) PER requires 40 msec per frame at rest and 20 msec per frame during exercise; and c) for the measurement of PFR, at least 40 msec per frame at rest and 20 msec per frame during exercise are needed. These results should hold for both first-pass and gated equilibrium studies.


J Nucl Med 20: 189-193, 1979

Curves of activity over the cardiac left ventricle as a function of time can be generated by either gated equilibrium or first-pass techniques. The information extracted from such curves can be influenced by the sampling rate and sampling period used to collect data-i.e., by the framing rate of the study $(1,2)$. Using the ejection fraction (EF) as the quantity of interest, Hamilton et al. (1) have shown that sampling with relatively coarse temporal resolution ( 40 msec 25 times per second) is sufficient to give only a slight underestimate of EF, even at

[^0]the rapid heart rates achieved during maximal exercise. However, other parameters can be derived from the left-ventricular volume (LVV) curve. The clinical utility of certain of these parameters $(3,4)$ is currently receiving attention in the literature (57). The influence of framing rate on the measurement of these other quantities derived from the LVV curve is unknown. It has been speculated that a framing rate significantly higher than 25 per second may be required for the analysis of certain portions of the LVV curve ( 1,5 ).

The present study was undertaken to determine the effects of framing rate on the measurements of peak ejection rate (PER) and peak filling rate (PFR)-that is, the maximal up and down slopes of the LVV curve, normalized to end-diastolic
counts-and on the measurement of times of occurrence of these quantitites (TPER, TPFR, respectively). In addition we have assessed, with clinical scintigraphic data, the conclusions concerning EF and framing rate reached by Hamilton et al. (1) from contrast cineangiographic data; we suggest a procedure for calculating peak ejection and filling rates; and we present some typical values of PER and PFR at rest and exercise in various disease categories.

## METHODS

There is, unfortunately, no known mathematic expression that adequtely describes all the important features of all LVV curves. The detailed features of such curves vary widely from patient to patient and from one disease group to another. It is therefore necessary to use actual patient data to study how measurement of quantities such as PER and PFR might vary with the framing rate of the study.

The population of individuals studied in the present work consisted of: a) 11 volunteers with normal cardiac function (NV); b) ten patients with coro-nary-artery disease (CAD)-namely, $50 \%$ stenosis in one or more of the major coronary vessels,including two with and nine without wall-motion defects at rest; and c) 11 patients with aortic regurgitation (AR). Equilibrium ECG-gated scintigraphy was performed on each subject, following administration of 10 mCi of Tc -99m-labeled human serum albumin. The details of this procedure and how it is used to produce an LVV curve have been described elsewhere $(8,9)$. The LVV curve had a temporal resolution of 10 msec per point (i.e., of 100 frames per second). Each subject was studied both at rest and at maximal exercise, resulting in a total of 64 volume curves, each with $10-\mathrm{msec}$ temporal resolution. Premature beats were excluded from the study by inspection of the distribution function of the R-R interval length.

An optimum method for calculating PER and PFR would be one that makes no assumptions (or as few as possible) regarding the shape of the LVV curve. The method explored in this study was based on the assumption that, over a narrow range of points near the time of PER amd PFR (Fig. 1), the LVV curve could be described by a third-degree polynomial. Empirically, terms of higher order were usually unnecessary to describe these two limited portions of the volume curve. Lower-order polynomials were found inadequate to fit the data in certain patients. The limited regions of the LVV curve to which the cubic function was fitted were determined iteratively by a minicomputer algorithm. For PER, a preliminary fit was performed


FIG. 1. Idealized plot of left-ventricular volume against time during a cardiac cycle. Region A shows span of points used in systolic polynomial fit, with origin at 1. Region B around origin 2 would be used to obtain diastolic fit.
over all of systole (for PFR, over the smaller of either a) all of diastole or b) the first 400 msec following systole). For PER the time of occurrence of steepest negative slope (or steepest positive slope for PFR) was determined from this preliminary fit. Using these points as the new origins, the algorithm iteratively reduced the span of points to a small number of points (but always greater than four) that gave an inflection point of the proper sign centered within the span. This range of points is illustrated diagramatically in Fig. 1. A least-squares technique (10) was used to fit the data to a thirddegree polynomial. The fit was weighted according to the statistical fluctuations expected for each point. The values for the peak slope and its time of occurrence were determined by setting the second derivative of the resultant polynomial equation equal to zero. Peak ejection rate and TPER (or the corresponding diastolic parameters) are then easily expressed as a closed-form function of the coefficients of the polynomials. Less careful methods attempting to fit the LVV curve may result in a dependence on framing rate that is more strongly influenced by the nature of the approximation used than on the actual shape of the LVV curve. The total minicomputer execution time for the procedure was less than two seconds.

To duplicate the effects of performing a study with decreased temporal resolution, each resting volume curve ( $10 \mathrm{msec} /$ point) was condensed into curves having $20,30,40$, and 50 msec per point by adding consecutive $10-\mathrm{msec}$ counts together. All exercise volume curves were condensed into curves having 20, 30, and 40 msec per point. The following procedure was used to determine end-diastolic (ED) and end-systolic (ES) counts. End-diastolic counts were always a 3-point sum of the first points on the 10 -msec curve, a $1 \frac{1}{2}$ point sum for the $20-\mathrm{msec}$ curve, or simply the first point for curves of coarser resolution. End systole was not chosen as the lowest point on the volume curve, since to choose ES
in this manner would consistently overestimate EF at high framing rates. To minimize this systematic error, the region near the minimum of the LVV curve was fitted to a quadratic function, and the time of occurrence of the minimum of the quadratic was taken as first estimate of the time of occurrence of ES. The actual data point on the original LVV curve closest to this time was then taken as the ES point, and ES counts were calculated as a $20-\mathrm{msec}$ average about this point (for the $10-\mathrm{msec}$ curves), or the single point itself for resolutions coarser than 10 msec . This procedure should reduce the systematic errors associated with the choice of ES. Rather than consistently underestimating ES, this scheme will underestimate and overestimate ES in an approximately random fashion, according to the fluctuations of counting statistics. These fluctuations are included in the error associated with ES (and thus EF). Errors in the polynomial coefficients, combined with the assumed Poisson errors in the end-diastolic counts and background counts, were used to determine the errors in PER and PFR.

Errors in the coefficients of the polynomial were calculated using the Poisson assumption rather than the more usual residuals of the fit. Correlations between relevant coefficients of the third-degree polynomial were made negligible by shifting the origin to the times of PER and PFR, respectively.

## RESULTS AND CONCLUSIONS

Figures 2 and 3 present the principal results of this study. Numerical data descriptive of the patient population are shown in Table 1. The values of EF, PER, and PFR shown are the average values for each group. Each of the figures illustrates how the measured value of EF, PER, or PFR would change if the measurement were performed at coarser framing rates. Since it is the changes in these values


FIG. 2. Ejection fractions at rest and exercise as a function of framing rate for three subject groups. Error bars show $\pm$ 1 s.d., as discussed in text.
with framing rate that are of interest, the error brackets shown in Figs. 2 and 3 are not those associated with the absolute values of EF, PER, or PFR; rather, they are those that could be used to determine the statistical significance of the changes in these values as a function of framing rate. Each error bracket is calculated to be the standard deviation of the difference between the point of interest and its neighbor to the left. The first point is taken to have the same error as the second.

The standard deviations of the differences shown

FIG. 3. Maximum ejection rate and maximum filling rate, at rest and exercise, (in units of end-diastolic volumes per second) as functions of time per frame. Error brackets are $\pm 1$ s.d. as discussed in text. Note differences in ordinate scales.

table 1. average parameters describing each of three groups of subjects studied, at rest AND DURING EXERCISE

|  |  | HR | EF | Peak Ejection Rate | Peak Filling Rate |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Normal | Rest | $\begin{gathered} \hline 65 \\ (6) \end{gathered}$ | $\begin{gathered} 0.61 \\ (0.14) \end{gathered}$ | $\begin{gathered} 2.69 \\ (0.54) \end{gathered}$ | $\begin{gathered} 3.26 \\ (0.90) \end{gathered}$ | 11 |
|  | Exercise | $\begin{aligned} & 141 \\ & (12) \end{aligned}$ | $\begin{gathered} 0.74 \\ (0.20) \end{gathered}$ | $\begin{aligned} & 4.93 \\ & (1.3) \end{aligned}$ | $\begin{aligned} & 8.81 \\ & (2.1) \end{aligned}$ |  |
| CAD | Rest | $\begin{aligned} & \hline 67 \\ & (6) \end{aligned}$ | $\begin{gathered} 0.60 \\ (0.16) \end{gathered}$ | $\begin{aligned} & 2.85 \\ & (.67) \end{aligned}$ | $\begin{gathered} 2.32 \\ (0.87) \end{gathered}$ | 10 |
|  | Exercise | $\begin{aligned} & 105 \\ & (19) \end{aligned}$ | $\begin{gathered} 0.43 \\ (0.10) \end{gathered}$ | $\begin{gathered} 2.40 \\ (0.90) \end{gathered}$ | $\begin{gathered} 3.67 \\ (1.30) \end{gathered}$ |  |
| AR | Rest | $\begin{aligned} & \hline 79 \\ & \text { (9) } \end{aligned}$ | $\begin{gathered} 0.60 \\ (0.12) \end{gathered}$ | $\begin{gathered} 3.02 \\ (0.48) \end{gathered}$ | $\begin{aligned} & \hline(3.08 \\ & (1.10) \end{aligned}$ | 11 |
|  | Exercise | $\begin{aligned} & 134 \\ & (18) \end{aligned}$ | $\begin{gathered} 0.58 \\ (0.15) \end{gathered}$ | $\begin{aligned} & 3.76 \\ & (1.2) \end{aligned}$ | $\begin{aligned} & 5.96 \\ & (1.8) \end{aligned}$ |  |

$H R=$ heart rate, $E F=$ ejection fraction. Units for ejection and filling rates are end-diastolic volumes per second. Numbers shown in parentheses are standard deviations of distribution about population mean. They are not errors in calculating these quantities for any one patient, but rather, fluctuations in values from one patient to the next.
in Figs. 2 and 3 were calculated in two ways. First, they were calculated in the usual way, considering only the errors of the polynomial coefficients, in the ED counts (and ES counts for EF), and in the background counts. Second, the errors were computed by observing the fluctuations of the differences in individual patients from the mean difference. In order to be conservative, the larger of these two calculated standard deviations was used in Figs. 2 and 3. The magnitude of these standard deviations does not differ much as a function of framing rate, since better statistics at coarser frame rates are offset by fewer points with which to perform the polynomial fit. In the discussion that follows, therefore, two values whose error brackets do not overlap are considered to be significantly different from each other (at $95 \%$ confidence level), whereas "no change" will signify a change of less than 2 s.d.

Several important conclusions can be drawn from Figs. 2 and 3. Examining Fig. 2, we see that EF does not vary significantly in any of the groups for times per frame up to 50 msec at rest and 40 msec under exercise. This agrees with the data of Hamilton et al. (1). The PER, when measured at rest, was unchanged up to 50 msec per frame in the CAD and AR groups, but remained unchanged up to only 40 msec per frame in the normal group. The PFR measured at rest was unchanged up to 50 msec for CAD and AR, but remained unchanged in the normal group up to only 40 msec . This seems consistent with the higher absolute values of PER and

PFR in the normal group, presumably due to the greater high-frequency content in the curves.

At rest, then, a framing rate of 40 msec per frame would be adequte for measurement of EF, PER, and PFR, providing changes less than those indicated by the error brackets are not critical to the experimenter. During exercise, measurement of PER seems to require 20 msec per frame, since values for the normal group of subjects dropped significantly beyond that framing interval. The indicated peak filling rates measured during exercise dropped significantly from 10 to 30 msec , especially for the high filling rates encountered in the normal group. For these subjects then, at least 50 frames per second are necessary for accurate measurement of PFR.

The average behavior of the groups shown in Figs. 2 and 3 cannot, of course, be used to predict the behavior of a single individual drawn from the group. Framing rates that may be adequate, on averages, could be inadequate for certain individuals making up the population. However, in the AR and CAD groups, no individual's behavior deviated significantly from the average behavior shown in Figs. 2 and 3. In the group of normal subjects, one of the 11 had an exercise PFR that fell significantly faster than that shown in Fig. 3. The remaining individuals did not exhibit behavior significantly different from that presented in Figs. 2 and 3.

The absolute values of PER and PFR obtained from the fitting technique (Table 1) agreed excellently with those obtained by Hammermeister et al.
$(3,4)$ (using contrast cineangiography) for both the normal and the CAD groups. The AR group was not directly comparable, due to a different patient population.

The variation of the measured value of TPER and TPFR as a function of framing rate was also studied. No significant deviations in the measured values of TPER and TPFR were found for times per frame of from 10 msec to 50 msec at rest and of from 10 to 40 msec under exercise. The standard deviations of the differences were, averaged over all patients, $\pm 15 \mathrm{msec}$ for TPER or TPEF at rest, and $\pm 22 \mathrm{msec}$ under exercise. If changes in TPER or TPFR by the above amounts are not important to the experimenter, 50 msec per frame at rest and 40 msec per frame under exercise are sufficient.

In summary, we conclude that with the methods of calculation described above, and within the error brackets shown, the following frame rates are sufficient: 50 msec per frame at rest and 40 msec per frame during exercise are adequte for measurement of EF alone; 40 msec per frame is required to measure PER at rest and 20 msec per frame is necessary during exercise; and 40 msec per frame is required to measure PFR at rest and 20 msec or less during exercise. These conclusions should be applicable to both first-pass and gated equilibrium studies.

## ACKNOWLEDGMENTS

The authors thank Bonnie Mack for aiding with the patient acquisition and Luella Benz for typing the manuscript.

## REFERENCES

1. Hamilton GW, Williams DL, Caldwell JH: Frame rate requirements for recording time-activity curves by radionuclide angiocardiography. In Nuclear Cardiology: Selected Computer Aspects, New York, Society of Nuclear Medicine, 1978, pp 75-83
2. Bowyer KW, Konstantinow G, Rerych SK, et al: Optimum counting intervals in radionuclide cardiac studies. In Nuclear Cardiology: Selected Computer Aspects, New York, Society of Nuclear Medicine, 1978, pp 85-95
3. Hammermeister KE, Brooks RC, Warbasse JR: The rate of change of left ventricular volume in man. I. Validation and peak systolic ejection rate in health and disease. Circulation 49: 729-738, 1974
4. Hammermeister KE, Warbasse JR: The rate of change of left ventricular volume in man. II. Diastolic events in health and disease. Circulation 49: 739-747, 1974
5. Wagner HN: The use of the nuclear stethoscope for temporal imaging of left ventricular function. In Nuclear Cardiology: Selected Computer Aspects, New York, Society of Nuclear Medicine, 1978, pp 45-54
6. Bianco JA, Makey DG, Shafer RB: Application of radionuclide left ventricular systolic ejection rate (dV/dt). J Nucl Med 19: 726, 1978 (abst)
7. Marshall RC, Berger HJ, Costin JC, et al: Assessment of cardiac performance with quantitative radionuclide angiocardiography. Sequential left ventricular ejection fraction, normalized left ventricular ejection rate, and regional wall motion. Circulation 56: 820-829
8. Bacharach SL, Green MV, Borer JS, et al: A real-time system for multiimage gated cardiac studies. J Nucl Med 18: 79-84, 1977
9. Green MV, Brady WR, Douglas MA, et al: Ejection fraction by count rate from gated images. J Nucl Med 19: 880-883, 1978
10. Bevington PR: Data Reduction and Error Analysis for the Physical Sciences. New York, McGraw Hill, 1969, pp 172 175

## PACIFIC NORTHWEST CHAPTER ANNUAL SPRING MEETING

## April 27-28, 1979

Salishan Lodge
Glenedon, Oregon
The Pacific Northwest Chapter of the Society of Nuclear Medicine will hold its Annual Spring Meeting on April 27-28, 1979, at Salishan Lodge, Glenedon, Oregon.
The program will consist of 1) a tutorial on approaches to nuclear cardiology: pathophysiology techniques, interpretation, and clinical utility of current procedures-Chairman: Dr. Glen Hamilton; 2) a panel discussion with representatives of the major nuclear medicine computer companies-Chairman: Dr. Hamilton; and 3) a clinical refresher course on pediatric nuclear medicine: handling of the pediatric patient, sedation, restraint, special problems and interesting cases, conducted by Drs. Gary Gates and Thomas Rudd.

For further information contact:

Justine Parker<br>P.O. Box 40279<br>San Francisco, Ca 94140<br>(415) 647-0722


[^0]:    Received Aug. 15, 1978; revision accepted Nov. 9, 1978.
    For reprints contact: Stephen L. Bacharach, Nuclear Medicine Dept., CC, Building 10, Rm 1B48, National Institutes of Health, Bethesda, MD 20014.

