Measurement of Ventricular Function by ECG Gating during Atrial Fibrillation

Stephen L. Bacharach, Michael V. Green, Robert O. Bonow, Sharon L. Findley, Harold G. Ostrow, and Gerald S. Johnston

National Institutes of Health, Bethesda, Maryland

The assumptions necessary to perform ECG-gated cardiac studies are seemingly not valid for patients in atrial fibrillation (AF). To evaluate the effect of AF on equilibrium gated scintigraphy, beat-by-beat measurements of left-ventricular function were made on seven subjects in AF (mean heart rate 64 bpm), using a high-efficiency nonimaging detector. The parameters evaluated were ejection fraction (EF), time to end-systole (TES), peak rates of ejection and filling (PER,PFR), and their times of occurrence (TPER,TPFR). By averaging together single-beat values of EF, PER, etc., it was possible to determine the true mean values of these parameters. The single-beat mean values were compared with the corresponding parameters calculated from one ECG-gated time-activity curve (TAC) obtained by superimposing all the single-beat TACs irrespective of their length. For this population with slow heart rates, we find that the values for EF, etc., produced from ECG-gated time-activity curves, are very similar to those obtained from the single-beat data. Thus use of ECG gating at low heart rates may allow reliable estimation of average cardiac function even in subjects with AF.

J Nucl Med 22: 226–231, 1981

Atrial fibrillation (AF) causes wide variations in cardiac cycle length, and consequently in some parameters describing left-ventricular function (*1–4*). It has long been known that subjects in AF possess end-diastolic volumes (EDV), end-systolic volumes (ESV), and ejection fractions (EF) that vary greatly from cycle to cycle as a function of the length of the preceding cycle. Cycles preceded by cycles of long duration have large EDVs and large EFs, and conversely for cycles preceded by cycles of short length. The mechanisms underlying these observations are fairly well understood and are primarily related to the increased or decreased time available for filling when a cycle is preceded by a long or short cycle.

Many institutions have avoided applying the techniques of equilibrium ECG gating to subjects in AF. The basic assumptions upon which ECG gating is based are presumably violated by the wide fluctuations in cycle length exhibited by subjects in AF. The purpose of this study is to investigate how AF affects the measurement of left-ventricular (LV) function by gated equilibrium scintigraphy.

Received Aug. 4, 1980; revision accepted Oct. 31, 1980.

For reprints contact: Stephen L. Bacharach, PhD, National Institutes of Health, Dept. of Nuclear Medicine, Bldg. 10, Rm. 1B48, Bethesda, MD 20205.

METHODS

Seven subjects in AF were studied. They had a variety of cardiac diseases: four mitral-valve disease, one coronary-artery disease, one aortic regurgitation, one asymmetric septal hypertrophy. The mean heart rate was 64 bpm. Five subjects were receiving digoxin, one quinidine, and one no medication. An ECG-gated equilibrium cardiac study, in modified LAO orientation, was performed on each subject at rest, using a procedure described elsewhere (*5–7*). At the conclusion of this study, with the gamma camera still in place, a lead annulus (7.6 cm i.d.) was positioned over the LV. The visual information provided by the computerized gamma camera was used to exclude the atria and right ventricle from the inner circle formed by the annulus. When the

annulus was properly located over the LV, its position was traced on the subject's chest with a pen. The gamma camera was then raised, and a nonimaging, single-crystal detector, with a very-high-efficiency, parallel-hole collimator (7.6 cm diameter) was placed over the LV (mLAO). The correct placement of this device was assured because the collimator face of the nonimaging detector was made to coincide exactly with the pen markings on the subject's chest.

The nonimaging detector recorded from the LV a count rate that was typically in excess of 10^5 events/sec. Fast electronics minimized deadtime corrections. Such high count rates were essential in order to construct statistically reliable time-activity curves (TACs), with 10-msec resolution, for each of the 600 single beats that comprised a study. The data for each subject, then, consisted of 600 single-beat TACs, and a gated gamma-camera equilibrium study.

Background correction. For each subject a histogram was constructed showing number of beats for each beat duration (R wave to R wave); this resulted in the very wide histogram typical of AF. For the sole purpose of determining a proper single-beat background, the gated gamma-camera data were analyzed, using only beats whose lengths lay in the middle third of the R-R histogram, regardless of the length of the previous beat. An EF was calculated from the gated camera data of each subject. The camera EF was determined using a single fixed region of interest. For background a crescent-shaped ring was used, approximately ¾ cm removed from the ED profile, along the LV free wall. A single value of background was used to correct each of the single-beat TACs for a given subject. This background value was calculated by first adding together all those single-beat TACs whose lengths lay in the same beat-length range (the middle third of the R-to-R distribution) as was used for the gamma-camera study (regardless of the length of the preceding beat). The resulting summed single-beat TAC was then compared with the gamma-camera TAC. A background value for the summed single-beat TAC was chosen so as to give an EF identical to that obtained from the camera's TAC. This background value was then applied separately to each of the 600 single-beat TACs obtained from the subject under study.

Parameters of ventricular function. The value of each of the eight parameters used to described LV function—EDV, ESV, EF, time to end-systole (TES), peak ejection rate (PER), peak filling rate (PFR), and the times of occurrence of the latter two quantities (TPER, TPFR)—were calculated separately for each of the 600 TACs from each subject. The variance in each of these parameters due to counting statistics was also calculated for every single-beat TAC. A single-beat average for each parameter in a given subject was calculated by computing the weighted mean of that parameter over all 600 single-beat values. The weighting factor used was the reciprocal of the variance. Thus:

$$\langle P\rangle_s = \frac{\Sigma \frac{P_i}{\sigma_i^2}}{\Sigma \frac{1}{\sigma_i^2}}$$

where: $\langle P\rangle_s$ = single-beat mean of parameter P, P_i = value of parameter P for i^{th} beat, σ_i^2 = variance (computed from counting statistics alone) of parameter P_i. In the discussion that follows $\langle P\rangle_s$ will be referred to simply as the single-beat value of parameter P. This value represents the true mean value of a parameter.

One ECG-gated TAC was created for each subject by adding together all the single-beat TACs, irrespective of beat length. Each of the eight parameters of LV function mentioned above was calculated from this single, gated TAC. Henceforth the value of a parameter so calculated will be referred to simply as the gated value. Parameters calculated from this gated TAC represent the true means of those parameters only if each TAC making up the gated TAC is identical in shape and timing.

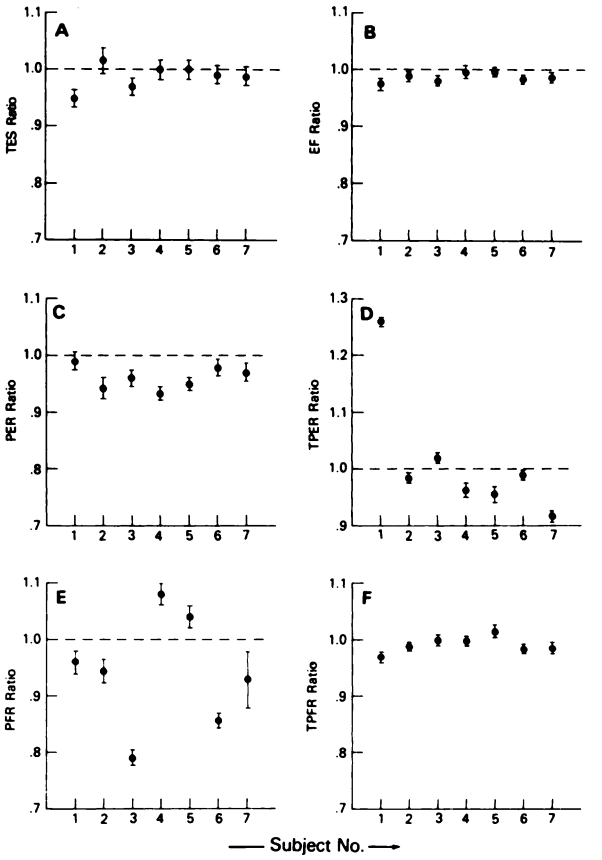

FIG. 1. Ratio of ECG-gated value to single-beat value for various parameters of ventricular function in each of seven subjects. Dashed line indicates unity ratio — gated value equaling true (single-beat) value of a parameter. Error bars indicate one s.d. as determined from counting statistics.

TABLE 1. ABSOLUTE VALUES OF VARIOUS PARAMETERS DESCRIBING VENTRICULAR FUNCTION AS CALCULATED FROM AN ECG-GATED TAC OR FROM AN AVERAGE OF ALL THE SINGLE BEAT TACs COMPRISING A STUDY*

	ES	TES	EF	PER	TPER	PFR	TPFR
Single beat value	1203	361.5	0.43	2.07	185	1.93	495
Gated value	1206	365.0	0.42	1.98	187	1.86	491
Random counting deviations	20	8.3	0.05	0.56	91	0.87	68
Observed deviations	32	24.0	0.07	0.64	51	1.11	43

* ES is the relative end systolic volume counts. The timing quantities TES, TPER, and TPFR are all in msec. PER and PFR are in end-diastolic volumes per second.

RESULTS

The ratio of the gated value of a parameter to its single-beat value is shown in Fig. 1 for each subject. This ratio provides a relative indication as to how accurately the parameter's gated value reproduces the true mean for that parameter as determined from the single-beat measurements. The error bars shown represent one standard deviation calculated from random counting errors alone. The error bars do not reflect the observed beat-to-beat fluctuations. The average absolute values of each parameter are given in Table 1. The first row of this table shows the single-beat value of each parameter, averaged over all the subjects studied. The gated value of each parameter, averaged over all subjects, is listed in the second row. The third row contains the standard deviation of each parameter (averaged over all subjects) based on counting statistics alone. In the fourth row are the observed fluctuations of the single-beat values about the mean (averaged over all subjects), expressed as one standard deviation. Comparison of Row 4 with Row 3 will indicate (with two exceptions) the increased parameter variability due to beat-to-beat fluctuations, over the inherent variability resulting from random counting errors.

Figure 2 illustrates the dependence of each parameter on the length of the previous beat, for one typical subject. To produce this figure, all the single-beat parameters obtained from TACs preceded by a beat of a specified length (± 50 msec) were averaged together.

DISCUSSION

The agreement between gated and single-beat parameters shown in Fig. 1 was unexpected. It was presumed that the extremely wide fluctuations in beat length would cause the gated TACs to be grossly distorted, resulting in a similar distortion in the parameter values derived from the gated TACs. This latter distortion did not occur. Instead, Figs. 1A and B show only a 3% maximum underestimate in gated EF, and a 5% underestimate in gated time to systole. The gated against single-beat differences were larger for parameters of maximum filling and emptying. Even here, however, the disagreement was not much more than might be expected from subjects not in AF (*8*). The times to peak ejection varied from at most 27% too high to 9% too low, whereas the values of peak ejection rate were at most 6% underestimated. Similarly, the filling parameters from the gated TACs (Figs. 1E and F) were as much as 21% low (PFR) or 4% low (TPFR). Again, this is not more than might be obtained from subjects not in AF.

Figure 2 allows the reader some insight into why atrial fibrillation does not cause a more drastic alteration in the gated parameters of LV function. The relationships between relative volumes (ES and ED) and the length of the preceding beat, shown in Figs. 2A and B, were as expected. Similar data have been reported by others, using invasive techniques and grouping together data from many subjects (*1-4*). With the beat-by-beat radionuclide technique, these data are produced from a single subject. For the typical subject (No. 6) shown in Fig. 2, the EDV first increases rapidly, then flattens, as a function of previous beat length. This is as expected, and mirrors the shape of the LV volume curve in late diastole. The rapidly rising portion of Fig. 2A is due to beats terminated during the latter part of active filling. The nearly flat portion occurs when the preceding beat is terminated during diastasis. Only minor changes in ESV are observed with preceding beat length (Fig. 2B), with ESV dropping slightly for long preceding beat lengths (and thus large EDVs), as might be predicted from Starling's law.

The behavior of EF, shown in Fig. 2C, reflects the change in EDV as a function of preceding beat length. With such a strong dependence on preceding beat length (the EF more than doubles) why does gating still work? The answer lies in Fig. 2D. Time to end-systole increases measurably as a function of preceding beat length. This would tend to reduce the gated EF, since curves are added together whose minima occur at different locations. Ignoring the 550-msec point of Fig. 2D (there was only a single beat as short as 550 msec for this subject), TES varied by about 50 msec. It has been shown previously (*9,10*) that sampling frequencies (i.e., framing

rates) as coarse as 50 msec will cause no significant reduction in EF. More directly, Brash et al. (*11*) have simulated LV volume curves with sinusoidal functions. When they gated (i.e., added together) curves with varying lengths (and similarly varying TESs), they found that a 7–10% coefficient of variation in cycle length reduced EF by only 2–2.5%. This simulation is in accord with the data of Figs. 1B and 2D. As shown in Table 1, the observed deviations in TES about the mean were 24 msec out of 360 msec, or about a 7% coefficient of variation.

No similar simulation data exist for the ejection or filling-rate parameters. However, it seems reasonable to hypothesize that again it is the fluctuation in timing of PER and PFR that will cause underestimation of those quantities, rather than fluctuations in the quantities themselves. Figure 2F illustrates the typical variation of TPER with length of preceding beat. The first point (at 550 msec) is omitted because its error is as large as the ordinate axis shown. The remaining data are suggestive of a decline in TPER as preceding beat length increases; that is, earlier emptying for larger EDVs and larger EFs. The maximum change in TPER was small—only 35 msec for this subject. On average, the seven subjects in Table 1 exhibited a deviation of 50 msec about the mean TPER. Some portion of this 50-msec deviation was due simply to random error, the remaining portion was due to true deviations in function. The observed 50-msec deviation was less than would be expected solely on the basis of counting errors (90 msec), because occasionally the filling portion of the curve was nearly linear, causing a great statistical uncertainty in

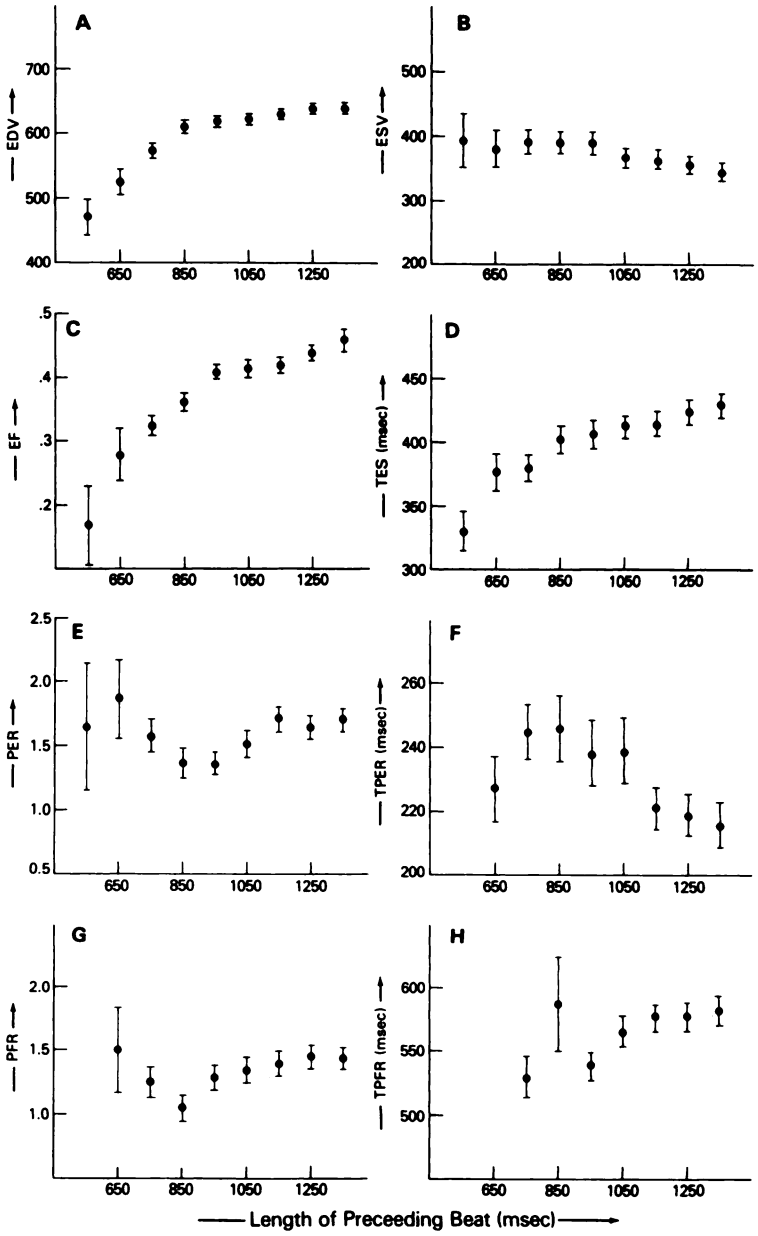

FIG. 2. Parameters of LV performance in a typical subject, as a function of length of preceding cardiac cycle. EDV and ESV are in units of relative counts. PER and PFR are in units of end-diastolic volumes/sec. Error bars indicate one s.d. as determined from counting statistics.

the time of occurrence of the peak slope. In these cases, however, the computer algorithm for finding TPER did not randomly select a time, but rather used a fixed procedure, thereby reducing the observed deviations.

It is expected that fluctuations in TPER would reduce PER in a gated study. It is not known what the magnitude of this reduction might be. From the EF data of Table 1, it was seen that a 24-msec fluctuation in TES produced only a 2.5% reduction in EF. This was presumably because of the relatively broad minimum of the LV volume curve. A plot of ejection rate against time (i.e., the first derivative of the LV TAC) would exhibit a shape similar to the bottom of the LV curve itself. One might, however, expect the ejection-rate curve to be sharper at its (negative) minimum. If so, fluctuations in TPER would have a more pronounced effect on PER than those in TES had on EF. The observed 5% reduction in PER (Table 1) is indeed a greater reduction. Due to the high random fluctuations in TPER (91 msec average from Table 1), it is unclear how large the true fluctuations (due to AF) in TPER were. They may have been considerably less than the 51-msec value listed in Table 1.

The gated values of PFR are also close (about 4% on the average) to the single-beat values, but individual subjects were underestimated by as much as 21%. Two factors must be considered in trying to understand how AF affects PFR. First, the observed fluctuations in time (TPFR) are slightly smaller than for TPER (Table 1). From Fig. 2H, TPFR increases with increasing previous beat length. Note, however, that TPFR is measured from the R wave, not from TES. By inspection of Fig. 2D, it is seen that all the increase in TPFR is due to an increase in TES. Secondly, AF affects a given cardiac cycle in two additional ways: by influencing EDV through the length of the preceding cycle, and by shortening or prolonging the current cycle. The changes in EDV should have their major physiologic effect during systole; filling should not be affected as much, since ESV and the timing of the current cycle remain nearly unchanged. The shortening or lengthening of the current cycle, on the other hand, should not produce any physiologic effect on that particular cycle, since the myocardium does not "know" in advance whether the current cycle will be terminated prematurely or allowed to continue. Thus the length of a cardiac cycle in itself, should not influence systolic or diastolic behavior during that cycle. Obviously, a beat terminated during filling (or emptying) will not completely fill (or empty). Before termination, however, the contraction and relaxation (if any) will proceed normally. Furthermore, if a cycle is terminated before TPFR, there will be a distortion of the gated results when the TAC from that cycle is added to those of all the other cycles. In the present study, less than 2% of all the subjects' cardiac cycles were shorter than their respective mean single-beat TPFR, and no single subject had more than 3% of his cycles shorter than TPFR for that subject. The mean TPFR for all subjects was 495 msec, compared with the mean R-R interval of 940 msec. At R-R intervals of this length, most of the variations in cycle length occur during the diastasis period, accounting for the good agreement between the gated and single-beat calculations. The R-R interval of the subjects studied is, however, quite representative of that found in AF patients whose rates are being controlled by the usual medications. At higher heart rates, and with equally wide fluctuations of cycle length, the gated measurements of diastolic events may deviate considerably from the true mean as determined from the single-beat measurements. Further work is necessary to determine whether this is so.

CONCLUSION

These data suggest that at low heart rates, only a small underestimate is made by using gated equilibrium techniques to measure average values of EF, PER, etc. in subjects with AF. This surprising conclusion is due in part to the fortuitous way in which the timing of the cardiac cycle varies with preceding beat length. Further studies are necessary to determine the validity of this conclusion at high heart rates.

It must be emphasized that although ECG gating seems to allow estimation of the true average cardiac behavior, it is unknown whether this average behavior is diagnostically significant in subjects in AF. It is possible that more detailed single-beat data are needed (e.g., Fig. 2) to evaluate patients in AF.

ACKNOWLEDGMENTS

The authors thank Barbara Damske for her assistance in performing the patient studies and in analyzing the data. Thanks are also due Sue Harshman and Carole Rodill for preparing the final manuscript.

REFERENCES

1. McINTOSH HDD, MORRIS JJ: The hemodynamic consequences of arrhythmias. *Prog Cardiovasc Dis* 8: 330-363, 1966
2. GREENFIELD JC, HARLEY A, THOMPSON HK, et al: Pressure-flow studies in man during atrial fibrillation. *J Clin Invest* 47: 2411-2421, 1968
3. BRAUNWALD E, FRYE RL, AYGEN MM, et al: Studies on Starling's law of the heart. III. Observations in patients with mitral stenosis and atrial fibrillation on the relationships between left ventricular end-diastolic segment length, filling pressure and the characteristics of ventricular contraction. *J Clin Invest* 39: 1874-1884, 1960
4. KARLINER JS, GAULT JH, BOUCHARD RJ, et al: Factors influencing the ejection fraction and the mean fate of circumferential fiber shortening during atrial fibrillation in man. *Cardiovasc Res* 8: 18-25, 1974
5. BORER JS, BACHARACH SL, GREEN MV, et al: Real-time radionuclide cineangiography in the noninvasive evaluation of global and regional left ventricular function at rest and

during exercise in patients with coronary-artery disease. *N Engl J Med* 296: 839-844, 1977
6. BACHARACH SL, GREEN MV, BORER JS, et al: A computer system for clinical nuclear cardiology. In *Proceedings: Computer Applications in Medical Care.* Washington, DC IEEE Computer Society, 1978, Cat. No. 78CH1413-4, Long Beach, CA, pp 50-55
7. DOUGLAS MA, OSTROW HG, GREEN MV, et al: A computer processing system for ECG-gated radioisotope angiography of the human heart. *Comput Biomed Res* 9: 133-142, 1976
8. BACHARACH SL, GREEN MV, BORER JS, et al: Beat-by-beat validation of ECG gating. *J Nucl Med* 21: 307-313, 1980
9. HAMILTON GW, WILLIAMS DL: 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 75-84
10. BACHARACH SL, GREEN MV, BORER JS, et al: Left-ventricular peak ejection rate, filling rate and ejection fraction-frame rate requirements at rest and exercise: Concise communication. *J Nuc Med* 20: 189-193, 1979
11. BRASH HM, WRAITH PK, HANNAN WJ, et al: The influence of ectopic heart beats in gated ventricular blood-pool studies. *J Nuc Med* 21: 391-393, 1980