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Beat-by-Beat Validation of ECG Gating

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Ejection fraction, normalized peak ejection and filling rates, and the time of occurrence of these events relative to the R-wave were determined in each of 512 consecutive individual cardiac cycles in each of 30 patients using an ultra-high-efficiency nonimaging detector system. For a given patient the 512 measurements of each quantity were averaged and compared with the value of this same quantity as determined from an R-wave-gated left-ventricular (LV) time-activity curve (TAC) derived from the same 512 cycles. We conclude (a) that a small but detectable systematic underestimate occurs in some LV function parameters when they are derived from gated LV TACs; (b) that the magnitude of this underestimate is smaller and less variable for systolic than for diastolic measurements; (c) that the magnitude of the underestimate is not greater than 20% in any single patient for diastolic parameters, nor greater than 8% in any individual patient for systolic parameters, and is substantially less for most patients; and (d) that a small subset of patients may require beat-length windowing if the gated values of diastolic parameters are to fall within these limits. Thus LV function measurements obtained from gated TACs adequately reflect the true average of such values during the measurement interval.

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The method of additive superimposition, in the form of ECG gating, is a common technique in nuclear cardiology (*1–4*). In gated equilibrium blood-pool imaging or gated first-transit methods, data from a number of cardiac cycles are added to provide a single, "average", cardiac cycle. A time-activity curve (TAC) is constructed from this average by suitable definition of a region of interest (e.g., the left ventricle, LV). Parameters such as ejection fraction (EF), peak ejection rate (PER), etc., are then calculated from this cumulative TAC. It is assumed that the values calculated from this cumulative curve are the "mean" or "average" of such quantities for the cardiac cycles studied. This assumption is false. It is false because, striotly speaking, one must compute the mean of a parameter, such as EF, by first calculating the parameter separately from each single cardiac cycle studied. The mean value of the parameter is then calculated from the collection of its single-beat values. This will, in general, give a result different from that obtained by calculating EF, PER, etc., from a cumulative TAC, unless each single-beat TAC is identical in functional form and frequency to every other. Thus parameters calculated from a cumulative gated TAC will at best approximate the means calculated by the correct (but impractical) single-beat method.

It is the purpose of this study to determine the magnitude of the error made by using ECG gating techniques, rather than the correct single-beat averaging procedure. To this end, a very high-efficiency detector was built to allow statistically reliable, single-beat TACs to be created at high temporal resolution. Thirty subjects were studied with this device. From each subject, 512 or more consecutive single-beat TACs were obtained. Each

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of these was analyzed to determine, for each subject, 512 values of EF, PER, and peak filling rate (PFR), time to end-systole (TES), and the times to PER (TPER) and to PFR (TPFR). The means for each quantity could then be calculated in the correct single-beat manner and be compared with the results obtained from a cumulative, gated TAC derived from the same data.

METHODS

Instrumentation. It was necessary to create a statistically reliable left-ventricular TAC, with 10-msec temporal resolution, from a single cardiac cycle. To this end a nonimaging NaI detector 3 in. in diameter was used, together with a very high-efficiency parallel-hole collimator. The collimator was constructed from tantalum tubes, 13 mm long and 4 mm inner diameter. This collimator resulted in a (centered) point-source efficiency that was flat as a function of distance from the collimator up to 12 cm from the collimator face. The effects of deadtime were minimized by using fast shaping amplifiers and electronics for fast pulse-height analysis. The resulting systems deadtime was less than 600 nsec, as evaluated using a nonparalyzable model. The energy window accepted ~ 105–155 keV photons. Ten to 20 mCi Tc-99m-labeled red blood cells (in vivo, PPi) were administered to each subject. The tracer was permitted to equilibrate before measurements were started. Typical count rates ranged from ~60,000–120,000 cps when the detector and collimator were positioned over the LV. Discrete counts from the detector were stored by a minicomputer for real-time creation of the sequence of consecutive single-beat TACs.

After tracer equilibration, ECG-gated imaging (5) was first performed with a gamma camera (MLAO 35° left anterior oblique, 15° caudad modification) in order to locate the LV unambiguously for subsequent positioning of the nonimaging detector. The latter was then placed over the subject's left ventricle, and remained in place for at least 512 consecutive beats. For each subject studied, 512 consecutive TACs (one for each cardiac cycle) were created and stored on a magnetic disc. Each TAC began at the R-to-S transition of the ECG signal, and each had a resolution of 10 msec per point. These 512 TACs comprised the data set for each subject.

Positioning. It has previously been shown (6) that the shape and relative timing of left-ventricular TACs created with nonimaging detectors is not strongly dependent on exact detector positioning over the LV. We desired, however, to eliminate all ambiguity in the positioning of the probe over the left ventricle. To accomplish this, the subject was first placed under a gamma camera in the MLAO orientation noted above. A short gated image sequence was collected and displayed in cine mode. Based on the observed left-ventricular size, a lead annulus of either 6.35 cm or 7.62 cm i.d. was selected, and placed on the subject's chest. The annulus, using the same angulation as the gamma camera, was adjusted until the LV was isolated within it, as determined visually from a new gated scintigram taken with the annulus in place. After several attempts with each subject, we always succeeded in isolating the left ventricle from other cardiac structures and from extraneous high-activity regions (e.g., liver, spleen). Once the proper annulus size and position had been determined, its location was marked on the subject's chest, and the same annulus was used to restrict the single detector to either a 6.35 cm or a 7.62 cm field of view. The detector was then placed (at the same fixed angulation used for the camera) over the region of interest marked on the patient's chest. Since gated camera images were acquired with the annulus in place, the exact positioning of the probe could be visually verified. Of course the poor resolution of the parallel-hole collimator on the probe could cause inclusion of some extraventricular counts at the LV edges.

This use of the camera to position the detector over the LV was largely precautionary. The calculations performed with the detector data, as described below, are themselves insensitive to small errors in detector positioning.

Subject population. Each of 30 subjects was studied during supine rest. Before data collection, sufficient time was allowed to permit stabilization of each subject's heart rate. The subject population was selected at random from the hospital's cardiology admission; it consisted of nine patients with angiographically documented coronary artery disease, ten with aortic regurgitation, five with normal cardiac function, three with asymmetric septal hypertrophy, one patient undergoing adriamycin therapy, one with mitral regurgitation, and one postoperative patient with a coronary artery bypass graft. The heart rates of the subjects ranged from 56–105 bpm. The beat-length histograms (number of beats against beat length) for each subject contained a main, central peak and, occasionally, isolated ectopic beats or small secondary peaks. The full width at half maximum (FWHM) of the primary peaks ranged from 20–110 msec. Ectopic beats and secondary peaks, if present, were eliminated from the study.

Data analysis. With the detector positioned over the LV, data were collected for a minimum of 512 consecutive cardiac cycles. A separate time-activity curve (10 msec temporal resolution) was constructed for each of the cardiac cycles and written to disk. The first point of each single-beat TAC began at the first 10-msec time marker (using a real-time clock not synchronized with the ECG) after the R wave (peak slope of R-to-S transition). The last point of each TAC consisted of the data occuring during the last full 10-msec time interval before the subsequent R wave.

Background was subtracted from each TAC. The detector was not used to measure background; instead,

the value to be used was calculated from the background obtained with the gamma camera (*7*). The gated TAC background was taken such that EF from the gated-detector TAC was identical to EF as calculated from the gated camera. Background for each single-beat TAC was this same gated-TAC value divided by the total number of beats. The background (corrected for physical decay) was assumed to be constant for every one of the 512 cardiac cycles during the 5–10 min of data accumulation. Background was assumed to be error-free. These latter two assumptions can be made because the results (comparisons of single beat to cumulative data) are nearly independent of background. Background correction was employed primarily to allow comparisons of the results with the usual absolute values of EF, PER, etc.

Each of the 512 single-beat TACs for each patient was separately analyzed for end-diastolic counts, end systolic counts, EF, PER, PFR, TES, TPER, and TPFR. Random errors in each of these quantities were also computed, using techniques described in detail elsewhere (*8*). Basically, PER, PFR, and their associated times were calculated using a third-order polynomical fit to two small regions of the TAC near the points of maximum slope. EF and TES used a quadratic fit to the narrow region of the TAC near end-systole. For each subject this analysis produced 12 512-word arrays: six 512-word arrays of results (EF, etc.) and six arrays of the corresponding errors in these quantities. Figure 1 illustrates the procedure. Figure 1A shows the first four of the 512 consecutive single-beat TACs acquired from a typical subject. Figures 1C, D, E, and F show the 512 values of TES, EF, PER, and PFR, obtained from each of the 512 cycles of a typical study. The arrays in which the random errors of each of the values are stored are not shown. Each of the curves in Figs. 1C–F has been normalized to approximately the same height so that the reader may judge the relative fluctuations.

For each subject the mean value of each parameter calculated (EF, PER, etc.) was computed from the 512 single-beat values by weighting each single-beat value with the reciprocal of its normalized variance and summing over all beats. Hereafter, these means will be referred to as the "single-beat" values of EF, PER, etc.

The cumulative, gated TAC (Fig. 1B) was created by adding together all the single-beat TACs in the usual manner: R-wave alignment, pointwise addition. For comparison purposes, a second gated cumulative TAC was also created by a technique known as "reverse framing" (aligning each curve's end point before summing) to create the late-diastolic portion of the cumulative gated TAC (*5*). Because all studies were carried out at rest, the reverse framing was found unnecessary for calculation of any of the previously mentioned parameters. For each subject, a single value of EF, PER,

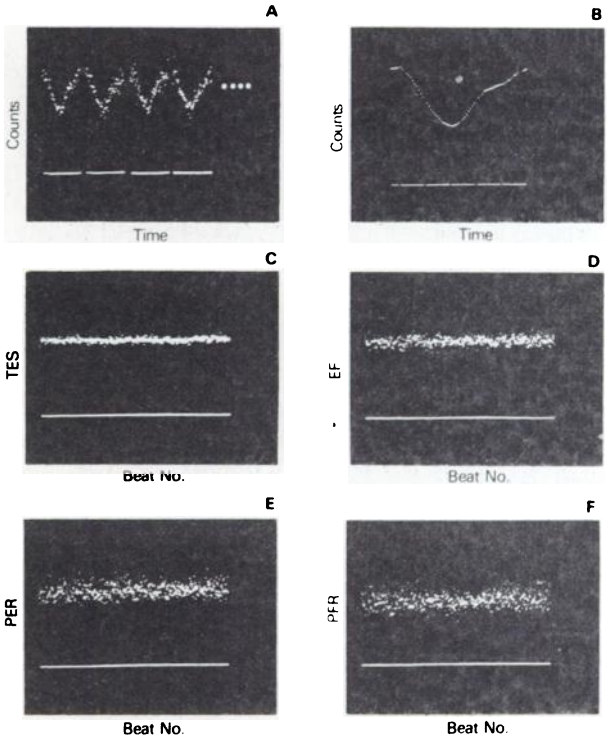

FIG. 1. (A) First four consecutive TACs from typical subject. (B) Gated TAC of typical subject. Note good statistics for each point due to high count rate achieved. (C–F) 512 values of TES, EF, PER, and PFR as functions of beat number, for typical subject.

PFR, TES, TPER, and TPFR was calculated from the gated, cumulative TAC. The identical background subtraction method was applied to the cumulative TAC and to the single-beat TACs. The method of calculating each parameter from the cumulative TAC was identical to that used for each single-beat TAC. Hereafter the value of EF, etc. calculated from the cumulative gated TAC will be referred to as the "gated" EF, etc.

We wished to compare single-beat parameters with the equivalent gated parameters, using a method of comparison that would minimize the dependence on absolute values. The method chosen was the ratio of the gated value of a given parameter to the single-beat value of the same parameter. The standard deviations of the gated parameters were calculated on the basis of counting statistics (and their influence on the appropriate polynomial fits) alone. In calculating the standard error of the single-beat parameters, we assumed that the single-beat parameters of a given subject distributed themselves about the mean as would be predicted from the fluctuations of counting rate alone. This was found to be not strictly true in several of the subjects. The difference between the measured distributions and the assumed ones were small enough, however, to justify estimating errors in the manner indicated.

RESULTS

The results of this study are contained in Fig. 2. To

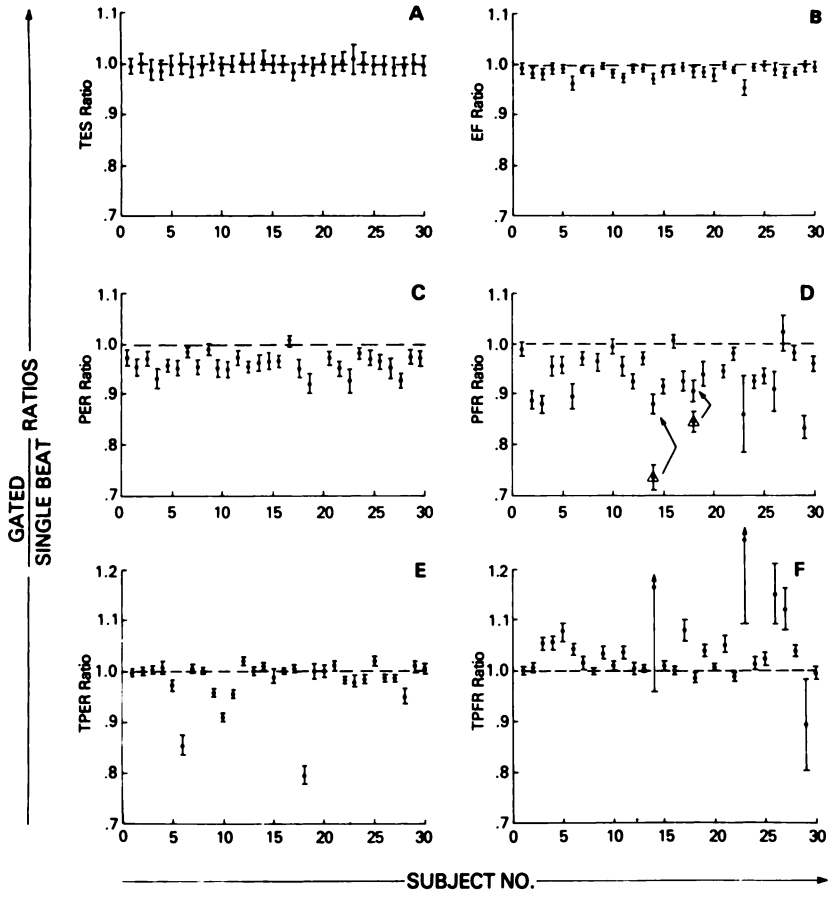

Fig. 2. For all 30 subjects, ratio of gated value to single-beat value of each parameter is shown. Triangles in Panel D refer to values not beat-length windowed (Figs. 3C, D). Arrows point to change in ratio when beat-length windowing was used (Figs. 3E, F).

construct this figure, each quantity of interest (EF, PFR, etc.) was first calculated by both the (correct) single-beat method and the gated method. The ratio of these two values (gated to single beat) was then plotted for each subject (Fig. 2). A ratio of 0.9, for example, indicates that the gated value underestimated the true value by about 10%. A dashed line is drawn to indicate a ratio of unity.

Table 1 summarizes the data of Fig. 2. In its first column are shown the absolute values of the population mean (over all 30 subjects) for all the parameters of interest (single-beat calculations). In order to show the spread of these values among subjects, one standard deviation of the population about the population mean is shown in parentheses.

The second column of Table 1 lists, for each parameter, the population mean of the parameter ratios of Fig. 2. These population means were calculated by weighting each subject's ratio with the inverse of the variance of that ratio, and averaging over all subjects. Note that these population means are presented for convenience only; the behavior of an individual subject is the important quantity, not the population mean. This is because an individual subject, (perhaps due to the substantial variability in the shape of a TAC from subject to subject) may possess a ratio that differs significantly from unity, even though the population mean may not differ from unity. For conservatism, the sigma values listed in parentheses in the table's second column are calculated either (a) by using the deviations of each individual subject's ratio from the population mean, or (b) by using the known (counting-statistical) error bars (as shown in Fig. 2) for each subject. The method chosen was the one that resulted in the largest estimate of sigma.

Time to end-systole. Panel A of Fig. 2 shows the ratio of TES as measured from the gated TAC to TES as measured from the single-beat TACs. It is seen that this ratio is not significantly different from unity for any of the 30 subjects. Also, the mean of the ratios for all 30 subjects, as shown in Table 1, does not differ significantly from unity. It may be concluded, then, that the time to end-systole may be measured acceptably by either of the two techniques in the present group of subjects.

Ejection fraction. Panel B of Fig. 2 shows the ratios of the ejection fractions, gated to single-beat. The weighted mean of the ratios for all subjects was 0.988, which is significantly lower than unity ($P < 0.001$). In addition, four of the 30 subjects individually had ratios significantly lower than unity ($P < 0.05$). The subject with the largest difference between gated and single-beat EF gave a 4.5% (0.022 EF units) underestimate in EF by the gated method compared with the single-beat method.

Peak ejection rate. The results for PER are shown in

TABLE 1.

Parameter	Single beat weighted mean (σ pop)*	Ratio: gated to single beat (σ mean)†
EF	0.508	0.988
	(0.14)	(0.002)
TES	350	0.998
	(33)	(0.004)
PER	2.728	0.967
	(0.92)	(0.004)
PFR	2.072	0.954
	(0.98)	(0.011)
TPER	183	0.980
	(24)	(0.012)
TPFR	481	1.005
	(47)	(0.011)

* Population means of single-beat values for each of six parameters describing LV function. Parentheses show spread of values (1 s.d.) among individual subjects about the population mean.

† Population means of ratios of gated value to single-beat value for each LV parameter. Parentheses show standard deviations in estimate of this mean ratio.

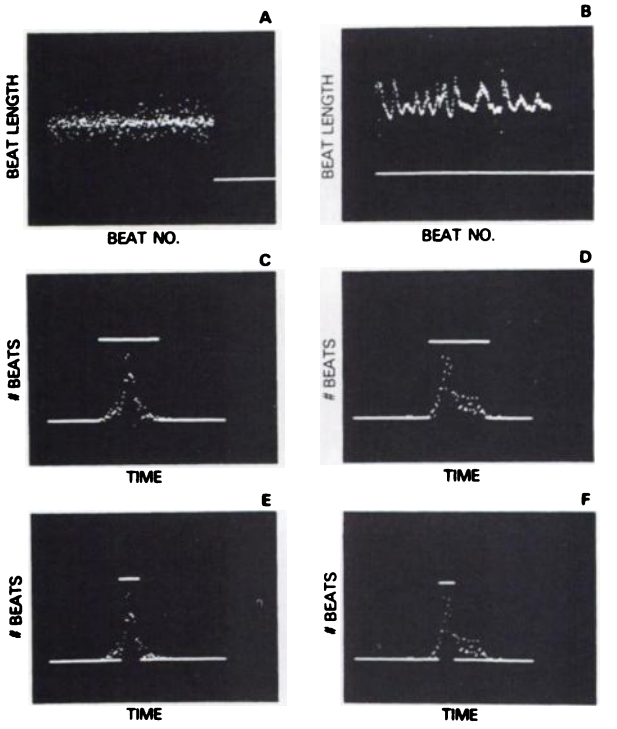

FIG. 3. (A, B) Beat length versus beat number for 512 beats in two different subjects (Nos. 14 and 18, see Fig. 2). (C–F) Beat-length histograms showing windowing used for the two subjects indicated by triangles in Fig. 2.

Fig. 2C. The population mean for the gated PER values was 4.6% lower than PER calculated from the single beats. No subject's PER ratio was significantly greater than unity. The largest differences between gated and single-beat calculations occurred for three of the 30 subjects, who had gated PER values 7–8% lower than the single-beat values. Eighteen of the 30 subjects had PER ratios 2.5–5% lower than unity ($P < 0.05$).

Peak filling rates. The results for PFR are shown in Fig. 2D. The population mean of the PFR ratios (0.954) was significantly lower than unity. Three of the subjects (Nos. 14, 18, and 29) had very low (<0.85) PFR ratios. Of these three, two (14 and 18) had R-to-R beat-length distributions that were unusually wide (see Fig. 3). The source of this wide distribution in these two subjects was not due to ectopic beats. Instead, Subject 18 had an EKG array (plot of beat length against beat number) with slow cyclic variations (Fig. 3B) perhaps related to respiration. Subject 14 exhibited a more random beat-length pattern, as evidenced by a scattered EKG array (Fig. 3A). Again, all beats used in the analysis were nonectopic, and there was no apparent pattern of long R-to-R following short. Both subjects had aortic regurgitation and markedly enlarged LVs. When all the (nonectopic) beats were included in the gated TAC (Figs. 3C, D), the values of PFR were markedly reduced from unity (triangles in Fig. 2D) for these two subjects. When the data from the two subjects were re-analyzed, excluding the longer and shorter beats as shown in Figs. 3E, F the values of PFR increased, as shown by the arrows in Fig. 2D. None of TES, EF, or PER was affected as a result of this "beat-length windowing", nor were the single-beat values of PFR significantly changed. This lends credence to the idea that beat length fluctuations at low heart rates will affect primarily diastolic phenomena. Since it was not the purpose of this study to investigate the effects of beat-length fluctuations, further windowing experiments were not performed.

Time to peak ejection rate. The time of occurrence of PER is depicted in Fig. 2E. For TPER the population mean of the gated to single-beat ratio is 0.967, significantly lower than unity. This figure, however, illustrates the difficulty (mentioned earlier) in using a population mean to describe the results. Three subjects (6, 10, and 18) show behavior markedly different from the rest of the population. Since the distribution of values among the population is so skewed, and seems to depend strongly on the highly individualistic shapes of the TACs, a population mean may be misleading. The lowest value of gated to single-beat TPER (0.80) occurred for Subject 18, the subject shown in Fig. 3B. Beat-length windowing did not alter this value. Subjects 6 and 10 possessed quite narrow beat-length histograms (60 and 50 msec, FWHM).

Time to peak filling. The final panel, Fig. 2F, depicts the gated to single-beat ratios for time of occurrence of PFR. The weighted population mean for this ratio (1.005) is not significantly different from unity, even

though 11 subjects had ratios significantly higher than unity ($P < 0.05$) and none was less than unity. As described previously, the deviations of each individual from the population mean were used to estimate the standard error of the mean.

If instead, the individual error brackets for each subject shown in Fig. 2 were used, the mean TPFR would be significantly higher than unity at $P < 0.01$. The gated TPFRs, then, tended to exceed slightly the single-beat values. Very large error brackets are shown for several of the subjects in Fig. 2F. Such errors occur whenever the diastolic filling region of a TAC is nearly linear with time. When filling is nearly linear, its maximum value can be quite accurately determined, but the time of its occurence is highly uncertain.

Background dependence. As a test of the influence of background on the above results, all the gated to single-beat ratios were recalculated with no correction for background, and none changed significantly whether background was or was not subtracted. This is not an obvious finding, since background enters nonlinearly into calculations of most of the parameters.

DISCUSSION

From the results in Fig. 2 and Table 1, the following generalizations may be made. First, for all the parameters, except TES and TPFR, gating results in a small but measurable underestimate in the parameter of interest. As seen in Table 1, this underestimate occurs not only in the population means, but—far more importantly—for a significant number of individuals in the population.

Second, we note that certain individuals making up the population can behave in a manner poorly described by the population mean (e.g., Subjects 6, 10, and 18 of Fig. 2E). This may be a reflection of variability in the shape of TACs from beat to beat in some subjects.

Finally, note that the errors in EF, PER, etc., achieved in this study were significantly lower than would be realized in a typical gated camera study. This is due to the very high-efficiency detector used. Deviations between gated and single-beat values that were statistically significant in the present study might be masked by the poorer statistics obtainable in a conventional gamma-camera study.

There are several reasons why one might expect results calculated from gated TACs to differ from those based on single-beat TACs (*9*). These reasons can be deduced from the two equations below, which express the two different methods of calculating parameters of interest (EF, PER, etc.).

$$\text{P gated} = \text{Pg} = \text{O}\sum_{i=1}^{N} f_i(t) \qquad (1)$$

$$\text{P single-beat} = \text{Ps} = \frac{1}{N}\sum_{i=1}^{N} \text{O}f_i(t) \qquad (1)$$

In the above expressions, Pg or Ps represents some parameter to be calculated from the gated or single-beat TACs, respectively. The function $f_i(t)$ represents the single-beat TAC for beat i, and N is the total number of beats in the study. O represents some operation that must be performed on the TAC in order to evaluate P, (e.g., it might stand for "find the time of occurence of the minimum of the TAC"). Equation 1, then, expresses the fundamental difference in calculation between the "correct", single-beat parameters, Ps, and the equivalent gated parameters, Pg. In Pg, all the TACs are first summed together and the operation, O, then performed on the sum. In calculating Ps, the operation, O, is performed on each TAC, $f_i(t)$, and the results of the operations summed and divided by the number of beats, N. It can be proved that, unless the single-beat TACs are identical for all beats, Pg is, in general, different from Ps, the magnitude and sign of the difference depending on the type of operation, O, being performed and the kind of variations found among the single-beat TACs, $f_i(t)$.

CONCLUSION

Theoretically, many parameters describing LV function are correctly calculated only by using the single-beat method. Our purpose was to determine how closely the results obtained with the ECG gating method approach the true results. We find that for TES and EF the two methods agree excellently. The gated EF underestimated the true value by at most 4.5% (0.022 EF units), whereas the average underestimate was only about 1%. Such small differences do not seem to be of any clinical significance.

Peak ejection rates tend to be slightly underestimated with the ECG gating techniques, but again the magnitude of the error is small. Gated values of peak filling rate, and the time to peak ejection rate, agree well, on average, with the true value. For certain isolated subjects, however, PFR and TPER may be significantly underestimated by ECG gating—as much as 17% for PFR and 20% for TPER. Even these underestimates, however, will probably be overshadowed by counting errors in any clinical situation.

Thus, although ECG gating gives results that differ measurably from the correct single-beat values, the magnitude of the difference is in general quite small, and is certainly smaller than the counting errors present in most clinical studies.

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