Factors of Variability in the Radionuclide Evaluation of Global and Regional Left Ventricular Ejection Fraction

Stuart A. Jackson, Rick Nickerson, Robert H. Martin, Sian Iles, and David Barnes

Victoria General Hospital, Halifax, Nova Scotia, Canada

This study was performed to establish the normal values and range of variability for three- and five-segment regional ejection fraction analysis. In addition, file conversion was utilized to compare global values produced by different vendors' systems. Global values show considerable differences between systems (15%-20% in most cases) which indicate the need for standardization and correction when comparing data. For regional analysis, with a mean global value of 60.6%, the mean regional ejection fractions varied from 47% to 81%. Interobserver variation of the regional parameters was between 2% and 6% (standard error of estimate) for a group of 50 "normals" (global ejection fraction >50%) with least variability in the apex and maximum in the septal segment. Intraobserver variability was between 1% and 4% with the same pattern. In a mixed population (global ejection fraction 10%-85%) all parameters exhibited more variability, and paying strict attention to patient positioning for repeat studies appears to have little effect on reducing this variation.

Multiple-gated equilibrium blood-pool (MUGA) imaging has become a routine method to determine left ventricular (LV) function (*1-3*). The global ejection fraction (EF) is the most commonly used functional parameter, and the evaluation of wall motion abnormality is typically assessed by visual observation of a sequence of gated images.

Attempts have been made to quantify wall motion by the introduction of regional ejection fraction (REF) analysis where several segments are defined separately within the left ventricle (*4*). However, this subdivision of the left ventricular region of interest can lead to increased variability in the data, attributed to object movement and normal variations in shape. Consequently, while REF analysis has the potential to identify volumetric abnormality which can be masked in the conventional two-dimensional display, it has not been widely adopted.

For reprints contact: Stuart A. Jackson, Victoria General Hospital, Halifax, Nova Scotia, Canada B3H 2Y9.

It has previously been shown that the parameters of LV function can be significantly affected by choice of region used for background subtraction and the LV edge-detection algorithm (*5*). It is of fundamental importance that when calculated parameters are significantly involved with the medical decision-making process they are both consistent and accurate. In addition, the magnitude of errors introduced by systematic factors need to be well defined before any confidence can be attached to measured values.

This study was undertaken to develop a practical framework within which our objective parameters of LV performance could be used effectively. Specific concerns were addressed as follows:

1. How does the global measure of EF vary between different vendors' systems?
2. What are the "normal" values and range of variability for REFs?
3. Does patient repositioning introduce significant variation of the calculated parameters?

MATERIALS AND METHODS

Comparison of Global EF

Thirty minutes after administration of 1 mg of stannous ion (cold pyrophosphate), 20 mCi (740 MBq) of technetium-99m- (^{99m}Tc) pertechnetate was injected to effectively label the blood pool. Gated sequences of 16 images each were collected over 600 heart cycles. The images were acquired in the left anterior oblique (LAO) 45° position using a 30° slant-hole collimator and in the anterior position using a general purpose collimator. Images were collected as 32 × 32 matrices and interpolated to a 64 × 64 matrix using a PDP11/23 (Digital Equipment Corp., Marlboro, MA) data acquisition system connected to a mobile gamma camera, and then transferred by floppy disk to a PDP11/34 system running gamma 11 software for initial analysis. Fifty patients were studied in whom contrast ventriculography was performed within 24 hr of the nuclear investigation. The radiography technique used was a standard biplane area-length method used to estimate LV volumes and EFs (*6*).

DATA ANALYSIS

In order to compare different systems, the gamma 11 data files were converted by a commercial contractor (7) into formats suitable for further analysis on system 1 (Star II, General Electric, Milwaukee, WI) and system 2 (APEX 009, Elscint, Boston, MA). The methods of data analysis for global EF calculations were as follows:

Gamma 11 manually picks end-diastolic and end-systolic frames, manually defines left ventricle, automatic positioning of background area between the end-diastolic and end-systolic outlines at ~3–6 o'clock position.

System 1 (Semiautomatic) manually picks center of LV edge-detection by maximum slope (second derivative), automatic background selection.

System 1 (Automatic) uses amplitude and phase images to define LV, second derivative for edge-detection and automatic background selection.

System 2 (Semiautomatic) uses amplitude and phase images to define LV, second derivative for edge-detection, but has break points to allow manual adjustment, if necessary, of regions of interest and background.

REF Observer Variability: Group 1, "Normal" Population

This group consisted of fifty patients who underwent clinically indicated routine gated blood-pool imaging for the evaluation of LV function. All patients had a "normal" EF (>50%), and demonstrated no wall motion abnormality. Gated blood-pool imaging was performed using a gamma camera (Elscint, Boston, MA), with an all-purpose collimator and a zoom factor of two. The patient was imaged in the best septal LAO position with a 5° caudal tilt. Data was analyzed on computer by two observers, in duplicate, using semiautomatic global, three- and five-segment REF programs. The REF programs used a single-end diastolic region of interest that is divided into equal segments excluding a 60° segment at the base of the heart (indicated as VP in all figures).

REF Positional Variability: Group 2A and 2B, Mixed Population

The study population for this phase consisted of two groups of 25 patients who underwent routine gated blood-pool imaging. The patients were selected at random and had global EFs that ranged from 10% to 85%. Data was acquired as previously described with the following exceptions:

(1) The patients in Group 2A had a second best septal LAO view acquired by another technologist with no knowledge of the camera angle used in the first view.

(2) The patients in Group 2B also had two LAO views performed, but during the first study the angle at which the view was acquired was measured with an inclinometer. The second LAO was then acquired by another technologist using the inclinometer to reproduce this angle. Data were analyzed in duplicate by one observer using the same semiautomatic global, three- and five-segment REF programs as used in Group 1.

TABLE 1. Correlation Between All Methods Used To Calculate Global LVEF

Pearson Correlation Matrix					
	Contrast	Gamma 11	System 1 (Auto)	System 1 (Semi)	System 2
Contrast	1.000				
Gamma 11	0.866	1.000			
System 1 Auto	0.887	0.936	1.000		
System 1 Semi	0.758	0.832	0.834	1.000	
System 2	0.899	0.956	0.972	0.818	1.000

$p < 0.001$

RESULTS

Global LVEF

The correlation between all methods used to calculate EF is tabulated in Table 1, the highest correlation being between system 1 and system 2 automatic methods and the lowest correlation being between the system 1 semiautomatic and the contrast ventriculography. However, all correlations are highly significant and using a linear regression model the relationships between any two of the analysis techniques are presented in Table 2. There is almost a one-to-one relationship between the system 1 automatic method and the system 2 analysis but most other relationships require modifying factors to make results comparable as indicated. Figures 1 and 2

TABLE 2. Relationships Between Global Ejection Fraction Measurements Performed on Different Systems

Relationships			
Contrast = 14.60	+	0.63 × Gamma 11	(s.e.e. = 8.5)
Contrast = 21.91	+	0.87 × System 1 Semi-Auto	(s.e.e. = 11.1)
Contrast = 17.36	+	0.82 × System 1 Auto	(s.e.e. = 7.9)
Contrast = 16.15	+	0.85 × System 2	(s.e.e. = 7.4)
Gamma 11 = 8.48	+	1.19 × System 1 Auto	(s.e.e. = 8.2)
Gamma 11 = 13.61	+	1.31 × System 1 Semi-Auto	(s.e.e. = 12.9)
Gamma 11 = 6.39	+	1.25 × System 2	(s.e.e. = 6.8)
System 2 Auto = 6.27	+	1.03 × System 1 Semi-Auto	(s.e.e. = 10.1)
System 2 Auto = 0.09	+	0.99 × System 2	(s.e.e. = 4.3)
System 1 Semi = 4.35	+	0.68 × System 2	(s.e.e. = 8.5)

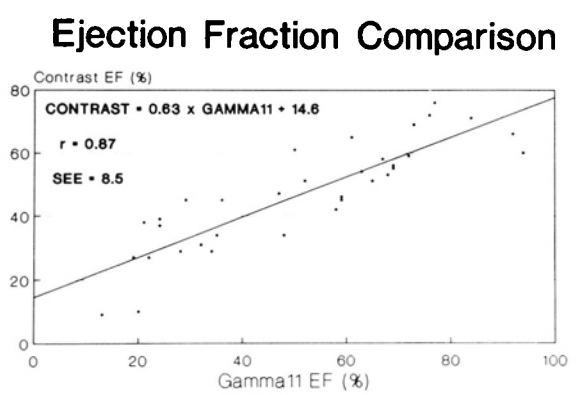

FIG. 1. Plot of LV ejection fraction measured by MUGA study and analyzed on Gamma 11 system, compared to contrast ventriculography.

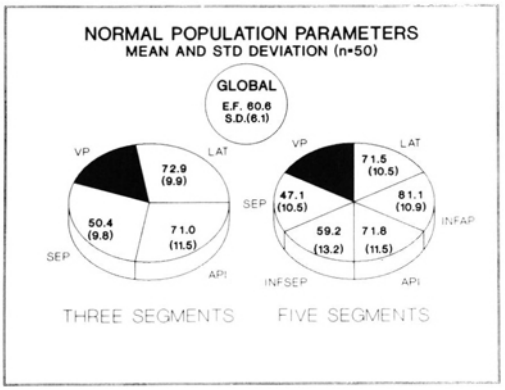

FIG. 3. Normal population (EF > 50%) parameters and (standard deviations) for three- and five-segment REF measurements.

show the relationship between contrast EF and gamma 11 EF and system 2 EF versus system 1 automatic, respectively, to give some idea of the data dispersion around the line of regression. Numerically, this is indicated by the standard error of the estimate.

REF "Normal" Parameters

Figure 3 summarizes the mean and standard deviations of the global and regional EF parameters as analyzed on system 2. The global EF for this group measured ~60% with a standard deviation of 6.1%. The REFs vary between 47% to 81% with standard deviations up to twice that of the global measure.

REF Observer Variability: Group 1, "Normal" Population

Inter- and intraobserver variability was measured by performing linear regression on repeated measures, and by expressing the variability as the standard error of the estimate (s.e.e.) of the regression line. In the "normal" population global inter- and intraobserver variability was ≤1% (s.e.e.). REF interobserver variability (Fig. 4) ranged between 2.2% and 6.6% (s.e.e.) with least variability in the apex and maximum in the septal and lateral segments. Interobserver variability was significant ($p < 0.05$ paired t-test) in the septal, infraseptal and apical segments. Intraobserver variability (Fig. 5) ranged between 1.3% and 4.6% with the same pattern, but differences were not statistically different at the 5% level.

Group 2 Positional Variation

For the mixed population, regional EF variability was between 4% and 10% (s.e.e.) and did not appear to be improved by paying strict attention to reproducing the camera angulation. The global variability is ~4%, compared to the 1% of the "normals" group, and regional variability is similarly greater. Figures 6 and 7 summarize these measurements.

DISCUSSION

In the calculation of global EF there are several intrinsic and extrinsic factors which can influence the result. In acquiring the data the resolution of the system, the number of frames used for the gated sequence, the count density, the shape of the patient, the shape of the heart and the adequacy of the gating will all have an effect to some degree on the measurement of global EF.

When it comes to data analysis the object in question can be defined either manually, semiautomatically or completely automatically with edge-detection mechanisms ranging from Fourier techniques to second derivative or simple threshold techniques. Currently, the second derivative technique is the most widespread method used for edge-detection, and fully

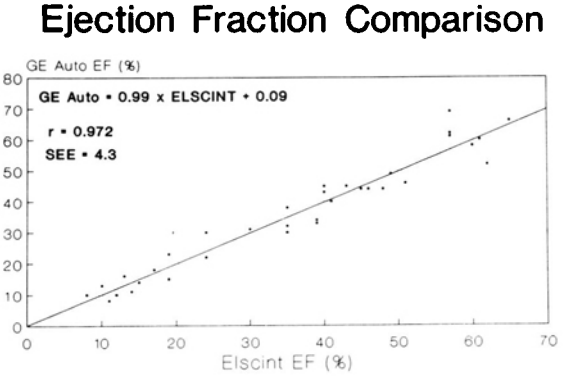

FIG. 2. Comparison of Systems 1 and 2 Automatic determination of LVEF.

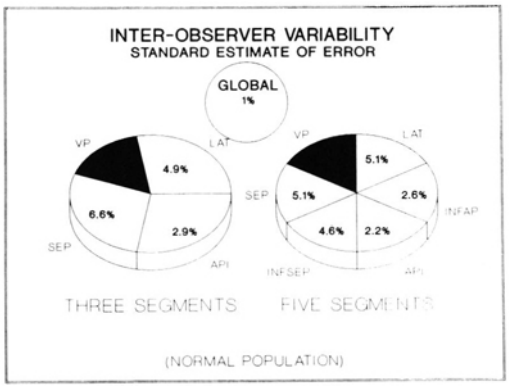

FIG. 4. REF interobserver variability (normal population).

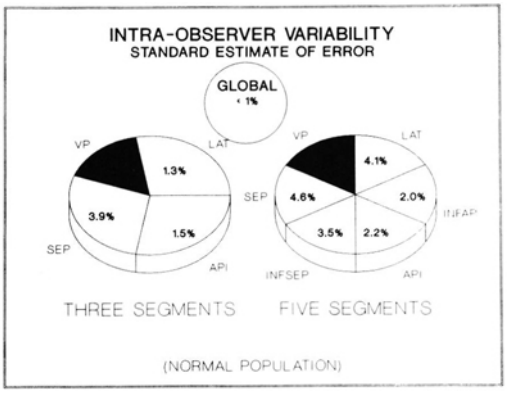

FIG. 5. REF intraobserver variability (normal population).

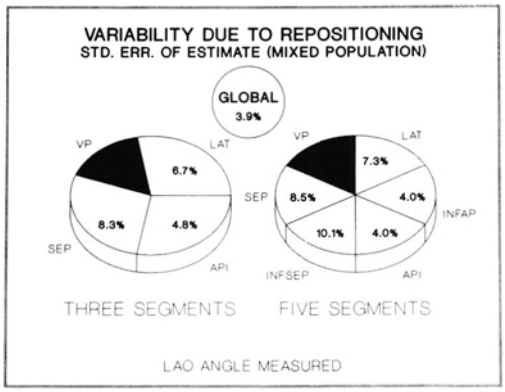

FIG. 7. REF variability when patient is repositioned for a second study and camera angulation is measured using inclinometer.

automatic methods of analysis appear to be consistent in their performance. However, the background-correction technique probably has the largest single effect on the calculated EF, and here again an automatic procedure would appear to provide a consistent approach. In practice, it may not be feasible to make adequate compensation for all of the different factors which cumulatively affect the outcome of this investigation. However, it would appear that the majority of variance is probably attributable to the method of data analysis.

It has been shown here that there are significant differences between the different manufacturers' systems and that when comparing results from different institutions or from different systems within the same department it is of the utmost importance to have some form of calibration or standardization when numerical values are used for clinical decision-making. This could take the form of phantom measurements (*8*) or comparison with an accepted radiologic technique.

There is a larger variability in both global and regional EF measurements in a mixed population as opposed to the "normal" group. This difference may be due in part to differences in ventricular geometry attributable to pathology, in the mixed group.

The variability of regional parameters is obviously greater in both groups than for global measurements. A dynamic region of interest which tracks the ventricular edges throughout the cardiac cycle is used in most global EF determinations.

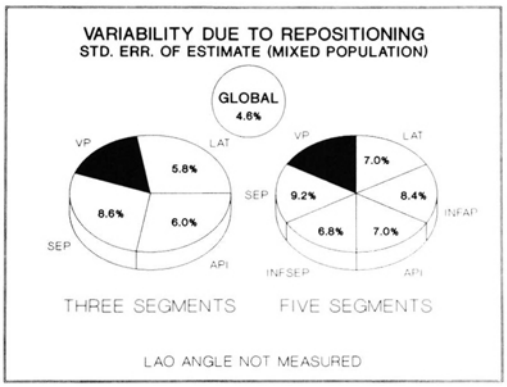

FIG. 6. REF variability when patient is repositioned for a second study and camera angulation is not measured.

In contrast, regional EF segments are defined only on the end-diastolic frame, hence, different degrees of translational or rotational movement of the heart will lead to more widely varying estimates of these parameters.

CONCLUSIONS

Large differences can be observed in cardiac parameters measured on different vendors' systems. It is, therefore, important to have some form of standardization procedure to facilitate comparison of data. For REF measurements, the total variability within a patient population can be very large, hence, the absolute values of calculated parameters must be used with caution. We recommend at this time, that REF analysis is best used in conjunction with the conventional observation of gated wall motion cine sequences.

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