Quantitative Assessment of Wall Motion in Multiple-Gated Studies Using Temporal Fourier Analysis

Pieter H. Vos, Albert M. Vossepoel, and Ernest K. J. Pauwels

University Hospital Leiden, and University of Leiden, The Netherlands

We describe a method for quantification of left-ventricular wall motion in multiple-gated studies, based on approximation of local time-activity curves by the first harmonic of the corresponding Fourier spectrum. The Fourier transform is adapted to the global left-ventricular time-activity curve by shortening the length of the base period. The degree of shortening depends on the corresponding power in the second and higher harmonics; the base period that resulted in minimal power in the higher harmonics was selected for a Fourier transform of the regional curves. This usually results in exclusion of both the diastasis phase and the left-atrial filling phase from the calculations. With a model of the left-ventricular volume curve it is shown that important advantages of this adaptation are (a) a better approximation of the maximum difference in the curves, and (b) less spread in the phase determination. Wall motion was related to the Fourier parameters. The combination of the mean amplitude and the standard deviation of the phase histogram gives the best results for global analysis of the motion of the wall.

J Nucl Med 24: 388–396, 1983

Programs for Fourier analysis of local, temporal activity changes detected during MUGA studies are available today for almost every nuclear medicine computer system.

Fourier parameters can be used for the detection of coronary artery disease (*1*) as well as abnormal conduction (*2*). It has also been suggested that both amplitude and phase of the first harmonic of the Fourier spectrum can be used for quantitative assessment of the motion of the left-ventricular wall (*3,4*). The approximation to the curves may be poor, however, particularly for the filling phase of the ventricle. Therefore in each individual case we have tried to adapt the base frequency of the Fourier transformation of the curve, seeking a better description of those parts of the curves that are pertinent to assessment of wall motion (*5*).

The aims of this study were to determine the usefulness of adaptation of the base frequency, and to evaluate the role of Fourier parameters in the quantitative assessment of wall motion (using the adapted base frequency) for patients with cardiovascular disease.

Theory for selection of the base frequency. The cardiac cycle is usually divided into four successive phases: those of isovolumetric contraction, ejection, isovolumetric relaxation, and filling. The last can be subdivided into three parts: rapid filling, slow filling (diastasis), and atrial contraction.

The phases of diastasis and left-atrial contraction are of no importance for assessment of left-ventricular contraction. Their fluctuations may severely affect the determination of amplitude and phase by Fourier analysis when the base frequency equals the heart rate.

Moreover the duration of diastasis shows severe fluctuations, particularly at low heart rates. In several studies a strong correlation was found between the length of the fluctuations in diastasis and in the entire RR interval (*6,7*). For instance, injection of catecholamine particularly affects the diastasis (the other intervals remaining relatively unaffected), resulting in a change of the cycle length (*8*).

This is illustrated in a mathematical model of a normal left-ventricular volume curve (see Appendix for a

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Received Aug. 3, 1982; revision accepted Dec. 28, 1982.

For reprints contact: Pieter H. Vos, PhD, Dr. Bernard Verbeeten Institute, Brugstraat 10, 5042 SB Tilburg, The Netherlands.

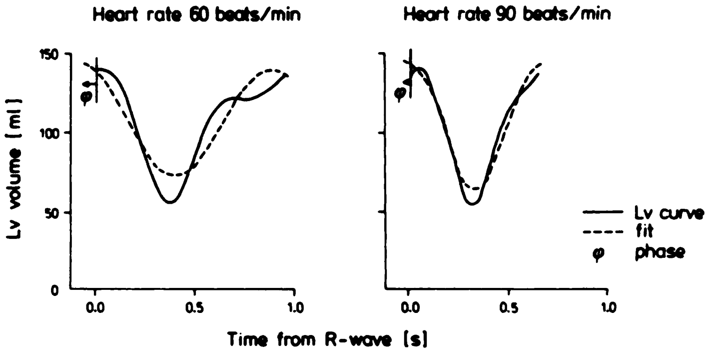

FIG. 1. Normal left-ventricular volume curve for two heart rates, with approximation of curve by first harmonic of Fourier spectrum. Base frequency for the Fourier transformation equals heart rate.

description of the model), where amplitude and phase of the first harmonic were calculated for various heart rates. The variation of the heart rate was obtained by extrapolation of random fluctuations in cycle length (Fig. 1). The approximation of the true maximum difference was expressed as the amplitude ratio, which is defined as the amplitude of the first harmonic divided by the true maximum difference in the volume curves:

$$\text{Amplitude ratio} = \frac{\text{amplitude first harmonic}}{\text{stroke volume}} \quad (1)$$

In addition we calculated the relative power, i.e., the power in the second and higher harmonics relative to the total power in the signal:

$$\text{Relative power} = \frac{\sum_{j=2}^{n} (\text{amplitude j-th harmonic})^2}{\sum_{j=1}^{n} (\text{amplitude j-th harmonic})^2}, \quad (2)$$

in which n equals the number of harmonics in the Fourier spectrum. In Fig. 2 amplitude ratio, phase, and relative power are plotted as a function of heart rate.

The same data were obtained using an adapted base frequency. This frequency was calculated by Fourier transformation of the left-ventricular volume curve, using base periods ranging from 10 to 28 consecutive curve points. (Our acquisition procedure was limited to 28 frames/cycle). The base period always started at the first point in the curve. Only points within the adapted base period were included in the transformation; thus, excluded curve points were always located at the end of the curve.

The model study showed that in almost all studies the base period producing the lowest relative power yielded a first harmonic that described the isovolumetric phase, ejection phase, and fast-filling phase quite well. The frequency related to this base period is referred to as the optimum base frequency (Figs. 2,3). In addition to the previously mentioned parameters, the so-called relative length of the base period, RLP (the length of the selected base period divided by the length of the cycle) is also given (see Fig. 2d).

When the base frequency equals the heart rate, the amplitude ratio, phase, and relative power are highly dependent on the fluctuations of the cycle length. When the optimum frequency is used, however, the parameters are almost independent of the fluctuations in cycle length. Since these fluctuations result almost entirely from variations in the duration of diastasis (*6,7*), this period is usually excluded from the calculations. The chosen base period is relatively short (RLP < 1) when diastasis is long; when diastasis is short, the chosen base period approximates the cycle length (RLP = 1).

MATERIALS AND METHODS

Patient selection. Seventy-five consecutive patients referred to our division of nuclear medicine for evaluation of left-ventricular function were selected.

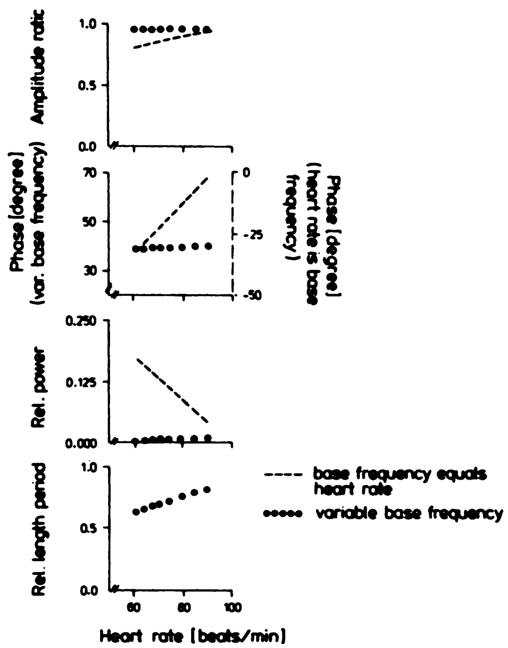

FIG. 2. Amplitude ratio, phase, relative power in second and higher harmonics, and relative length of base period, as a function of heart rate, for normal left-ventricular volume curves.

Amplitude ratio = (amplitude first harmonic)/(stroke volume)

$$\text{Relative length base period} = \frac{\text{optimum base period}}{\text{length of cardiac cycle}}.$$

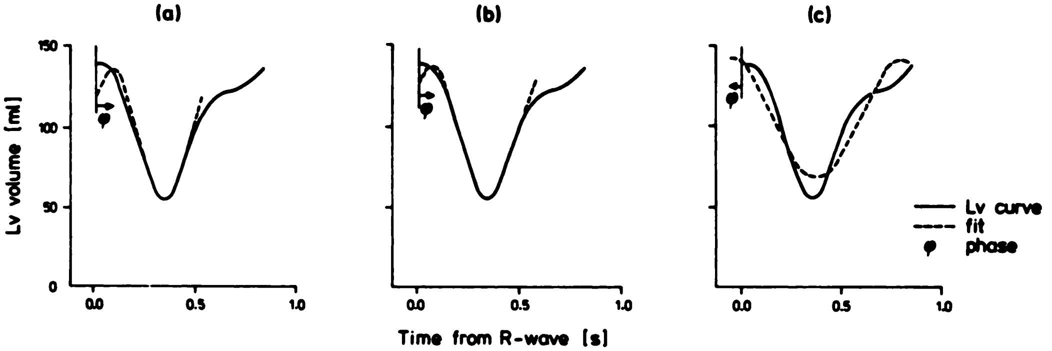

FIG. 3. Adaptation of base frequency for ejection and rapid-filling phases in left-ventricular volume curve.
(a) RLP = 0.62, a.r. = 0.964, phase = 54.7°, rel. power = 0.009;
(b) RLP = 0.70, a.r. = 0.954, phase = 38.7°, rel. power 0.007;
(c) RLP = 1.00, a.r. = 0.868, phase = −22.3°, rel. power = 0.123; where RLP = relative length of base period (a.r. = amplitude ratio; rel. power = relative power (see text).)

Patients with severe arrhythmia, bundle branch block, other conduction disorders, or severe valvular regurgitation were excluded from the study.

Scintigraphic studies. A large-field gamma camera (equipped with an all-purpose parallel-hole collimator) was arranged for an LAO projection, perpendicular to the septum, and tilted 30° caudalwards. Images were zoomed electronically into the heart region. Visualization of the heart cavities occurred after administration of 0.4 mg stannous chloride and 2.0 mg pyrophosphate dissolved in 0.5 ml saline, followed about 30 min later by an i.v. injection of 555 MBq (15 mCi) [Tc-99m]pertechnetate.

Gated frame-mode acquistion was performed at rest using a commercially available acquisition program*. Each cycle contained 28 intervals; 300kcounts/frame were acquired. The images were acquired in a 32 × 32 word-mode format and interpolated up to 64 × 64 pixels before analysis. Because the acquisition program did not allow for selection of RR interval, each study was corrected afterwards for distortion of the last frames due to RR-interval fluctuations within the acquisition period, using a small source placed in a corner of the field of view during acquisition.

Regional motion of the wall in three regions of the left ventricle (antero-septal, infero-apical, postero-lateral) was independently assessed visually by three cardiologists using a 4-point scale: 0 = normokinesia, 1 = hypokinesia, 2 = akinesia, 3 = dyskinesia. The averages of the observer scores for each region were used to indicate the severity of the abnormal wall motion in all experiments.

Parameter calculations in patient studies. The optimum base frequency was calculated for each patient using the technique described above. In addition, amplitude ratio, phase, relative power, and relative length of base period were determined for all normally contracting ventricles. In each study the optimum base frequency was used for the calculation of all local amplitudes and phases; subsequently amplitude and phase images were created.

The local amplitudes represent the magnitude of the change in absolute activity, which may vary from patient to patient because of differences in attenuation and dilution. To normalize the amplitudes of the local time-activity curves for the left-ventricular area, all amplitudes within the image were divided by the average value of the amplitudes within the left-ventricular area and multiplied by the ejection fraction. Thus the scale factor = EF/(average amplitude left ventricle) (*3*).

Regions of interest were chosen visually over the antero-septal, infero-apical, and postero-lateral regions of the ventricular area. The observer scores for these regions were related to the local amplitudes and phases. For this purpose an amplitude histogram and a phase histogram were created for each region, with the parameter values as abscissa and the corresponding frequency of occurrence within the left-ventricular area as ordinate. In addition, similar histograms were prepared for the total left-ventricular area. Mean, standard deviation, skewness, and kurtosis of all histograms were related to the average observer scores using both single and multiple regression analysis. The latter is necessary because information pertaining to abnormal wall motion may be duplicated in several parameters. To obtain the most useful combination of parameters, the parameter that explained the largest proportion of the wall-motion scores was selected first, next the parameter that added the most information, and then the remaining parameters in order of importance.

RESULTS

Selection of base frequency. Selection of the base frequency was evaluated using 25 patients from our group, all showing normal wall motion (that is, all three

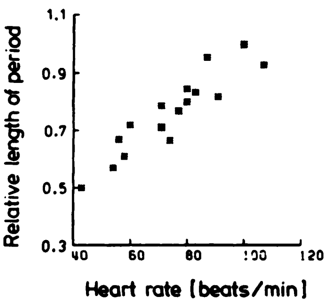

FIG. 4. Relative length of optimum base period as a function of heart rate for 25 patients with normal left-ventricular wall motion.

cardiologists considered wall motion to be normal in all regions). Moreover, no other signs of abnormal left-ventricular wall motion were present.

The optimum base period was considerably shorter than the cycle length for patients with a low heart rate (HR < 80 beats/min). For higher rates the optimum base period approximated the cycle length (Fig. 4). Correspondingly, the relative power in the second and higher harmonics clearly decreased in patients with a low heart rate when the optimum base frequency was used (Fig. 5).

As expected, the determination of amplitude—and phase in particular—improved for patients with a low heart rate.

The amplitude ratio did not correlate significantly with the heart rate when the optimum base frequency was used; in general the maximum difference was slightly underestimated (amplitude ratio = 0.95 ± 0.05). Use of heart rate as base frequency resulted in a significant correlation between amplitude ratio and heart rate:

$$\text{ampl. ratio} = 0.0027 \cdot \text{HR} + 0.71, \quad r = 0.60,\ p < 0.001, \qquad (3)$$

with heart rate in beats/min (Fig. 6a,b).

The major difference in phase between these two transformations was reduction of the spread in data when the optimum base frequency was used (Fig. 6b,d). The regression equations were:

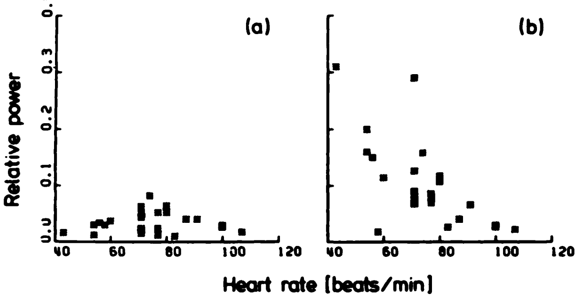

FIG. 5. Relative power as a function of heart rate for 25 patients with normal left-ventricular wall motion, calculated using optimum base frequency (a) and heart rate as base frequency (b).

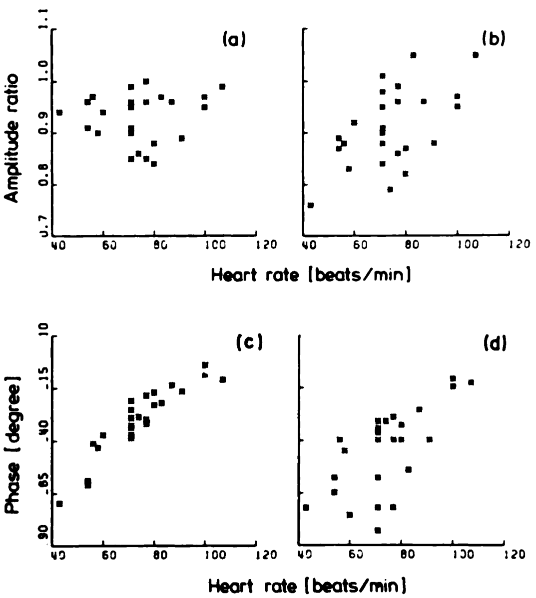

FIG. 6. Amplitude ratio and phase as a function of heart rate, for 25 patients with normal left-ventricular wall motion, calculated using the optimum base frequency (a,c) and heart rate as base frequency (b,d).

$$\text{phase} = 0.97 \cdot \text{HR} - 102\ (r = 0.91;\ p < 0.001;\ \text{opt. base frequency}); \qquad (4)$$

and

$$\text{phase} = 0.94 \cdot \text{HR} - 114\ (r = 0.69;\ p < 0.001;\ \text{heart rate}), \qquad (5)$$

assuming the phase is zero at the start of the R wave. The

TABLE 1. NORMAL VALUES FOR FOURIER PARAMETERS (N = 75)

Total left ventricle	Amplitude	Phase*
Mean	0.69 ± 0.11	0.0 ± 6.6
Standard deviation	0.243 ± 0.076	4.7 ± 2.2
Skewness	−0.011 ± 0.25	−0.09 ± 0.36
Kurtosis	−0.84 ± 0.29	−0.60 ± 0.43
Antero-septal region		
Mean	0.70 ± 0.13	1.0 ± 7.2
Standard deviation	0.222 ± 0.079	4.7 ± 2.2
Skewness	−0.12 ± 0.33	−0.1 ± 1.0
Kurtosis	−0.79 ± 0.52	0.3 ± 2.9
Infero-apical region		
Mean	0.65 ± 0.14	1.0 ± 7.6
Standard deviation	0.216 ± 0.068	3.6 ± 1.6
Skewness	−0.03 ± 0.29	−0.05 ± 0.52
Kurtosis	−0.97 ± 0.21	−0.48 ± 0.91
Postero-lateral region		
Mean	0.71 ± 0.11	−1.0 ± 8.1
Standard deviation	0.256 ± 0.071	4.1 ± 1.8
Skewness	−0.20 ± 0.34	0.09 ± 0.52
Kurtosis	−0.98 ± 0.32	−0.5 ± 1.1

* Phase (in degrees) corrected for heart rate.

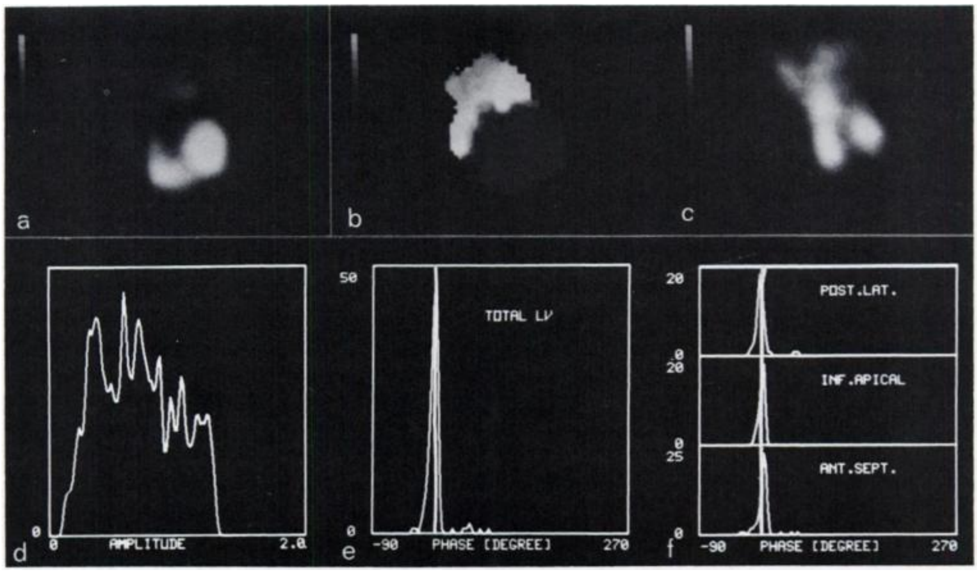

FIG. 7. Example of Fourier functional images and histograms for patient with normal left-ventricular wall motion (LAO 30° view, 30° caudal tilt; ejection fraction = 0.78).

(a) Amplitude image (scale runs from 0 to 0.8 amplitude units).
(b) Phase image (scale from −90° to 270°); pixels outside heart region are cleared.
(c) End-diastolic image.
(d) Amplitude histogram for total left ventricle.
(e) Phase histogram for total left ventricle.
(f) Phase histogram for three regions within left-ventricular area.

isovolumetric phase, ejection phase, and fast-filling phase were well described qualitatively in almost all cases when the first harmonic was calculated from the optimum base frequency. This base frequency was used for transformation of local curves in the following results.

Normal values for Fourier parameters. The phase was the only parameter that correlated significantly with the heart rate (Fig. 5c). The dependence of phase on heart

TABLE 2. CORRELATION COEFFICIENTS FOR FOURIER PARAMETERS AND WALL-MOTION SCORES (LINEAR REGRESSION; N = 75)

Total left ventricle	Mean	St. dev.	Skewness	Kurtosis
Amplitude	−0.80 $p < 0.0001$	−0.60 $p < 0.0001$	n.s.[†]	−0.37 $p < 0.001$
Phase*	n.s.	0.65 $p < 0.0001$	0.30 $p < 0.006$	n.s.
Antero-lateral region				
Amplitude	−0.65 $p < 0.0001$	−0.41 $p < 0.0002$	n.s.	n.s.
Phase*	n.s	0.36 $p < 0.001$	n.s.	n.s.
Infero-apical region				
Amplitude	−0.70 $p < 0.0001$	−0.59 $p < 0.0001$	n.s.	0.32 $p < 0.002$
Phase*	0.70 $p < 0.0001$	0.70 $p < 0.0001$	n.s.	n.s.
Postero-lateral region				
Amplitude	−0.65 $p < 0.0001$	−0.55 $p < 0.0001$	n.s.	n.s.
Phase*	n.s.	0.21 $p < 0.04$	n.s	n.s.

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* Phase corrected for heart rate.

[†] n.s. = not significant.

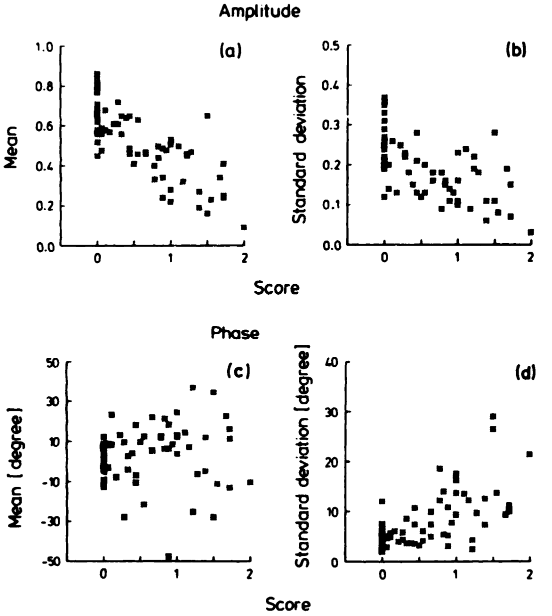

FIG. 8. Mean (a,c) and standard deviation (b,d) of amplitude and phase histograms for all studies, as a function of wall-motion score (data for total left ventricle, N = 75). Mean amplitude equals ejection fraction. (Phase is corrected for heart rate).

rate was excluded by subtraction of the phase value that can be expected in normals; this value was obtained from Eq. 4. Normal values for all histogram parameters for each region, and for the total left-ventricular area, are given in Table 1.

Because of the normalization procedure used, the mean amplitude for the total left ventricle represents the ejection fraction. Regional amplitude values normally show a slightly decreased movement of the apex. No regional difference in phase was registered between the three regions. A correlation with the spread of electrical activity was not found.

An example of a normal patient, the Fourier images, and the histograms is given in Fig. 7.

Analysis of motion of left-ventricular wall. The average wall-motion score for each region for all 75 studies was related to each of the histogram parameters (Table 2).

For the total left ventricle, both the mean and the standard deviation of the amplitude histogram correlated significantly with the wall-motion score (the wall-motion score for the total left ventricle represented the average of all regional scores, Fig. 8a,b). In addition, the standard deviation of the phase histogram (which represents the homogeneity of wall movement) increases when the wall-motion score increases (Fig. 8c,d). A correlation between mean phase and total score cannot be expected because, for example, the presence of either global hypokinesia or local dyskinesia in an otherwise normal left ventricle may produce the same total score.

Regionally, the mean amplitude and standard deviation of the amplitude histogram, as well as the standard deviation of the phase histogram, also correlate with the wall-motion score (Table 2). Only in the infero-apical region does the mean phase correlate with the wall-motion score, probably because in this study paradoxical moving segments were present only near the apex (Fig. 9).

Skewness and kurtosis proved to be of no value for wall-motion analysis. None of the regression showed marked improvement when a quadratic term was added.

Multiple regression analysis. Multiple regression analysis was performed using the mean and the standard deviation of both histograms. The resulting combinations, with corresponding correlation coefficients, are listed in Table 3.

For the total left ventricle, the mean amplitude

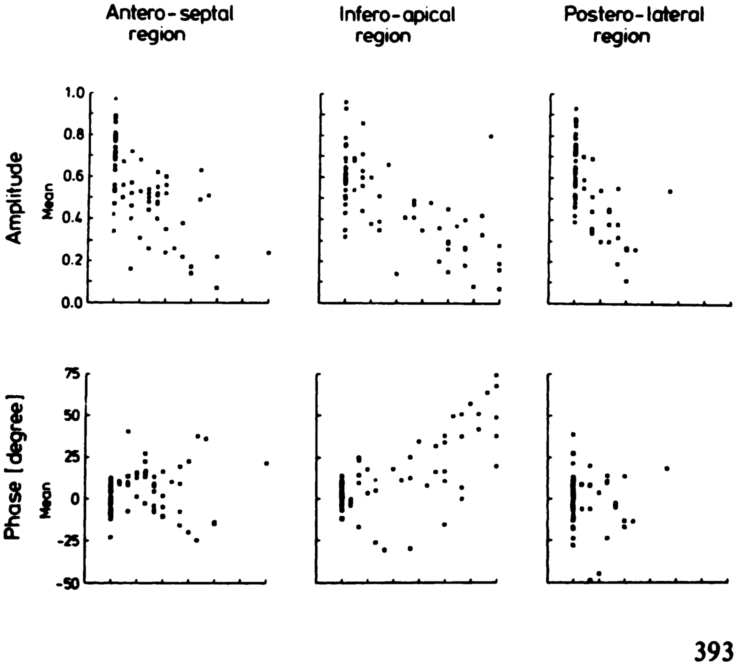

FIG. 9. Mean amplitude and mean phase as functions of wall-motion score for three regions within left-ventricular area (phase corrected for heart rate).

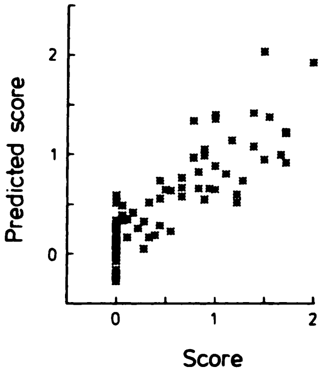

FIG. 10. Predicted wall-motion score vs. true wall-motion score for total left ventricle for all studies. Predicted score was calculated from regression equation obtained from multiple regression analysis:

$$\text{Score} = -2.06 \times (\text{mean ampl.}) + 0.034 \times (\text{st. dev. phase}) + 1.38$$

TABLE 3. CORRELATION COEFFICIENTS FOR COMBINATIONS OF FOURIER PARAMETERS AND WALL-MOTION SCORES (N = 75)

Total left ventricle	r^2
m.a.	0.637
m.a., s.p.	0.709
m.a., s.p., m.p.	0.722
m.a., s.p., m.p., s.a.	0.723
Antero-lateral region	
m.a.	0.420
m.a., s.a.	0.425
m.a., s.a., m.p.	0.430
m.a., s.a., m.p., s.p.	0.431
Infero-apical region	
m.a.	0.484
m.a., m.p.	0.644
m.a., m.p., s.p.	0.652
m.a., m.p., s.p., s.a.	0.653
Postero-lateral region	
m.a.	0.428
m.a., m.p.	0.432
m.a., m.p., s.p.	0.434
m.a., m.p., s.p., s.a.	0.435

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m.a. = mean amplitude.
m.p. = mean phase (corrected for heart rate).
s.a. = standard deviation amplitude histogram.
s.p. = standard deviation phase histogram.

(ejection fraction) was the first parameter to be selected (64% of the score was explained by mean amplitude). Addition of the standard deviation of the phase histogram resulted in 7% more information. Mean phase and standard deviation of the amplitude histogram added no further information. The predicted score is plotted against the true score in Fig. 10.

For the antero-septal and postero-lateral regions, the mean amplitude was the most informative parameter. Other parameters failed to add further information. In the infero-apical regions however, the mean phase provided added information. The discrepancy between regional results is probably due to the presence of paradoxically moving segments in the infero-apical region.

An example of a patient with regional paradoxical wall movement is shown in Fig. 11.

DISCUSSION

When the heart rate is used as base frequency, fluctuations in cycle length severely affect the amplitude and phase of the first harmonic in the Fourier spectrum of left-ventricular time-activity curves. In addition, the presence of diastasis causes the shape of the left-ventricular time-activity curve to deviate from a cosine function. Both phenomena are present, particularly at low heart rates (HR < 80 beats/min) in which case diastasis is prolonged and the fluctuations are the largest. Optimization of the base frequency allows a better determination of amplitude and phase, independent of the disturbances mentioned. With the method presented here, no relevant information regarding left-ventricular contractility is discarded because only diastasis and the left-atrial emptying interval are excluded from the computations. For time-activity curves this is of particular interest, since points located in these two intervals may be distorted because of fluctuations in cycle length. Note that the fundamental frequency is optimized for the left ventricle only. The approximation of curves in other areas of the images (such as the right-ventricular region) may be distorted using this technique.

The optimization procedure used in this paper can be carried out automatically and requires very little time. Because the base period is shortened, the calculation of local amplitudes and phases could be limited to about 1.5 min with our computer system.

Our data suggest that for assessment of wall motion of the total left ventricle, the mean amplitude (ejection fraction) is the major parameter. Mean phase (corrected for heart rate) is of no value for global analysis of wall motion. This is to be expected, since local paradoxical movement, combined with normally moving segments, may produce the same total wall motion score as overall hypokinesia. The standard deviation of the phase histogram is sensitive to local differences in wall movement, and therefore adds information to the global analysis of wall motion. Thus by measuring the magnitude of the changes in activity and the homogeneity of the contraction, a fairly reliable description of wall movement is obtained with Fourier parameters (see also Fig. 10).

Furthermore, our experiments suggest that for regional analysis the mean amplitude is also the most important parameter. The normal values for mean amplitude clearly show the smaller movements of the apex known from radiographic angiography. Mean phase,

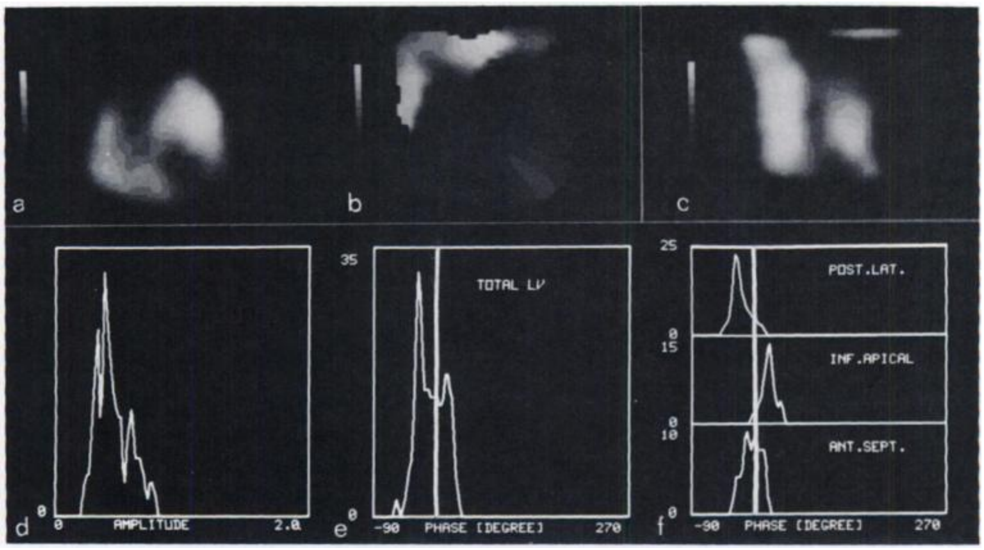

FIG. 11. Example of Fourier functional images, histograms, and parameters for patient with hypokinetic and dyskinetic movement of left-ventricular wall.

(a) Amplitude image;
(b) Phase image;
(c) End-diastolic image;
(d) Amplitude histogram for total left ventricle;
(e) Phase histogram for total left ventricle;
(f) Phase histogram for three regions within left-ventricular area.

Fourier parameters (phase corrected for heart rate):

	Total LV	Ant. sept.	Inf. ap.	Post. lat.
Score	1.00	0.66	2.33	0.00
Amplitude				
Mean	0.53	0.44	0.40	0.63
St. dev.	0.16	0.06	0.11	0.17
Phase (degree)				
Mean	24.3	27.1	50.8	8.8
St. dev.	17.6	12.7	7.5	6.9

corrected for heart rate, adds information only when paradoxical movement is present. The mean phase cannot be used for detection of local hypokinesia.

Regional analysis of wall motion by means of the regional mean amplitude and the regional mean phase offers several advantages over analysis using the regional ejection fraction:

1. All relevant intervals on the local time-activity curves are included in the analysis, whereas the local ejection fraction is calculated from only two points on the curve, and is therefore very sensitive to noise.
2. Regional differences in background do not affect local amplitudes and phases.
3. Paradoxical movement can be distinguished from akinesia.

We conclude that Fourier analysis of local time-activity curves can provide a valuable tool for analysis of the motion of the left-ventricular wall, provided that the

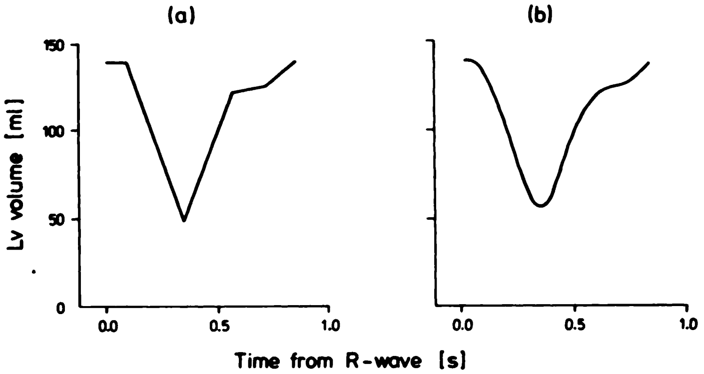

FIG. 12 (a). Computer-generated curve before Fourier filtering (see text); (b) same curve after Fourier reconstruction with first 5 harmonics in Fourier spectrum.

optimum base frequency is used and mean phase is corrected for heart rate.

FOOTNOTE

* MDS-MUGA; Modumed Trinary system.

ACKNOWLEDGMENT

The authors are indebted to Mr. M. Popkes for his competent preparation of the figures, and to Dr. H. ter Keurs, of the Department of Cardiology, University Hospital, Leiden, The Netherlands.

APPENDIX

MATHEMATICAL MODEL OF LEFT-VENTRICULAR VOLUME CURVE

Using data from normals (7), a typical global left ventricular volume curve was constructed (see Fig. 12a). Fifty points were used in each display of the model curve; this resulted in an almost continuous appearance of the curves.

The numerical values used were: end-diastolic volume = 140 ml; end-systolic volume = 50 ml; pre-ejection period/left-ventricular ejection time = 0.33 sec; pre-ejection period plus left ventricular ejection time = 0.36 sec; volume change in rapid filling phase = 80% of stroke volume; rapid filling time = 0.22 sec; duration of diastasis = 0.15 sec; atrial emptying time = 0.12 sec.

This curve was Fourier-transformed and reconstructed using only the first five harmonics because normal left-ventricular time-activity curves contain a maximum of five relevant harmonics (9). The curve after Fourier reconstruction is shown in Fig. 12b.

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