Determination of Diastolic Function Parameters: A Comparison of Two Methods

Janice S. Preslar, Mark T. Madsen, and Peter T. Kirchner

Division of Nuclear Medicine, Department of Radiology, University of Iowa Hospitals and Clinics, Iowa City, Iowa

Left ventricular diastolic function can be evaluated noninvasively from gated blood-pool studies. Two of the more useful indices of diastolic function are peak filling rate and time-to-peak filling rate. We have compared two analytic methods (third order polynomial and Fourier series) for determining these parameters. We evaluated both of these methods on a set of 24 subjects and a set of simulated curves. Although there was close agreement between the results obtained with the two methods, the polynomial fit requires operator selection of boundary points which influence the measured parameters and also requires an independent determination of the time-to-end-systole. The Fourier series method does not require operator intervention and determines all relevant quantities automatically from the single fitting procedure. Thus, we conclude that the Fourier series fit is less subject to methodologic bias and is, therefore, the preferred method for the evaluation of left ventricular diastolic function.

In recent years, measurement of left ventricular (LV) diastolic function has become an important investigative procedure due to the clinical significance of normal or abnormal rates of ventricular filling (*1–8*). In certain patients, the use of diastolic function parameters has been reported to be a more sensitive test for determining the presence or nature of cardiac disease than parameters of systolic function (*1*, *9*). Pathologic conditions such as coronary artery disease, myocardial infarction, constrictive pericarditis, cardiomyopathy, mitral stenosis, and hypoxia will produce impaired ventricular compliance due to incomplete or abnormal muscular relaxation (*10–18*). With radionuclide ventriculography, it is now possible to study the time-course of LV filling noninvasively and, thereby, characterize one aspect of LV diastolic function (*2*, *19*). Thus, analysis of left ventricular time-activity curves (TACs) obtained with multigated imaging of the labeled red blood cell pool in the left ventricle can be a useful tool in the evaluation of patients who may have certain forms of cardiac diseases.

The two methods used for the quantitative analysis of the TAC have been the third order polynomial fit and the Fourier series fit (*1*, *20*, *21*). The purpose of this study was to compare these two methods and to delineate their advantages and disadvantages. Two of the more useful indices of diastolic function are the peak-filling-rate (PFR) during the rapid filling phase of diastole and the time-to-peak-filling-rate (TPFR) (*22*). These two indices were used as parameters for the comparison of the third order polynomial fit and the Fourier series fit. The first method finds the PFR and TPFR from a third order polynomial fit which is applied only to the rapid filling phase of the LV TAC (*1*) (Fig. 1). In the second method, the entire LV TAC is fitted by a Fourier series which is then used to calculate the PFR and TPFR (*20*) (Fig. 2).

MATERIALS AND METHODS

Patient Studies

Scintigraphic studies were performed on two groups of patients. The first group consisted of 12 normal male volunteers, aged 23 to 35. They had no evidence of cardiovascular or pulmonary disease by physical examination. In each patient, the resting radionuclide ejection fraction (LVEF) was normal. The second group consisted of 12 patients, eight males and four females ranging in age from 58 to 76 with clinical evidence of cardiac disease.

Data Acquisition

The patients were studied with a small field of view scintillation camera* using a collar shield that limited the field of view to the left ventricle only. The camera was positioned in a left anterior oblique angulation, which was adjusted to achieve the best septal view possible. Twenty minutes after injection of 5.1 mg. stannous pyrophosphate,[+] 30 mCi of [^{99m}Tc]pertechnetate was injected intravenously. The changing pattern of radioactivity in the ventricle was recorded for a total of 10 million counts with serial mode acquisition using a gating device.[‡]

Data Analysis

Scintigraphic data from the patients were reformatted using a technique described by Bonow et al. (*1*). Temporal resolution of 10-20 msec per frame was used to produce 40-50 frames per cardiac cycle (*23*, *24*). Beat-to-beat uniformity was achieved by accepting cardiac cycles whose duration was within 15% of the dominant cycle length. This prevents distortion of the TAC by extrasystoles, post-extrasystolic cycles, and wide variations in sinus rhythm.

For reprints contact: J.S. Preslar, CNMT, Division of Nuclear Medicine, University of Iowa Hospitals and Clinics, Iowa City, Iowa 52242.

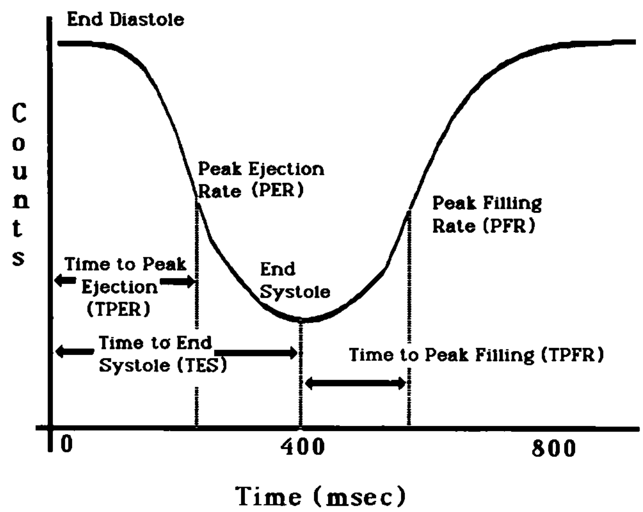

FIG. 1. Third order polynomial fit to the rapid filling phase of the LV time-activity curve used to find the values for the PFR and TPFR.

Stimulation Studies

The accuracy of both methods was evaluated from a set of stimulated LV TACs. These curves were generated analytically so that the PFR and TPFR were exactly known. Five sets of curves were generated with the PFR varying from 2.5 to 4.5 EDV/sec. Each set consisted of eight curves which were scaled to a maximum of 4,000 counts. Random noise with a Poisson distribution was added to each of the curves to simulate counting statistics. Each set was analyzed with both the third order polynomial (*1*) and the Fourier series fit (*24*) and the results were compared against the analytic values.

RESULTS

For each patient, the diastolic function values calculated by the two analytic methods were in close agreement for each parameter. Results are shown in Figure 3, where the y-axis denotes the parameter calculated with the third order polynomial fit and x-axis shows the parameters derived from the Fourier series fit. For the PFR parameter, shown at the top, the slope of the correlation was 0.96, the intercept was 0.02, and the correlation coefficient was r = 0.972. For TPFR values, shown in the middle, the slope of correlation between the two techniques was 1.01, the intercept was −5.1, and the correlation coefficient was r = 0.94. Comparing the EF values derived from the Fourier fit and the EF values derived from routine analysis of the TAC, we found a slope of correlation of 1.01, an intercept of 0.6, and a correlation coefficient of r = 0.995. With the third order polynomial technique, values for the PFR, TPFR, and EF ranged from 1.44 to 4.55 EDV/sec, 127 to 237 msec, and 26% to 81%, respectively. With the Fourier series technique, values for the PFR, TPFR, and EF ranged from 1.5 to 4.5 EDV/sec, 125 to 250 msec, and 27% to 80%, respectively.

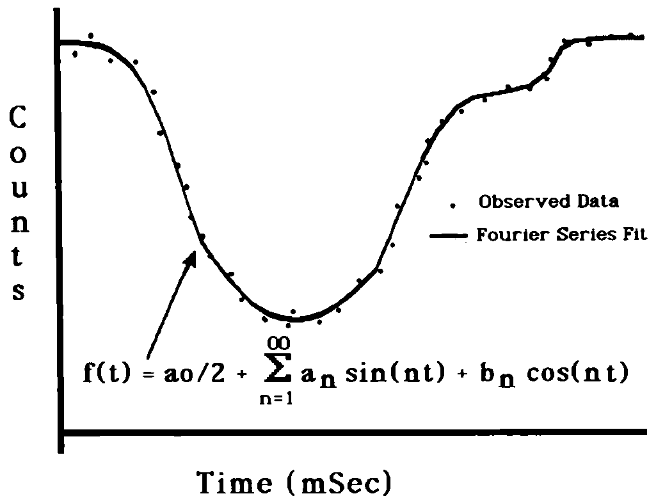

FIG. 2. Entire LV time-activity curve fitted by a Fourier series which is used to calculate the PFR and TPFR.

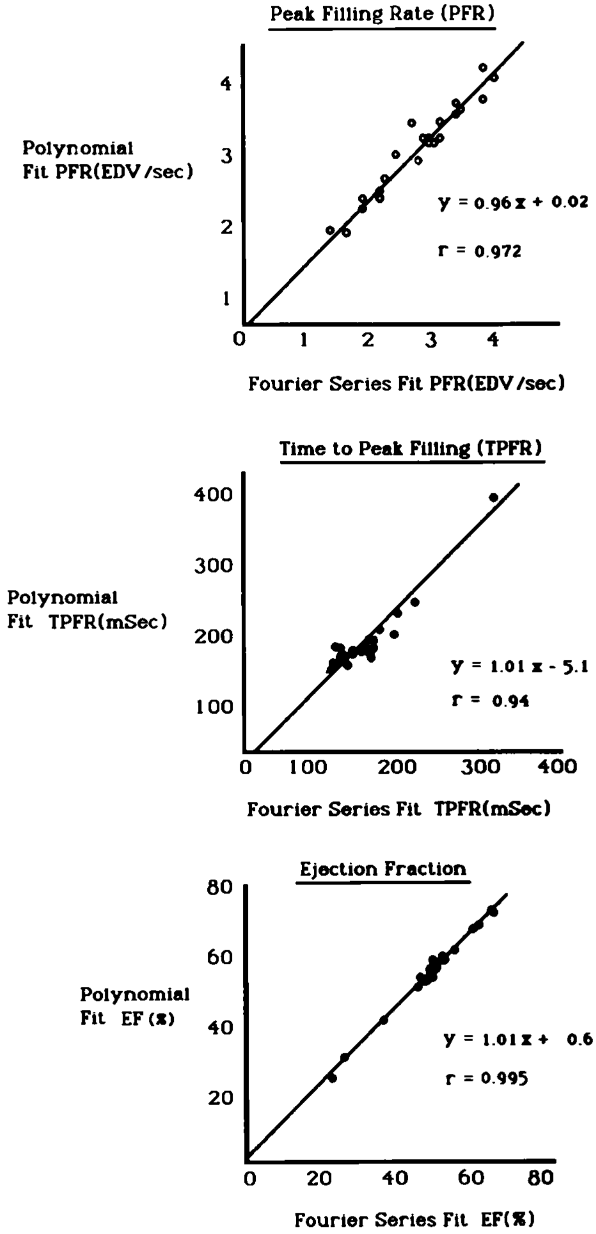

FIG. 3. PFR, TPFR, and EF determinations derived with each of the two methods (third order polynomial and Fourier series) independently correlated utilizing linear regression analysis.

Correlations were determined by comparing the third order

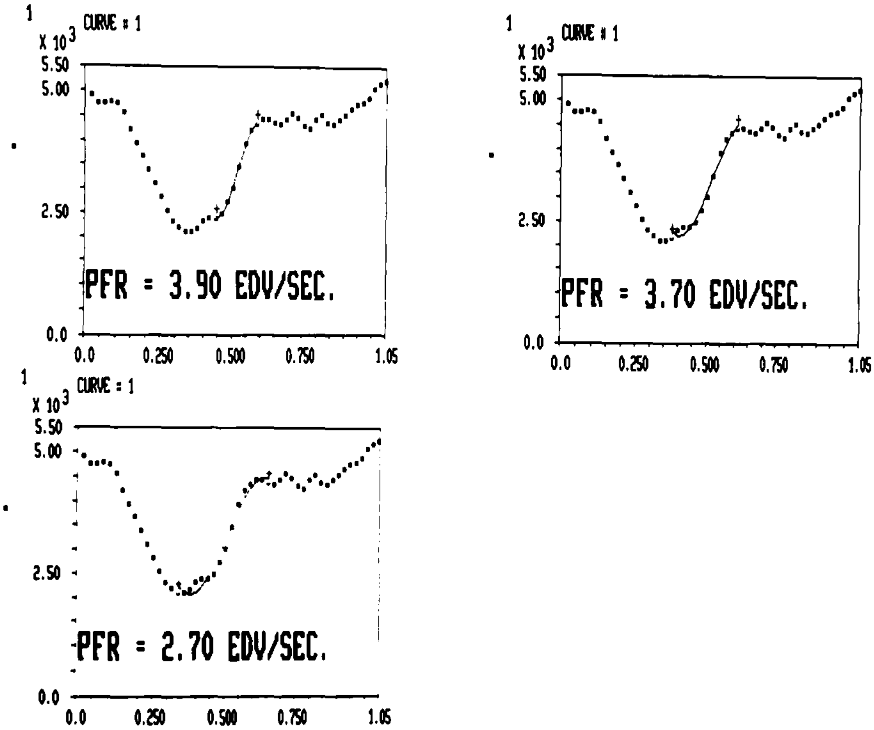

FIG. 4. Variation in PFR values related to the number of frames incorporated and the selection of boundary points when the third order polynomial fit method is used.

polynomial and Fourier series fit values to the simulated curve values. With the third order polynomial fit, r values of 0.99 were obtained for both PFR and TPFR. With the Fourier series fit, r values of 0.99 and 0.98 were obtained for PFR and TPFR, respectively. Interobserver variation was evaluated for each method by comparing the results of each patient's data done by four different operators. When different operators used the third order polynomial fit method to derive filling parameters from a single TAC, PFR values ranged from 2.70 EDV/sec to 3.90 EDV/sec (Fig. 4). The interobserver variation in the PFR values was as little as 0.04 and as high as 1.35. This wide range of variation was related to the number of frames incorporated and the selection of boundary points used by the operator (see Figure 4, which shows an example of different values for PFR when a different operator uses the third order polynomial fit). The Fourier series-fit values did not exhibit any variation since there is no operator intervention for the determination of boundary points and the values were determined with a single fitting procedure.

DISCUSSION

Both the third order polynomial method and the Fourier series method provide a readily available noninvasive means of evaluating diastolic function parameters (*9*). While each method was accurate when checked against a gold standard provided by simulated curves, we conclude that the Fourier series fit is the preferred method. The third order polynomial fit requires the selection of boundary points and also requires an independent determination of the time-to-end-systole. In addition, the measured parameters are sensitive to the selection of boundary points demonstrated by our data where interobserver variation in the PFR values was as little as 0.04 and as high as 1.35 (Fig. 4). Furthermore, the third order polynomial method requires a large amount of processing time because 40-55 frames per cardiac cycle are needed to analyze the diastolic values. The Fourier series method does not require operator intervention and determines all relevant values from the single fitting procedure. This type of fitting produces a systematically reproducible method and requires less computer time. These conclusions are consistent with those of Zatta et al. (*9*), who performed a similar study. Based on the results of our comparison study, we have chosen to use the Fourier series fit for a more reproducible and time-efficient method to determine LV diastolic function parameters.

NOTES

* LEM, Siemens, Schaumburg, IL
† TechneScan PUP, Mallinckrodt, Inc., St. Louis, MO
‡ Lifepak 6, Physio-Control, Redmond, WA

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REFERENCES

1. Bonow RO, Bacharach SL, Green MV, et al. Imparied left ventricular diastolic filling in patients with coronary artery disease: Assessment with radionuclide angiography. *Circulation* 1981;56:315–323.

2. Grossman W, Barry WH. Diastolic pressure-volume relations in the diseased heart. *Fed Proc* 1980;39:148–155.

3. Dwyer EM. Left ventrciular pressure-volume alterations and regional disorders of contraction during myocardial ischemia induced by atrial pacing. *Circulation* 1970;42:1111–1122.

4. Rickards AF, Seabra-Gomes R. Observations on the effect of angina on left ventricle, with special reference to diastolic behavior. *Eur J Cardiol* 1978;7(suppl):213–238.

5. Bristow JD, Van Zee BE, Judkins MP. Systolic and diastolic abnormalities of the left ventricle in coronary artery disease: Studies in patients with little or no enlargement of ventricular volume. *Circulation* 1970;42:219–228.

6. Diamond G, Forrester JS. Effect of coronary artery disease and acute myocardial infarction on left ventricular compliance in man. *Circulation* 1972;45:11–19.

7. Gaasch WH, Levine HJ, Quinones MA, et al. Left ventricular compliance: Mechanisms and clinical implication. *Am J Cardiol* 1976;38:645–653.

8. Parmley WW, Sonnenblick EH. Relation between mechanics of contraction and relaxation in mammalian cardiac muscle. *Am J Physiol* 1969;216: 1084–1091.

9. Zatta G, Tarolo GL, Palagi B, et al. Computerized analysis of equilibrium radionuclide ventriculography time-activity curve in the assessment of left ventricular performance: Comparison of two methods. *Eur J Nucl Med* 1985;10:198–202.

10. McLaurin LP, Rolett EL, Grossman W. Impaired left ventricular relaxation during pacing induced ischemia. *Am J Cardiol* 1973;32:751–757.

11. Barry WH, Brooker JZ, Alderman EL, et al. Changes in diastolic stiffness and tone of the left ventricle during angina pectoris. *Circulation* 1974;49:255–263.

12. Grossman W, Mann JT. Evidence for impaired left ventricular relaxation during acute ischemia in man. *Eur J Cardiol* 1978;7(suppl):239–249.

13. Frist WH, Palacios I, Powell WJ, et al. Effect of hypoxia on myocardial relaxation in isometric cat papillary muscle. *J Clin Invest* 1978;61:1218–1224.

14. Bing CH, Keefe JF, Walk MJ, et al. Tension prolongation during recovery from myocardial hypoxia. *J Clin Invest* 1971;50:660–666.

15. Weisfeldt ML, Armstrong P, Scully HE, et al. Incomplete relaxation between beats after myocardial hypoxia and ischemia. *J Clin Invest* 1974;53:1626–1636.

16. Mann T, Goldberg S, Mudge GH, et al. Factors contributing to altered left ventricular diastolic properties during angina pectoris. *Circulation* 1979;59:14–20.

17. Miller TR, Goldman KJ, Sampathkumaran KS, et al. Analysis of cardiac diastolic function: Application in coronary artery disease. *J Nucl Med* 1983; 24:2–7.

18. Gibson DG, Prewitt TA, Brown DJ. Analysis of left ventricular wall movement during isovolumic relaxation and its relation to coronary artery disease. *Br Heart J* 1976;38:1010–1019.

19. Mancini BJ, Slutsky RA, Norris SL, et al. Radionuclide analysis of peak filling rate, filling fraction, and time to peak filling rate: Response to supine bicycle exercise in normal subjects and patients with coronary disease. *Am J Cardiol* 1983;51:43–51.

20. Bacharach SL, Green MV, Vitale D, et al. Optimum Fourier filtering of cardiac data: A minimum-error method: Concise communication. *J Nucl Med* 1983;24:1176–1184.

21. Miller TR, Sampathkumaran KS, Goldman KJ, et al. Quantitation of diastolic function in fourier analysis of cardiac studies [Abstract]. *J Nucl Med* 1982;23:P62.

22. Grossman W, McLaurin LP. Diastolic properties of the left ventricle. *Ann Intern Med* 1976;84:316–326.

23. Green MV, Ostrow HG, Douglas MA, et al. High temporal resolution ECG-gated scintigraphic angiocardiography. *J Nucl Med* 1975;16:95–98.

24. 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 Nucl Med* 1979;20:189–193.