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Resting Early Peak Diastolic Filling Rate: A Sensitive Index of Myocardial Dysfunction in Patients with Coronary Artery Disease

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Resting first-pass radionuclide angiocardiography (RNA) was used to derive left-ventricular (LV) peak diastolic filling rates (PFR) in normals (Group 1: N = 12) and in patients with coronary artery disease (CAD), both without (Group 2: N = 27) and with previous myocardial infarction (Group 3: N = 23). Resting peak filling rates were significantly depressed in both Group 2 (1.61 ± 0.36; $p < 0.01$) and Group 3 (1.35 ± 0.26; $p < 0.001$) patients when compared with Group 1, normals (2.14 ± 0.63). Even though LV systolic function of Group 2 patients was normal and comparable to that in Group 1 (EF = 0.55 ± 0.06 against EF = 0.55 ± 0.06 NS), diastolic dysfunction [PFR < 1.61 end diastolic volume/sec (EDV/sec)] was present at rest in 14 of 27 (52%). Depressed PFR values were also seen in 20 of 23 Group 3 patients (87%). It appears that (a) resting PFR is a sensitive and easily obtainable parameter of the diastolic dysfunction associated with CAD; (b) abnormal PFR values are seen in almost all patients with previous myocardial damage, and (c) a significant proportion of CAD patients without any evidence of abnormal systolic function have depressed resting PFR of the LV.

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Ischemia is well known to modify the mechanical properties of the heart. One of its principal effects is to induce a series of metabolic changes that interfere with the Ca^{2+} binding mechanisms at the level of the myofibrils and therefore affect myocardial contraction (*1–3*). An interesting sequel would be the perturbation of myocardial relaxation, since for relaxation to occur Ca^{2+} would have to be removed from the vicinity of the contractile proteins by an active, energy-dependent mechanism (*1*).

Evidence now suggests that such phenomena have repercussions at the macroscopic level and may therefore affect the mechanical behavior of the ventricle as a whole. To measure such changes, parameters of myocardial relaxation are derived from measurements of ventricular volume, pressure, and the first derivative of pressure (dp/dt), as obtained during catheterization. Thus, changes in the shape and position of pressure-volume curves during diastole (*4–6*), in the maximum negative value of dp/dt during isovolumic relaxation (*7–9*), or of the constant of exponential decay of pressure during isovolumic relaxation (*10–13*) were seen to occur during myocardial infarction or acutely induced ischemia. Such changes may also precede evidence of systolic dysfunction (*14*).

Ventricular filling rates during early diastole have also been shown to be systematically modified when normal patients were compared with those having coronary artery disease (CAD) (*15,16*). The results of these early studies have been confirmed by noninvasive measures derived from either gated or first-pass radionuclide ventriculography (*17,18*). The present study was undertaken in order to characterize the clinical usefulness of a resting parameter of diastolic function—maximal

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left-ventricular filling rate normalized to end-diastole—and to test the hypothesis that such a parameter is a good indicator of the myocardial diastolic dysfunction associated with CAD. We used first-pass radionuclide ventriculography to assess this index of myocardial function in normal subjects and to determine to what extent ventricular filling is altered in CAD patients with myocardial damage, as documented by wall-motion abnormalities with or without electrocardiographic changes, and in CAD patients without evidence of systolic dysfunction.

METHODS

Patient population. Three groups of individuals were studied. Group 1 included 12 individuals considered to be normal on the basis of negative histories for cardiac disease, normal physical examinations, and normal electrocardiographic and/or echocardiographic evaluations. Three of these patients also underwent coronary angiography for the investigation of atypical chest pain, and were found to have less than 25% luminal diameter narrowing in their coronary vessels. The mean patient age was 39 yr (range 24–54). Nine patients were male and three female. One individual in this group was taking propranolol at the time of the radionuclide study.

Groups 2 and 3 consisted of individuals referred to our institution for cardiac catheterization for coronary artery disease (CAD). They were selected on the basis of availability of satisfactory radionuclide and angiographic and supportive clinical data. Propranolol was administered to 90% of patients in Group 2 and to 75% of those in Group 3. There were no differences in the number of patients in Groups 2 and 3 who were on propranolol therapy ($p > 0.05$ by chi-square analysis). Equal portions of Group 2 and Group 3 patients received nitrate treatment.

Group 2 (N = 27) patients had significant coronary artery disease at cardiac catheterization but did not have historical, electrocardiographic, or ventriculographic evidence of a previous myocardial infarction. Mean age in this population was 57 yr (range 48–67) and all were male. Four patients had single-vessel disease, six had two-vessel disease, while 17 had three-vessel disease.

Group 3 patients (N = 23) had both significant coronary artery disease and significant wall-motion abnormalities at catheterization. Electrocardiographic changes were seen in 16 patients and ventriculographic contraction abnormalities were present in all. Electrocardiographically, myocardial infarction was considered to be present if Q waves (≥ 0.04 sec) were seen in leads III, F (inferior MI) or I, II, L, V_1–V_4 (anterior MI). Angiographically, 12 of the 23 had evidence of an old anterior infarct, while 11 had had inferior infarcts. Significant single-vessel disease was seen in five patients, while two vessels were involved in seven, and three in 11. The mean age of this group was 54 yr (range 38–81) and all were male.

Angiographic study. Coronary angiography was performed using the Judkins method. Significant coronary artery disease was present whenever a more than 70% narrowing of the luminal diameter was seen in either of the major coronary arteries or smaller branches. LV angiography was performed in the 30° RAO projection, the ventriculograms being obtained following the injection of 50–70 ml of Renografin-76 in 3–4 sec. Three cardiologists scored these ventriculograms, taking care to exclude premature ventricular contractions as well as the first and second postpremature beats. Normokinesis was considered to be present if wall motion appeared normal to all three observers. Asynergy was considered present when hypokinesis, akinesis, or dyskinesis was seen (*19*). Group 2 patients always had normokinesis of all segments, whereas all Group 3 patients exhibited asynergy of at least one portion of the ventricle.

Radionuclide technique. First-pass radionuclide angiography was performed at rest with a multicrystal gamma camera.* The detector was oriented in a 30° LAO projection with a slight (20°) caudal tilt. An average dose of 20 mCi of pertechnetate(Tc-99m) was injected into an antecubital vein and the first transit of the bolus through the major vessels and heart chambers was stored on a minicomputer system associated with the camera. The framing rate was 25 msec. Preliminary data processing included temporal smoothing and corrections for deadtime and field uniformity. The operator then selected a left-ventricular region of interest (ROI), based on a dynamic replay of the acquired study. A completely automated algorithm subsequently detected the main cardiac beat as the one with the highest concentration of radiopharmaceutical at left-ventricular end-diastole (ED). Four to eight cardiac beats were selected on the basis of the following criteria: maximal counts at ED $\geq$ 70% of the main beat's end-diastolic counts and ejected volume (measured as counts) $\geq$ 50% of the counts ejected during the main beat. A representative cardiac cycle was then constructed. The systolic portion of this representative beat was obtained by summing forward from the end-diastolic frame all selected beats until a global minimum was attained. The diastolic portion of this cycle was then created by summing forward from the end-systolic frame of each of the selected beats until a global maximum was reached. Background (BKD) subtraction was performed according to an algorithm that takes into consideration activity in the left-ventricular ROI before the appearance of the bolus and also activity outside the left ventricle during passage of the bolus through the left-ventricular cavity (*20*).

The peak diastolic filling rate (PFR) was determined by a method similar to one described by Bacharach et al. (*21*). First, a third-order polynomial was fitted to the first 400 msec (16 frames) of diastole. For this, a general

TABLE 1. HEART RATE, SYSTOLIC, AND DIASTOLIC INDEXES (MEAN ± s.d.)

	Group 1 (n = 12)	Group 2 (n = 27)	P (vs. 1)	Group 3 (n = 23)	P (vs. 1)
Heart rate, beats/min	74 ± 14	63 ± 15	< 0.05	60 ± 9	< 0.002
Ejection fraction	0.55 ± 0.06	0.55 ± 0.06	NS	0.45 ± 0.08	< 0.001
PFR, EDV/sec	2.14 ± 0.63	1.61 ± 0.36	< 0.01	1.35 ± 0.26	< 0.001
TPRP, msec	151 ± 38	183 ± 54	NS	176 ± 60	NS

unweighted least-squares method was used. The point of maximal filling was then determined by setting the second derivative of the polynomial expression to zero. This point flagged the time of occurrence (Ti) of the maximum diastolic filling rate. The third-order polynomial was then differentiated once and the resultant expression, when evaluated at Ti, yielded the maximum filling rate. This value represented filling rate as counts/25 msec; it was subsequently scaled and normalized to total end-diastolic counts. PFR, therefore, expresses diastolic filling rate as a fraction of end-diastolic volume per second.

Left-ventricular ejection fraction (LVEF) was also derived from these left-ventricular time-activity curves by the equation EF = (ED − ES)/(ED − BKG). LVEF values obtained by first-pass radionuclide ventriculography (RNEF) have been correlated with angiographic EF in our laboratory in multiple series, with r values ranging between 0.78 and 0.90. In a recent group of 24 subjects, the RNEF is related to contrast ventriculography (CVEF) by the regression equation CVEF = 0.9 RNEF + 0.13, r = 0.84.

Statistical analysis. All numerical data are expressed as means ± s.d. Linear correlation coefficients were computed to assess the relationships PFR vs. HR, PFR vs. EF, EF vs. HR, and TPFR vs. HR. The intergroup slopes of the regression equations were compared using the Student's t-test. To evaluate the relative contributions of heart rate and EF to PFR, multivariate equations were derived using a statistical program.† Differences among variates were assessed during an unpaired t-test (*22*); when necessary, chi-square analysis and the Mann-Whitney test for unpaired samples were used.

RESULTS

Values for heart rate, left-ventricular ejection fraction, early diastolic peak filling rate, and time to peak filling rate are shown in Table 1. The mean heart rates of Groups 2 and 3 were similar to each other but were significantly less than those in Group 1 patients ($p < 0.05$ and $p < 0.002$). Mean left-ventricular ejection fraction for Group 3 patients was significantly lower than those for Group 1 ($p < 0.001$) and Group 2 ($p < 0.001$) patients. This parameter was not significantly different between Groups 1 and 2 (p = NS). Patients from Groups 1 and 2 all had LVEF values within the range of normal for our laboratory (lower limit = 46%).

For purposes of display, Fig. 1 shows interpolated left-ventricular time-activity curves from two patients—a Group 1 (L) and a Group 2 (R)—with similar heart rates and ejection fractions. The differences between maximal slopes of the diastolic portion of these curves and between the time from end-systole to the point of peak filling rate can be appreciated visually. The individual values for early diastolic peak filling rates are plotted for all three groups in Fig. 2. The mean PFR values are progressively lower for Group 2 and 3 patients compared with Group 1. Differences between groups are significant when comparisons are made between the normals and CAD patients (1 vs. 2: $p < 0.01$; 1 vs. 3: $p < 0.001$) and between the different classes of CAD patients (2 vs. 3: $p < 0.01$).

In Fig. 3, individual values of PFR are plotted against heart rate for the three patient populations. Weak correlations exist between these two parameters for the three groups studied (Group 1: r = 0.42; Group 2: r = 0.39; Group 3: r = 0.50). The slope of this relation differs significantly between Group 1 and Group 3 ($p < 0.01$). A correlation between PFR and LVEF is also apparent when these values are plotted (Fig. 4) and analyzed (r = 0.56 for the three groups). It is clear from Fig. 4 that, for an equivalent LVEF, Group 2 and 3 patients have lower PFR than Group 1 patients. Further analysis reveals that the slopes for the three groups are statistically different (Group 1 vs. 2: $p < 0.002$; Group 1 vs. 3: p <

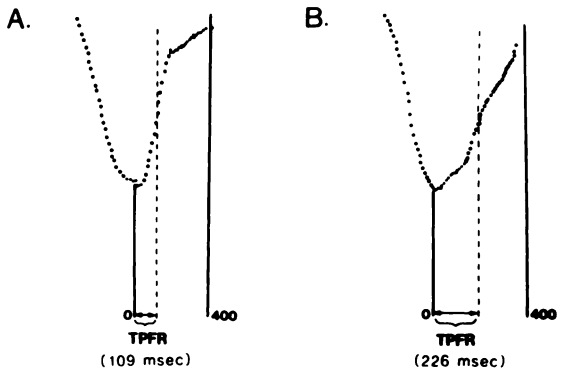

FIG. 1. Smoothed time-activity curves of representative beats from normal subject (A) and patient with three-vessel CAD (B). Normal curve rises earlier and more rapidly.

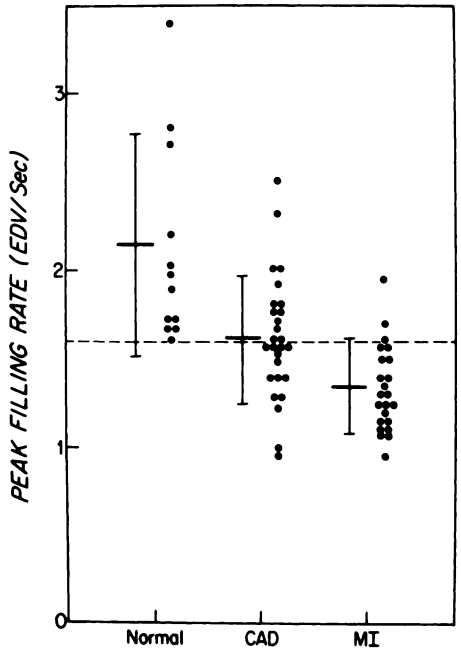

FIG. 2. Peak filling rates of individuals in three groups of subjects: (1) Normal subjects, (2) patients having CAD but normal systolic function, and (3) patients with previous MI and impaired systolic function (1 vs. 2 $p < 0.01$, 1 vs. 3 $p < 0.001$). Dotted line is lowest value of normal.

0.001), and that a change in 0.1 LVEF units for Group 1 subjects leads to a change in 0.7 PFR units, whereas this results in a smaller increase for members of Group 2 (0.31 PFR units) and Group 3 (0.12 PFR units). There are no significant differences between the group-mean values for the times to peak filling rate for either of the CAD groups compared with normals (Fig. 5).

When an arbitrary cutoff point of 1.61 EDV/sec is chosen, this being the lowest value seen in our normals, abnormally depressed PFR values are seen in 14 of the 27 patients (52%) in Group 2 and, similarly, in 20 of the 23 patients (87%) in Group 3. Again, using the highest

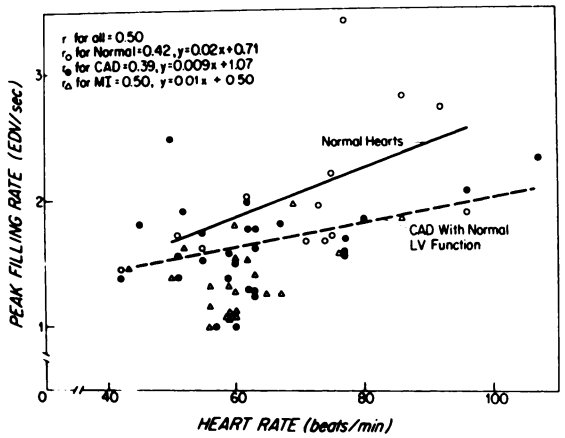

FIG. 3. Relationship of PFR to heart rate of individuals in three groups of subjects. Solid line shows regression for normal subjects, and dotted line for CAD patients with normal systolic function. (Regression for CAD patients with MI not shown.)

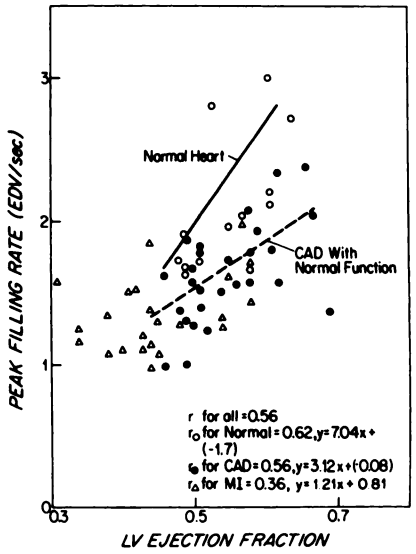

FIG. 4. Relationship of PFR to LVEF of individuals in three groups of subjects. Solid line shows regression for normal, and dotted line for CAD patients with normal systolic function. (Regression line for CAD patients with MI not shown.)

value for TPFR seen among our normals (200 msec), this time was significantly prolonged in seven of the 27 Group 2 patients and in five of the 23 Group 3 patients. The presence of either abnormal value was seen in 56% and 91% of Group 2 and 3 patients, respectively (Table 2). The incidence of abnormally depressed PFR values among patients without previous myocardial infarction is similar when subjects with three-vessel disease (7/17; 41%) are compared with those with either one- or two-vessel disease (7/10; 70%, Table 3).

Further study of PFR values for given ranges of heart

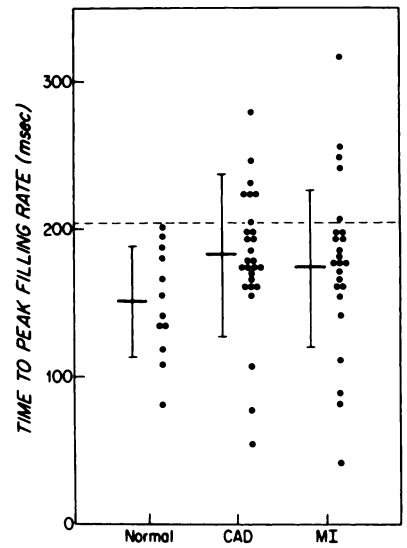

FIG. 5. Time to PFR for individuals in three groups of subjects: (1) normal subjects, (2) CAD patients with normal systolic function, and (3) patients wtih previous MI and impaired systolic function. There is no significant difference between mean values for groups.

TABLE 2.

	Normal systolic function	Abnormal systolic function due to M.I.	Total
Sensitivity PFR	14/27 = 0.52	20/23 = 0.87	34/50 = 68%
Sensitivity TPFR	7/27 = 0.26	4/23 = 0.17	11/50 = 22%
Sensitivity TPFR + PFR	15/27 = 0.56	21/23 = 0.91	36/50 = 72%

rates yielded significant differences between Groups 2 and 3 ($p < 0.05$) for rates spanning 40 to 59 BPM, and between Group 1 and Groups 2 and 3, respectively ($p < 0.01$, $p < 0.01$) for rates between 60 and 79 BPM (Table 4). A similar prevalence of abnormally depressed PFR was seen in Groups 2 and 3 for these heart-rate categories (Table 4).

Multivariate regression analysis was also performed to assess the relative relationships of heart rate and ejection fraction to PFR in these groups. Results were: *Group 1*, PFR = 6.2EF + 0.011BPM − 2.06 (r = 0.66); *Group 2*, PFR = 3.15EF + 0.010BPM − 0.67 (r = 0.67); and *Group III*, PFR = 1.51EF + 0.017BPM − 0.38 (r = 0.67). Thus, with a fixed heart rate, a unit change in EF will result in PFR changes of 0.06, 0.03, and 0.015 in Groups 1, 2, and 3. Likewise, with a fixed EF, a heart-rate change of 1 BPM will result in PFR changes of 0.011, 0.010, and 0.017 in Groups 1, 2, and 3. It is apparent that changes in PFR secondary to changes in heart rate are relatively constant in the three groups, and are smaller than changes secondary to alterations in EF.

Furthermore, the changes in PFR as related to changes in EF are greater for Group 1 than for Group 2, which in turn is larger than for Group 3. We would expect this relationship to exist, since PFR has been shown to be a more sensitive indicator of severity of CAD.

DISCUSSION

We were able to demonstrate that resting normalized peak diastolic filling rate (PFR), as determined by first-pass radionuclide angiography, is a sensitive indicator for the presence of resting myocardial dysfunction in CAD patients with and without antecedent myocardial infarction. These results agree with the work of Hammermeister and Warbasse (contrast ventriculography) (*16*) and with the more recent contributions by Bonow et al. (gated radionuclide ventriculography) (*17*) and Reduto et al. (first-pass radionuclide ventriculography) (*18*). Although our results confirm the sensitivity of the peak filling rate and time to peak filling rate as indices for the presence of resting myocardial dysfunction in CAD patients, the incidence of abnormal values among our subjects without previous myocardial infarction (56%) is lower than that reported by Bonow et al. (85%). We do observe, however, a similar incidence of depressed diastolic filling for patients with previous myocardial infarction (91% vs. 90%).

There is a systematic prolongation in the time necessary to reach peak diastolic filling rates among patients with coronary artery disease (Group 2: 183 ± 54 msec, Group 3: 176 ± 60 msec) compared with normals (Group 1: 151 ± 38 msec). Since this parameter alone is abnormally prolonged in only 22% of our CAD patients, it appears to be a poor discriminator for presence or absence of disease (Table 2 and Fig. 5).

Although we applied a method of analysis similar to that adopted by Bonow et al. (*17,21*), our ranges for normal and abnormal peak filling rates are slightly lower than their values. We believe that this is due to the algorithm used to construct our ventricular time-activity curves. Previously these curves had been extracted from ventricular time-activity curves synchronized to the patient's electrocardiogram. Our algorithm constructs the global diastolic filling curve by aligning end-systole on the end-systolic points of the individually selected cardiac beats. The determination of these local minima, although heavily dependent on the counting statistics, does not seem to affect the reliability of the obtained data and of the subsequently derived peak filling rates. The generally lower PFR values are in line with the ranges

TABLE 3. PFR IN GROUP 2 PATIENTS ACCORDING TO SEVERITY OF CAD

Number of vessels diseased	PFR (EDV/sec)		Heart rate (BPM)		No. of patients wtih PFR < 1.61 EDV/sec
	Range	Mean	Range	Mean	
1 VSD*	0.9–2.33	1.49 ± 0.44*	51–109	64.3 ± 16.5*	7/10
2 VSD					
3 VSD	1.37–2.49	1.71 ± 0.29*	45–96	63.2 ± 14.1	7/17

* p = N.S. according to Mann-Whitney test.
VSD = vessels diseased.

TABLE 4. PFR ACCORDING TO DIFFERENT RESTING HEART RATES

	Heart rates	40–59 BPM	60–79 BPM	80–99 BPM
GROUP 1	PFR (EDV/sec)	1.67 ± 0.09	2.14 ± 0.72$^{O,\Delta}$	2.49 ± 0.52
	% abnormal (< 1.61 EDV/sec)	0/2	0/7	0/3
GROUP 2*	PFR (EDV/sec)	1.62 ± 0.41†	1.55 ± 0.29^{O}	1.97 ± 0.15
	% abnormal (< 1.61 EDV/sec)	60% (6/10)	54% (7/13)	0% (0/2)
GROUP 3	PFR (EDV/sec)	1.23 ± 0.18†	1.42 ± 0.27$^{\Delta}$	1.85
	% abnormal (< 1.61 EDV/sec)	91% (10/11)	82% (9/11)	0% (0/0)

* Two outlying points are at 2.33 and 1.37 EDV/sec for heart rates of 109 and 42 BPM, respectively.

† Significant, $p < 0.05$ for Group 2 vs. 3.

$^{O,\Delta}$ Significant, $p < 0.01$ for Group 1 vs. 2 and 1 vs. 3.

of our RVG global EFs. These have been well correlated with values obtained by contrast angiography but are systematically lower (CVEF = 0.9 RNEF + 0.13). We also limited the procedure used to determine TPFR and PFR to a single fitting of a third-order polynomial over the first 400 msec of diastole or the whole of diastole, whichever is shorter. This was done in order to prevent inconsistent results due to the additional random noise created during the fusion of the component beats into a representative cardiac cycle; the smoothing properties of such a polynomial would not have been as effective over a shorter data range. The use of such a polynomial over a larger range of data, however, does filter out some higher-order information and, therefore, reduces the amplitude of its first derivative, the curve describing filling rates.

The validity of time-activity curves derived from first-pass radionuclide angiography for the investigation of diastolic filling has been confirmed by another group. Reduto et al. (*18*) were able to obtain accurate and reproducible values for indices of diastolic function using left-ventricular time-activity curves obtained and processed by instrumentation similar to our own. These investigators analyzed the diastolic portion of the time-radioactivity curve of the individual beats with subsequent smoothing instead of using the representative cycle as we did. They emphasized the sensitivity of the filling fraction as an index of the presence of coronary artery disease. They also correlated the radionuclide method with echocardiographic parameters of diastolic function.

We observe a mild correlation between LVEF and PFR (Group 1: r = 0.62; Group 2: r = 0.56; Group 3: r = 0.36). A similar relationship had been described by Bonow et al. (*17*) and, similarly, by Hammermeister and Warbassee (*16*) for the relation between peak filling rate and stroke volume. Whether this represents a direct relationship between these parameters of a common dependence on preload, afterload, and contractility is impossible to ascertain at this time. There appears, however, to be a significant difference between our normals and patients with CAD when peak filling rates are compared at equivalent ejection fractions (Fig. 4). There is also significant modification in the slope of this relationship for patients with CAD (Fig. 4). For an equivalent increase of 0.1 EF value, CAD patients are unable to increase PFR values by more than 0.31 units (Group 2) and 0.12 units (Group 3), whereas normals show an increase of 0.70 units. Furthermore, there is a systematic difference between CAD patients with and without systolic myocardial dysfunction, the greatest impairment being seen in the former group. These observations agree well with the belief that impaired ventricular distensibility is an early and persistent manifestation of coronary artery disease.

We also note a mild correlation between peak filling rate and heart rate in normals and CAD patients, whereas Hammermeister and Warbasse (*16*) did not observe a similar phenomenon. Interestingly, this relation is different for each of the three groups studied (Fig. 3). Normal subjects seem to increase their PFR values, for a given increment in heart rate, more than CAD patients do. This suggests that the discriminative ability of PFR may be enhanced at higher heart rates. However, our study population is too small to confirm such an effect with any certainty. The group differences in heart rates between our CAD and non-CAD patients are easily explained by the high prevalence of propranolol administration in our CAD population. The potential effect that this drug might have and the heterogeneous nature of our control group limit the applicability of our results to the proper screening of patients with or without CAD. The lack of any direct effect on diastolic filling rates by the negative chronotropic action of propranolol has been demonstrated both in patients with CAD (*18*) and in those with hypertrophic cardiomyopathy (*23*). This can

be understood further in light of Hammermeister's findings (*16*) for heart rates with normal physiological ranges; the shortening of the cardiac cycle due to increases in heart rate affects mostly the later portions of diastole and causes a disproportionate reduction in the duration of diastasis. More importantly, despite similar distributions for age, drug history, and resting heart rate, there are significant differences in the PFR values of our Group 2 and 3 patients. Such a finding best fits the hypothesis that the depression in peak filling rate parallels the change in the functional status of the myocardium in CAD patients. A more precise characterization of the dependence of PFR on other parameters must await further studies with larger patient groups, or experiments in rigidly controlled canine preparations. Our preliminary analysis of the incidence of abnormal PFR values in patients with three-vessel disease compared with those with either 1 or 2 VSD does not reveal any clustering of abnormal values toward the former group. This finding has recently been confirmed (*37*).

Recent evidence suggests that parameters measuring diastolic function are more sensitive than those measuring systolic function for detecting the effects of acutely induced myocardial ischemia (*24*). There is also evidence that the diastolic properties of the left-ventricular myocardium are chronically modified in patients with coronary artery disease (*25*). Parameters associated with early ventricular relaxation are depressed in these patients. Both maximal negative dp/dt and the derived relaxation-time index "T" are significantly different between normals and patients with CAD (*24,25*). These indices of myocardial relaxation have also been shown to depend slightly on both heart rate and ejection fraction. Since the maximum rate of change of ventricular volume during diastole occurs later than peak $-dp/dt$, at a time when LV pressure changes are actually at a minimum, the two phenomena are probably not directly related, but may instead reflect different facets of the ventricular dysfunction engendered by CAD.

Changes in ventricular compliance are another of the manifestations of myocardial dysfunction seen in patients with CAD. The diastolic pressure-volume curves of these patients can be acutely displaced during myocardial infarction (*6*) or ischemia (*26*). It appears unlikely that changes in ventricular compliance ($\Delta V/\Delta P$) can adequately explain our findings and others', since the peak filling rates occur in a portion of diastole that corresponds more closely to the point of minimum left-ventricular pressure. At this time, compliance bears no physical significance, since it is near a point of mathematical discontinuity as ΔP approaches zero (*27*). Furthermore, changes in the pressure-volume relationships are apt to occur during ischemia or exercise and seem to be sensitive to the mechanical effects of right-ventricular function (*28,29*). Such mechanisms are unlikely to explain any of the resting abnormalities in left-ventricular diastolic function that are seen in our patients.

Early diastolic filling, in contradistinction to late filling caused by atrial systole, is responsible for the presence of quite a significant amount of blood in the ventricle even before diastolic pressure reaches a minimum (*30,31*). Unfortunately, there are few ventricular models capable of describing the complex dynamics and interactions between pressure and volume during this portion of the cardiac cycle. It is reasonable, however, to expect that early ventricular filling is dependent on both the pressure gradient across the mitral valve and on the resistance of the ventricular wall to distension. Given that ventricular relaxation is responsible for a continued and independent monoexponential decay in LV pressure during a significant amount of time following the opening of the mitral valve, then maximum filling rates would occur later and reach lower maximum values when the time constant of pressure decay is prolonged. Some authors have reported such a prolongation of this time constant in CAD patients at rest (*25*) and during exercise (*24*). Another mechanism would involve alteration of ventricular viscoelastic properties. In such a case, ventricular filling would be damped by the myocardium's inability to expand quickly enough during periods of rapid filling. Such a theory would concur with the hypothesis that myocardial viscosity depends not only on volume but also on the rate of volume change; thus, ventricular pressure would be inexplicably elevated during rapid filling (*32–34*). Experimental observations showing deviations in the pressure-volume relationship at the point of rapid atrial filling are explained by such an effect (*34–36*). That ischemia could affect this relation detrimentally is possible, but there are as yet no conclusive data that would confirm the existence of such an effect during early diastole.

It has yet to be determined whether either or both of these mechanisms could explain the alterations in myocardial distensibility that we and others have observed at rest in patients with CAD. We conclude that there is a resting abnormality in the ventricular diastolic function of patients with CAD. This modification of diastolic mechanics is reflected by a significant decrease in the early peak diastolic filling rate. It is seen in almost all patients with previous infarction and in over half of CAD patients without measurable myocardial damage as evidenced by normal EFs. The noninvasive detection of this abnormality is easily implemented by first-pass radionuclide ventriculography. Potentially, its value for the detection of CAD may be further enhanced when it is used with some form of myocardial stress (*18*).

FOOTNOTES

* Baird System 77.
† Hewlett-Packard 67.

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