Diastolic Function in Acute Myocardial Infarction: A Radionuclide Study

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We studied left ventricular diastolic function by equilibrium gated radionuclide angiography in patients as follows: 75 with acute myocardial infarction (AMI), 35 with anterior or anteroseptal necrosis (Group A) and 40 with inferior, inferolateral, or posterior necrosis (Group I). The ejection fraction (EF) was lower in Group A than Group I (41.9 ± 2.5 vs. 57.1 ± 2.0%, $p < 0.001$), as was peak diastolic filling rate normalized to end diastolic volume (PDFR-EDV/sec) (1.9 ± 0.1 vs. 2.4 ± 0.1 EDV/sec, $p < 0.05$). PDFR normalized to stroke volume was similar in both groups. An excellent linear correlation was found between EF and PDFR-EDV/sec in the total study population. Isovolumic relaxation period (IRP) was beyond our upper normal value of 94 msec in 64% of patients and it was shorter in Group A than I (95.8 ± 12.7 vs. 147.0 ± 13.6 msec, $p < 0.05$). The presence of shorter IRP in Group A than in I is probably a result of an earlier mitral valve opening as a consequence of higher left atrial pressure.

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Left ventricular (LV) diastolic filling abnormalities are common in patients with coronary artery disease, even in those with normal global and regional LV systolic function (*1–5*). Ischemia appears to reduce LV distensibility by way of several mechanisms, among which are impaired LV relaxation, LV asynchrony, and altered composition of left ventricular wall (i.e., increased fibrosis) (*1*). In patients with previous myocardial infarction, the extent and site of fibrosis are likely to play a major role in the impairment of diastolic function.

Limited data are available concerning LV diastolic function in patients with acute myocardial infarction (AMI) (*1–5*). Furthermore, few data are available concerning the influence of different sites of myocardial necrosis on left ventricular diastolic filling (*6*).

The purpose of this study was to investigate LV diastolic function utilizing radionuclide angiography (RNA) in patients with AMI and to evaluate the relationships between diastolic parameters and systolic function.

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MATERIALS AND METHODS

Study Population

We studied 75 patients (59 males and 16 females, mean age 57.6 yr, range 27–75 yr) referred to our Coronary Care Unit for a first transmural AMI between July 1985 and June 1986. All patients underwent RNA between the seventh and tenth day after the onset of symptoms and were in sinus rhythm at the time of the study. Acute myocardial infarction was diagnosed when two of the following criteria were met: ischemic chest pain lasting for more than 30 min, typical EKG changes, and elevation of creatine kinase levels. A transmural AMI was diagnosed when a new Q wave appeared. The patients were divided as follows: 35 patients (Group A) with anterior or anteroseptal AMI and 40 patients (Group I) with inferior, infero-lateral or posterior AMI. There was no difference in drug administration between the two groups; nitrates and calcium channel blockers were discontinued 12 hr before the study, while antiplatelet drugs and anticoagulants were allowed; five Group A and three Group I patients were taking digitalis which was not discontinued at the time of the study. No patient was on beta-blocking drugs.

Radionuclide Angiography

High temporal resolution equilibrium gated RNA was performed with the patient at rest in the supine position. Red blood cells were labeled in vivo with 25 mCi of technetium-99m (*7*). Imaging was performed with a small field-of-view

Anger camera equipped with a low-energy, general purpose, parallel hole collimator, oriented in the 45° left anterior oblique position with a 15° of caudal tilt. Data were acquired in frame mode by computer-based EKG gating, with 2× digital zoom. The imaging rate was 20 msec/frame (i.e., 50 frames/sec) with a gate tolerance of 5%, to minimize distortion in the diastolic part of curve; at least 150,000 counts per frame were collected. Ejection fraction (EF) was measured on the raw time-activity curve by standard technique (*8*). The following parameters were calculated on the time-activity curves filtered using a Fourier expansion with five harmonics: time to end systole (TES, msec) was measured from R wave to the nadir of the time-activity curve; peak diastolic filling rate of the first half of diastole (PDFR) was normalized to end diastolic volume (PDFR-EDV/sec) as described by Poliner et al. (*9*) and it was also normalized to stroke volume (PDFR-SV/sec) (*10*); time to peak diastolic filling rate (TPDFR, msec) was defined as the interval between end-systole and PDFR. The isovolumic relaxation period (IRP, msec) was calculated as previously described (*11*): IRP is terminated by the onset of rapid filling, represented by an inflection point followed by an abrupt increase in slope on the raw time-activity curve (Fig. 1). This point was automatically identified on the second derivative curve as the first maximum occurring between end systole and TPFR. An algorithm was designed to measure automatically the time interval from the R wave to the onset of rapid filling. From this time interval, TES was subtracted and the resulting value was defined as IRP. Accuracy and reproducibility of previous measurements have been reported elsewhere (*12*).

Statistical Analysis

All data were expressed as mean ± S.E. Comparison between groups was performed by unpaired t-test; the relationships among parameters were assessed by linear regression; p values < 0.05 were considered significant (*13*).

RESULTS

Mean values and standard errors for all variables studied are given in Table 1.

Ejection Fraction

EF in the total study population was 50.0 ± 1.8% and was lower in Group A than in Group I (41.9 ± 2.5 vs. 57.1 ± 2.0%, $p < 0.001$).

Time to End Systole

No significant difference was found between Group A and Group I.

Peak Diastolic Filling Rate

PDFR in the total population was 2.2 ± 0.1 EDV/sec. It was below our lower normal limit of 2.8 EDV/sec (*12*) in 29 (83%) Group A and 26 (65%) Group I patients; hence, the mean value of PDFR-EDV/sec was lower in Group A than in Group I. When PDFR was measured in SV/sec Group A values were similar to those of Group I.

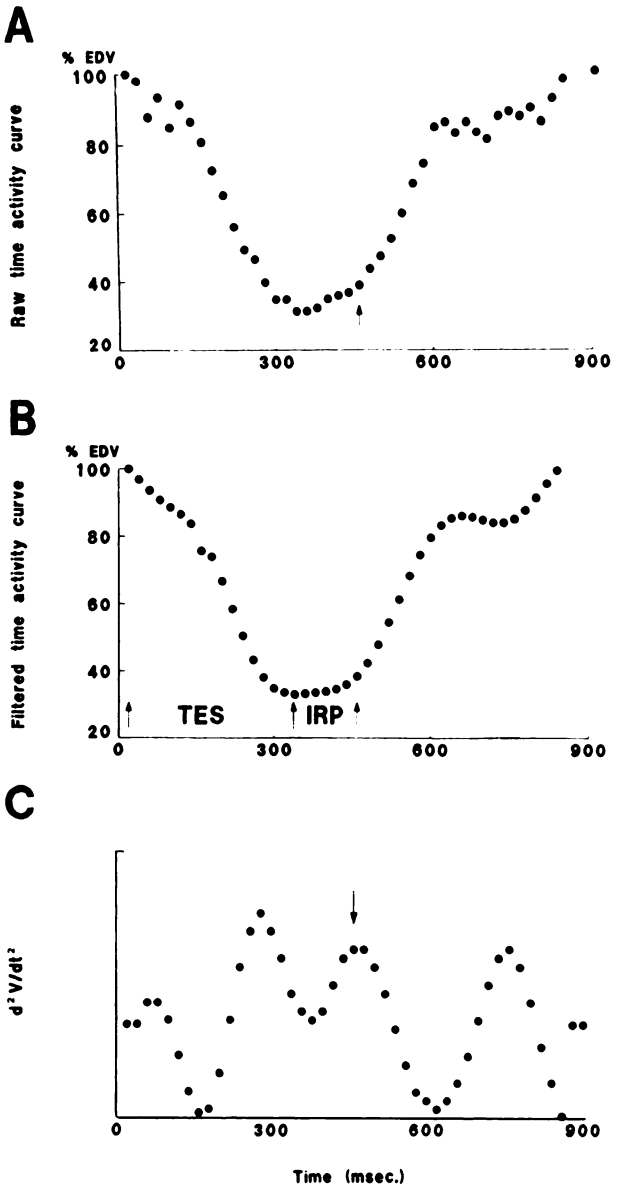

FIGURE 1
A: Raw time-activity curve of a patient. B: Time-activity curve after Fourier filtering with five harmonics. C: Second derivative curve obtained from the filtered curve in B. A maximum after end systole is present on the derivative curve (arrow) and corresponds to the termination of the isovolumic relaxation period and to the onset of rapid filling in A and in B. Each point represents 20 msec. TES = time to end systole, EDV = end diastolic volume.

Time to Peak Diastolic Filling rate

TPDFR was lower in Group A than I ($p < 0.05$).

Isovolumic Relaxation Period

IRP was measured in only 55 patients (25 Group A and 30 Group I) because our automatic program did not identify the onset of rapid filling in the other 20 patients, either because the transition between relaxation and filling was too smooth or there was statistical noise in the raw time-activity curve. The mean value

TABLE 1
Left Ventricular Systolic and Diastolic Parameters Obtained by Radionuclide Angiography

	Total study population	Group A	Group I
EF%‡	50.0 ± 1.8	41.9 ± 2.5	57.1 ± 2.0*
TES msec§	328.2 ± 8.8	330.7 ± 14.7	323.4 ± 10.5
PDFR EDV/sec¶	2.2 ± 0.1	1.9 ± 0.1	2.4 ± 0.1†
PDFR SV/sec	4.3 ± 0.1	4.5 ± 0.2	4.2 ± 0.2
TPDFR msec**	178.3 ± 7.6	161.1 ± 10.6	193.3 ± 10.3†
IRP msec††	123.9 ± 9.9	95.8 ± 12.7	147.2 ± 13.6†

* $p < 0.001$.
† $p < 0.05$ vs. Group A.
‡ Ejection fraction.
§ Time to end systole.
¶ Peak diastolic filling rate.
** Time to peak diastolic filling rate.
†† Isovolumic relaxation period.

was 123.9 ± 9.9 msec in the total study population and was lower in Group A than in Group I; IRP was >94 msec (the upper value of the 99% confidence limit in our normal population) in ten (40%) Group A and 25 (83%) Group I patients.

We found an excellent linear correlation between EF and PDFR-EDV/sec in the total population ($r = 0.79$, $p < 0.001$) (Fig. 2), as well as in Group A ($r = 0.80$, $p < 0.001$) and in Group I ($r = 0.76$, $p < 0.001$). No correlation was found between EF and PDFR-SV/sec.

DISCUSSION

Peak Diastolic Filling Rate

In our study 55 out of 75 patients (73%) had abnormal diastolic filling manifested by depressed PDFR-EDV/sec, which agrees with findings by Bonow et al. in patients with previous myocardial infarction (*1*). Although many patients with AMI had depressed systolic function, the diastolic impairment observed was not due solely to reduced systolic performance. In fact, despite the direct correlation observed between EF and PDFR-EDV sec, when we analyzed patients with normal EF (i.e., >55%), we found a subnormal PDFR (i.e., < 2.8 EDV/sec) (*12*) in 45% of them, with no differences between Group A and I.

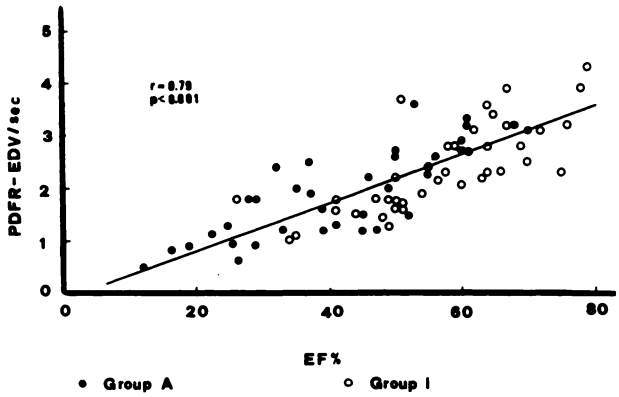

FIGURE 2
Relationship between ejection fraction (EF) and peak diastolic filling rate normalized to EDV/sec (PDFR) in study population.

Normalization of PDFR to SV has been suggested to be superior to PDFR-EDV/sec in terms of ability to distinguish normals from coronary artery disease patients (*10*). In our study PDFR-SV/sec was unable to distinguish Group A from I. This result is in agreement with that of Shaffer et al. who were able to distinguish patients into groups according to EF utilizing PDFR-EDV/sec but not other PDFR normalizations (*14*). Shaffer concluded that any normalized PDFR may not be related to true filling, although any parameter which actually separates two groups may be useful independent on what it, in fact, measures. In our study the extent of myocardial damage and ventricular enlargement rather than the site of necrosis probably, influences PDFR-EDV/sec. Moreover, the role of other determinants, such as abnormal LV relaxation and stiffness and the driving pressure of LV, cannot be disregarded. It has been demonstrated that myocardial ischemia prolongs LV relaxation (*15*) and that abnormal relaxation influences the diastolic pressure/volume relationship of the intact working left ventricle (*16,17*). However, an increased chamber stiffness also could contribute to this phenomenon in humans with ischemic heart disease (*17*).

Despite these limitations, rapid filling is an important and clinically useful parameter that is readily measured noninvasively by scintigraphic technique. Our data suggest that in AMI patients normalization to EDV rather than to SV distinguishes patients with different diastolic filling impairment.

Isovolumic Relaxation Period

No data are currently available concerning IRP in patients with AMI, but the results of the present study indicate that this parameter is prolonged. The difference between patients with anterior and inferior myocardial infarction remains to be explained. In the setting of a more compromised LV function, one would expect Group A patients to have abnormally prolonged IRP values. However, this was not the case. In fact, isovolumic relaxation was longer in patients with inferior than anterior infarction; moreover, it was abnormal in 83% of Group I and in only 40% of Group A patients.

Our method of computing isovolumic relaxation subtracts TES from the time interval from the R wave to the beginning of rapid filling. Therefore, a prolonged TES could be responsible for the shorter IRP in Group A patients. However, in both groups, TES values were comparable, so that an earlier onset of rapid filling in Group A must be the mechanism responsible.

Rapid filling starts with mitral valve opening: during isovolumic relaxation, left ventricular pressure falls toward left atrial pressure; at the point of atrioventricular pressure crossover, the valve opens quickly and rapid early filling starts without delay (*18*). Ishida et al. demonstrated in dogs that volume loading induces an increase in left atrial pressure and a shortening in IRP (*19*). Although hemodynamic data are not available in this study, it is likely that our Group A patients had higher LV end diastolic pressure which induces higher left atrial pressure; we suppose that during isovolumic relaxation, if left atrial pressure is more elevated the atrioventricular pressure crossover and the mitral valve opening occur earlier. This mechanism may be responsible for the relatively short IRP in Group A patients.

Therefore, during the acute phase of myocardial infarction, if left ventricular end diastolic pressure and left atrial pressure remain in the normal range, myocardial ischemia may result in an IRP prolongation, but if left atrial pressure is increased this may induce shortening of the left ventricular IRP. It should be considered that none of the parameters discussed above is independent and all factors interact during isovolumic relaxation. In AMI patients, IRP may be more or less prolonged according to the prevalence of factors that prolong relaxation, i.e., myocardial ischemia, or that induce the mitral valve to open early, i.e., left atrial pressure.

CONCLUSION

Our study demonstrates that LV diastolic filling abnormalities are common in patients with AMI. The EF and PDFR-EDV/sec are more severely compromised in patients with anterior than inferior myocardial infarction. Peak diastolic filling rate normalized to EDV/sec is a useful index for identifying AMI patients with different diastolic filling impairment. Isovolumic relaxation period is prolonged in patients with AMI, but less in anterior than in inferior infarcts, probably as a consequence of an increase in left atrial pressure.

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