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Effects of Regional Systolic Asynchrony on Left Ventricular Global Diastolic Function in Patients With Coronary Artery Disease

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Patients with coronary artery disease often have impaired left ventricular diastolic filling despite normal global systolic function. The influence of regional systolic asynchrony on diastolic function was assessed by radionuclide angiography in 60 patients with coronary artery disease and normal ejection fraction at rest: group 1 (n = 30) with normal wall motion at rest and group 2 (n = 30) with abnormal wall motion. Data were compared with those obtained from 19 normal volunteers.

Age, heart rate, ejection fraction and echocardiographic end-diastolic dimension did not differ among the three groups. Peak filling rate in group 1 and group 2 was similar (2.5 ± 0.5 and 2.3 ± 0.6 end-diastolic counts/s, respectively) and significantly lower than that in the normal subjects (2.8 ± 0.7 end-diastolic counts/s; $p < 0.01$ vs. group 2, $p < 0.05$ vs. group 1). Time to peak filling rate was prolonged in group 2 (184 ± 27 ms) compared with that in normal subjects (162 ± 19 ms; $p < 0.01$) and group 1 (172 ± 15 ms; $p < 0.05$). Left ventricular end-diastolic pressure was significantly higher in group 2 than in group 1 (14 ± 7 vs. 10 ± 5 mm Hg, respectively; $p < 0.05$).

Asynchrony was assessed by sector analysis of the radionuclide left ventricular region of interest. Diastolic asynchrony was similar in the two patient groups (30 ± 23 ms in group 2, 26 ± 16 ms in group 1) and was higher in both groups than in the normal subjects (16 ± 8 ms; $p < 0.01$). However, systolic asynchrony was higher in group 2 (32 ± 15 ms) than in both group 1 (14 ± 6 ms; $p < 0.01$) and the normal group (9 ± 6 ms; $p < 0.01$). In the total group of patients with coronary artery disease, systolic asynchrony correlated with global time to peak filling rate ($r = 0.53$; $p < 0.001$). This correlation became stronger when only group 2 was considered ($r = 0.62$; $p < 0.001$). Moreover, in group 2 systolic asynchrony correlated with the duration of the isovolumetric relaxation period ($r = 0.58$; $p < 0.001$) and the isovolumetric relaxation period, in turn, correlated with global time to peak filling rate ($r = 0.72$; $p < 0.001$).

Thus, left ventricular systolic asynchrony affects both the relaxation and filling phases of diastole, thereby contributing to the impairment of diastolic function commonly observed in patients with coronary artery disease.

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Left ventricular diastolic function is often impaired in patients with coronary artery disease and normal global systolic function at rest (1,2). The impairment of filling observed in many patients with normal systolic wall motion has been related to increased diastolic asynchrony (3–5). The possible contribution of systolic asynchrony to alterations of diastolic function has been less extensively investigated. Experimental (6–9) and clinical data (10,11) suggest that systolic asynchrony may decrease the rates of relaxation and filling in patients with coronary artery disease. As a consequence of systolic inhomogeneity, it is conceivable that some regions of the left ventricle may be developing tension or be incompletely relaxed at the onset of mitral valve opening, thus delaying the filling process and contributing to compromise of global diastolic function. Moreover, abnormalities in regional contraction may also exert abnormal end-systolic loading conditions on relaxing myocardium (12–15). Accordingly, in the present study we investigated the influence of regional systolic asynchrony on indexes of global diastolic filling at rest in patients with coronary artery disease and normal ejection fraction at rest.

Methods

Study patients. We studied 60 patients with coronary artery disease who underwent radionuclide angiography at rest, left ventriculography and coronary arteriography. There were 56 men and 4 women from 40 to 74 years old.

All patients fulfilled the following criteria: 1) significant coronary artery disease, defined as the presence of a significant stenosis (>50% reduction in lumen diameter) in at least one major coronary vessel; 2) normal left ventricular ejection fraction at rest, as determined by radionuclide angiography; and 3) no electrocardiographic (ECG) evidence of conduction abnormalities. The lower limit of normal for ejection fraction at rest in our laboratory is 45% (2). Studies were performed in all patients after administration of cal-

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cium channel blocking agents and beta-adrenergic blocking agents had been discontinued for ≥48 h, long-acting beta blocking agents for ≥72 h and nitrate preparations for ≥6 h. All patients gave informed written consent to the protocol, which was approved by the Institutional Human Research Review Committee in 1977. The estimated radiation exposure from the radionuclide angiography was 0.36 rad total body dose.

Patients were classified into two groups: group 1 comprised 30 patients with normal left ventricular regional wall motion at rest as assessed by both radionuclide angiography and contrast ventriculography; and group 2 comprised 30 patients with rest regional wall motion abnormalities as assessed by both studies. No patient in group 1 had abnormal ECG Q waves compared with 22 (73%) of 30 patients in group 2.

Radionuclide data in the two groups with coronary artery disease were compared with those obtained from 19 asymptomatic, normal volunteers (13 men and 6 women) who had no evidence of cardiovascular diseases on the basis of history, physical examination, blood pressure, ECG findings and echocardiographic examination.

All normal subjects and 40 of the 60 patients (22 in group 1 and 18 in group 2) underwent M-mode and two-dimensional echocardiography to measure left ventricular end-diastolic dimension and wall thickness of the free wall and interventricular septum. Only one patient in group 1 showed a septal wall thickness >13 mm; no other patient showed echocardiographic evidence of left ventricular hypertrophy.

Gated blood pool scintigraphy. Radionuclide angiography was performed with the patient in the supine position with use of red blood cells labeled in vivo with 15 to 25 mCi of technetium-99m and a conventional Anger camera equipped with a high sensitivity, parallel hole collimator oriented in a modified left anterior oblique position. A total of 10.5 million counts were collected for each study. High temporal resolution (20-ms/frame) cardiac image sequences were constructed by computer-based ECG gating using list mode data acquisition with exclusion of extrasystolic and postextrasystolic beats and combined forward and reverse gating from the R wave (16). Left ventricular time-activity curves representing relative changes in left ventricular volume during the average cardiac cycle were generated from the cardiac image sequence after background correction with a fixed region of interest, which was constructed manually to conform to the borders of the left ventricle as identified from the end-diastolic image, stroke volume image and amplitude image. This latter functional image was created by approximating each single-pixel time-activity curve from the first harmonic of its temporal Fourier expansion (17). After the region of interest was identified in this manner, the time-activity curve was constructed from the raw image sequence without spatial or temporal smoothing processes.

Analysis of global left ventricular function. Indexes of global left ventricular function were derived by computer analysis of the background-corrected time-activity curve. Ejection fraction was computed on the basis of relative end-diastolic and end-systolic counts. Time to end-systole was measured from the R wave to the nadir of the time-activity curve. Peak filling rate was computed by fitting third-order polynomial functions to the rapid diastolic filling portions of the time-activity curve by a least squares technique (2). Time to peak filling rate was obtained by setting the second derivative of the polynomial function to zero and was measured relative to end-systole. Peak filling rate was computed in left ventricular counts/s, normalized for the number of counts at end-diastole and expressed as fractional end-diastolic counts/s.

The isovolumetric relaxation period was defined as the interval of the time-activity curve between minimal left ventricular volume and the onset of rapid filling. This interval was identified, as previously described (18), by automatically filtering the time-activity curve with a Fourier expansion with four harmonics and computing the second derivative of this filtered curve. The first maximum on the second-derivative curve occurring between end-systole and the time to peak filling rate was considered to be the inflection point marking the onset of rapid filling. An algorithm was designed to measure the time interval between the R wave and this inflection point automatically. From this time interval, time to end-systole was subtracted and the resulting value was considered the isovolumetric relaxation period. Previous studies (18) in our laboratory in patients with hypertrophic cardiomyopathy demonstrated an excellent correlation between the onset of rapid diastolic filling assessed by this method and that measured by the timing of mitral valve opening by echocardiography.

Analysis of regional left ventricular nonuniformity. The left ventricular region of interest was divided into 20 sectors of equal arc (18°), each emanating from the end-diastolic left ventricular center of gravity, as previously described (19). The inner one third of each sector was excluded, yielding annular sectors comprising the outer two thirds of the left ventricle. From these fixed regions sectorial time-activity curves were constructed, representing the change in the number of counts within each sector during the average cardiac cycle. To evaluate regional systolic asynchrony, we approximated the time to minimal volume of the 20 sectors from the nadir of the sector time-activity curves. The standard deviations of these values were considered an index of systolic asynchrony. To improve precision and reduce errors stemming from counting fluctuation within these smaller regions, we created quadrants by combining the 20 sectors into four quadrants of 5 sectors each (4). Regional time-activity curves were then generated from each quadrant and were fitted to a Fourier expansion with three harmonics. From each fitted curve, the time to minimal volume and the time to peak filling rate were computed. Time to minimal volume was computed from the R wave, whereas time to peak filling rate, as in the global left ventricular curve, was computed from each quadrant's time to minimal volume. As

Table 1. Characteristics of the Study Groups

	Normal Subjects	CAD Group 1	CAD Group 2
Age (yr)	57 ± 9	59 ± 8	56 ± 9
HR (beats/min)	67 ± 10	67 ± 10	64 ± 11
SBP (mm Hg)	131 ± 13	136 ± 15	139 ± 25
DBP (mm Hg)	83 ± 10	80 ± 9	80 ± 11
LVEDD (mm)	48 ± 6	48 ± 5	50 ± 6
LVEDP (mm Hg)	—	10 ± 5	14 ± 7*

*Different from group 1, $p < 0.05$. CAD = coronary artery disease; DBP = diastolic blood pressure; Group 1 and Group 2 = patients with, respectively, normal and abnormal wall motion at rest; HR = heart rate; LVEDD = left ventricular end-diastolic dimension; LVEDP = left ventricular end-diastolic pressure; SBP = systolic blood pressure.

Table 2. Radionuclide Indexes of Global Left Ventricular Function in the Three Study Groups

	Normal Subjects	CAD Group 1	CAD Group 2
Ejection fraction (%)	56 ± 6	56 ± 5	52 ± 5
Time to minimal volume (ms)	374 ± 22	369 ± 24	361 ± 32
Isovolumetric relaxation period (ms)	62 ± 27	77 ± 14	72 ± 40
Peak filling rate (end-diastolic counts/s)	2.8 ± 0.7*	2.5 ± 0.5	2.3 ± 0.6
Time to peak filling rate (ms)	162 ± 19	172 ± 15	184 ± 27*

*Different from group 1, $p < 0.05$ and from group 2, $p < 0.01$; †different from normal group, $p < 0.01$ and from group 1, $p < 0.05$. Abbreviation as in Table 1.

an index of left ventricular systolic asynchrony, we averaged the absolute differences between quadrant time to minimal volume and the global value of time to minimal volume. Similarly, diastolic asynchrony was assessed as the average absolute difference between quadrant time to peak filling rate and the corresponding global value. Reproducibility of this method has been previously described (4).

Statistical analysis. All data are expressed as mean values ± SD of the mean. One-way analysis of variance was used for overall comparison among groups. Then the Bonferroni method was used to compare each group with the others. Percent data were compared by chi-square analysis. All correlations reported were analyzed by linear regression analysis. As a minimal level of significance a p value < 0.05 was accepted throughout the study.

Results

Clinical characteristics (Table 1). Age, heart rate and systolic and diastolic blood pressure did not differ among the three groups of subjects. Left ventricular end-diastolic pressure (measured in 24 patients in group 1 and 24 patients in group 2) was significantly higher in patients in group 2 with wall motion abnormalities at rest than in patients in group 1 with normal wall motion at rest despite similar left ventricular end-diastolic dimensions.

Coronary angiographic findings. Of the 30 patients in group 1, 13 showed three-vessel, 9 two-vessel and 8 one-vessel coronary artery disease. These findings were similar to those in group 2 in which 11 patients had three-vessel, 10 had two-vessel and 9 had one-vessel coronary artery disease. However, 21 (70%) of the 30 patients in group 2 showing wall motion abnormalities at rest had at least one totally occluded epicardial coronary artery compared with 13 (43%) of group 1 patients with normal wall motion at rest ($p < 0.05$).

Global left ventricular function (Table 2). Ejection fraction and global time to minimal volume were not different among the three groups of subjects. Isovolumetric relaxation period (measured in 9 normal subjects and in 33 of the 60 patients) was prolonged in the two patient groups compared with values in normal subjects, although this difference did not reach statistical significance. Peak filling rate was similar in the two patient groups (2.5 ± 0.5 end-diastolic counts/s in group 1 and 2.3 ± 0.6 end-diastolic counts/s in group 2), and both values were significantly lower than that observed in normal subjects (2.8 ± 0.7 end-diastolic counts/s; $p < 0.05$ vs. group 1 and $p < 0.01$ vs. group 2). Global time to peak filling rate was prolonged in group 2 patients compared with that observed in the normal subjects ($p < 0.01$) and group 1 ($p < 0.05$).

Regional left ventricular function (Fig. 1). Systolic asynchrony was greater in group 2 (32 ± 15 ms) than in group 1 (14 ± 6 ms; $p < 0.01$) and in normal subjects (9 ± 6 ms; $p < 0.01$). The value in group 1 was also greater than that in the normal group ($p < 0.01$). Although diastolic asynchrony was also significantly higher ($p < 0.01$) in both patient groups than in the normal group (16 ± 8 ms), it did not differ between group 1 and group 2 patients (26 ± 16 vs. 30 ± 23 ms).

Relation between left ventricular asynchrony and global filling (Fig. 2 and 3). In the combined group of patients with coronary artery disease, global time to peak filling rate correlated significantly with regional systolic asynchrony as assessed by the standard deviation of sector time to minimal volume ($r = 0.53$; $p < 0.001$) (Fig. 2). This correlation was stronger when only patients in group 2, that is, those with wall motion abnormalities at rest, were considered ($r = 0.62$; $p < 0.001$).

In group 2, regional systolic asynchrony also correlated with the duration of isovolumetric relaxation period ($r = 0.58$; $p < 0.001$) (Fig. 3). Thus, an increase in systolic asynchrony corresponds to a delay in opening of the mitral valve. The isovolumetric relaxation period, in turn, correlated with the global time to peak filling rate ($r = 0.72$; $p < 0.001$).

Discussion

Asynchrony in patients with coronary artery disease. Homogeneity of left ventricular contraction and relaxation is a major determinant of left ventricular function (12,14,15).

JACC Vol. 19, No. 4
March 15, 1992:739–44

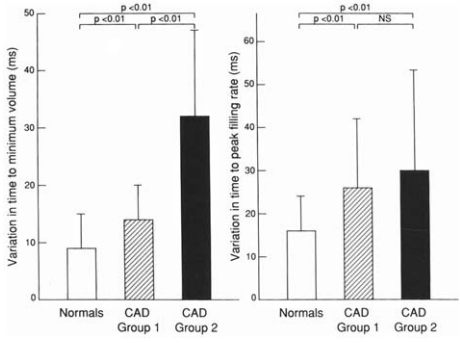


Figure 1. Left panel. Left ventricular systolic asynchrony, expressed as the regional variation in time to minimal volume among four left ventricular quadrants in normal subjects and in patients with coronary artery disease (CAD) with normal (Group 1) and abnormal (Group 2) regional wall motion. **Right panel,** Left ventricular diastolic asynchrony expressed as the regional variation in time to peak filling rate among four left ventricular quadrants.

Alterations in the homogeneity of the diastolic filling phase were previously reported in patients with coronary artery disease, normal systolic function and compromised global diastolic filling at rest (3–5). In those studies increased diastolic asynchrony was directly related to the impairment of global left ventricular filling; however, because the patients selected for study had no regional wall motion abnormalities by visual analysis, they did not manifest alterations in the timing of regional systolic events.

In the present study we investigated the role of systolic inhomogeneity in the impairment of diastolic function at rest in patients with coronary artery disease and normal left ventricular ejection fraction who were selected for the presence or absence of regional wall motion abnormalities at rest. Our findings confirm the results of the earlier investigations (3–5) in that the patients had impaired left ventricular filling compared with that of normal volunteers (Table 2), and the reduced rate and prolonged duration of rapid filling were associated with diastolic asynchrony (Fig. 1). However, although patients with regional wall motion abnormalities at rest had greater impairment of diastolic function than did patients without such abnormalities, the magnitude of diastolic asynchrony did not differ between the two groups. Both patient groups also manifested augmented systolic asynchrony at rest compared with values in the normal subjects. As expected from the selection criterion, systolic inhomogeneity was greater in the patient group with wall motion abnormalities at rest, reflecting the greater prevalence of abnormal ECG Q waves and greater severity of coronary artery disease in these patients.

Although the increased dispersion in regional timing of contraction is not surprising in patients with visually discernible contraction abnormalities, the evidence of systolic asynchrony at rest in patients with qualitatively normal ventriculograms is more unexpected. Although this observation differs from earlier reports in which patients with normal regional wall motion by visual analysis did not manifest systolic asynchrony (3,4), this apparent discordance may be explained by the high prevalence (43%) of patients with totally occluded coronary arteries in the group with normal wall motion in the current study. This finding is compatible with the earlier data of Holman et al. (20), showing regional

Figure 2. Relation between systolic asynchrony expressed as the standard deviation (S.D.) of time to minimal volume (TMV) among 20 left ventricular sectors and global peak filling rate in the patients with abnormal regional wall motion (**left**) and in all patients with coronary artery disease (**right**).

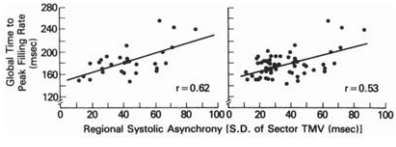
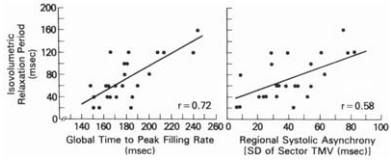


Figure 3. Relation between isovolumetric relaxation period and global time to peak filling rate (**left**) and between isovolumetric relaxation period and systolic asynchrony (**right**) expressed as the standard deviation (SD) of time to minimal volume (TMV) among 20 left ventricular sectors in the group of patients with coronary artery disease and abnormal regional wall motion.



nonuniformity of systolic function as evaluated by regional ejection fraction in patients with coronary artery disease, even in the absence of visually apparent abnormalities of regional wall motion. These data suggest an early, regional systolic disturbance identified by quantitative analysis of regional ventricular function but not detectable by routine qualitative analysis of left ventricular wall motion by both radionuclide angiography and contrast ventriculography.

Relation between systolic asynchrony and global diastolic filling. Several experimental studies (6–9) have focused on the effects of altered activation sequence on left ventricular relaxation and filling. In these studies left ventricular asynchrony, induced by right ventricular pacing (6), simultaneous right atrial and ventricular pacing (7), right atrioventricular sequential pacing (8) or intracoronary isoproterenol infusion (9), resulted in slowed relaxation and reduced peak velocity of filling.

Takeuchi et al. (10) demonstrated impaired left ventricular relaxation in patients with coronary artery disease and even in normal persons when asynchrony was induced by right ventricular pacing. However, in that study only the effects on left ventricular relaxation, not those on filling, were considered. In these previous studies no attempt was made to distinguish between the effects of regional systolic asynchrony from those of diastolic asynchrony on global diastolic function. The present data provide a means to assess these effects separately and indicate an effect of systolic asynchrony on global ventricular filling that is additive to the effect of regional diastolic asynchrony. When the total group of patients with coronary artery disease was considered, a positive linear correlation was found between the degree of systolic asynchrony and the global time to peak filling rate (Fig. 2). Thus, a left ventricle with more asynchronous contraction has greater delay in the timing of maximal filling velocity. This relation became stronger when only patients with qualitative wall motion abnormalities, and hence more pronounced systolic asynchrony, were considered. A similar relation between global peak filling rate and systolic asynchrony was previously reported (11) in a less selected population of patients with coronary artery disease with use of a different approach to assess left ventricular asynchrony.

Mechanisms. Although our findings do not elucidate the mechanisms by which altered systolic asynchrony can compromise global filling, some hypotheses can be made. Ejection timing has been shown to influence the rate of relaxation (21). Thus, it is conceivable that a different sequence of contraction in some areas of the left ventricle might affect relaxation not only by delaying its onset, but also by altering its rate. In addition, delayed contraction of ischemic areas of the ventricle could lead to persistent tension development and incomplete relaxation of those regions at the time of mitral valve opening (22–24). Moreover, the inhomogeneity of the regional contraction and relaxation phases might also affect late diastolic filling by reducing the extent of global ventricular relaxation (25). These changes might contribute to the higher left ventricular end-diastolic pressure in the patients with than in those without wall motion abnormalities, a finding that indicates reduced compliance because left ventricular dimensions were similar in the two groups (Table 1). Finally, abnormal regional contraction may also result in altered regional end-systolic loading conditions, which also affect the relaxation process (12–15).

Relation between isovolumetric relaxation period and systolic asynchrony. Impaired relaxation in both groups of patients with coronary artery disease is suggested by the trend toward a longer isovolumetric relaxation period in these groups compared with that in the normal subjects. Because both global time to peak filling rate and isovolumetric relaxation time are measured on the left ventricular time-activity curve from the time to minimal volume, this observation suggests that the prolongation of time to peak filling rate in these patients is, at least in part, accounted for by a prolonged isovolumetric relaxation time. This concept is supported by the significant correlation between the duration of isovolumetric relaxation period and global time to peak filling rate in the patients with regional wall motion abnormalities. This finding confirms the influence of relaxation in the subsequent filling phase of the ventricle during early diastole previously reported in patients with coronary artery disease (26). A similar relation between the isovolumetric relaxation period and the time to peak filling rate has also been reported (18) in patients with hypertrophic cardiomyopathy in whom impaired diastolic function at rest is commonly observed.

In the patients with regional wall motion abnormalities, and hence those with more severe systolic asynchrony, a significant relation was also observed between the degree of systolic inhomogeneity and the duration of isovolumetric relaxation. Thus, the more pronounced the dispersion in time to minimal volume throughout the ventricle, the longer is the delay in mitral valve opening and the beginning of rapid filling, presumably as a consequence of delayed pressure decrease in the ventricle (10). These findings are in agreement with previous data of Green et al. (27) showing that the duration of isovolumetric relaxation in the dog is influenced by systolic asynchrony produced by regional myocardial ischemia.

Limitations of the study. In the present study only the duration of the isovolumetric relaxation was measured, not the time constant of left ventricular relaxation. However, the duration of isovolumetric relaxation at a given preload was recently reported (28) to accurately reflect the time constant of relaxation and thus to be a reliable marker of the relaxation process.

Conclusions. Left ventricular systolic asynchrony plays an important role in determining abnormalities at rest of both the relaxation and rapid filling phases of diastole in patients with coronary artery disease. Systolic inhomogeneity leads to prolonged, inhomogeneous and presumably incomplete relaxation. In turn, prolonged relaxation contributes to reduced maximal velocity of filling and delay in the peak

velocity of filling, thus impairing rapid filling of the ventricle during early diastole.

References

1. Reduto LA, Wickemeyer WJ, Young JB, et al. Left ventricular diastolic performance at rest and during exercise in patients with coronary artery disease: assessment with first-pass radionuclide angiography. Circulation 1981;63:1228–37.
2. Borow RO, Bacharach SL, Green MV, et al. Impaired left ventricular diastolic filling in patients with coronary artery disease: assessment with radionuclide angiography. Circulation 1981;64:315–23.
3. Yamagishi T, Ozaki M, Kumada T, et al. Asynchronous left ventricular diastolic filling in patients with isolated disease of the left anterior descending coronary artery: assessment with radionuclide ventriculography. Circulation 1984;69:933–42.
4. Bonow RO, Vitale DF, Bacharach SL, Frederick TM, Kent KM, Green MV. Asynchronous left ventricular regional function and impaired global diastolic filling in patients with coronary artery disease: reversal after coronary angioplasty. Circulation 1985;71:297–307.
5. Perrone-Filardi P, Bacharach SL, Dilsizian V, Bonow RO. Impaired left ventricular filling and regional diastolic asynchrony at rest in coronary artery disease and relation to exercise-induced ischemia. Am J Cardiol 1991;67:356–60.
6. Blaustein AS, Gaasch WH. Myocardial relaxation. VI. Effects of beta-adrenergic tone and asynchrony on left ventricular relaxation rate. Am J Physiol 1983;244:H417–22.
7. Babler RC, Martin P. Effects of loading conditions and inotropic state on rapid filling phase of the left ventricle. Am J Physiol 1985;H523–33.
8. Zile MR, Blaustein AS, Shimizu G, Gaasch WH. Right ventricular pacing reduces the rate of left ventricular relaxation and filling. J Am Coll Cardiol 1987;10:702–9.
9. Lew WYW, Rasmussen CM. Influence of nonuniformity on rate of left ventricular pressure fall in the dog. Am J Physiol 1989;256:H222–32.
10. Takeuchi M, Fujitani K, Kurogane K, et al. Effects of left ventricular asynchrony on time constant and extrapolated pressure of left ventricular pressure decay in coronary artery disease. J Am Coll Cardiol 1985;6:597–602.
11. Perrone-Filardi P, Betocchi S, Giustino G, et al. Influence of left ventricular asynchrony on filling in coronary artery disease. Am J Cardiol 1988;62:523–7.
12. Brutsaert DL, Rademakers FE, Sys SU. Triple control of relaxation: implications in cardiac disease. Circulation 1984;69:190–6.
13. Gaasch WH, Blaustein AS, Bing OHL. Asynchronous (segmental early) relaxation of the left ventricle. J Am Coll Cardiol 1985;5:891–7.
14. Brutsaert DL. Nonuniformity: a physiologic modulator of contraction and relaxation of the normal heart. J Am Coll Cardiol 1987;9:341–8.
15. Bonow RO. Regional left ventricular nonuniformity: effects on left ventricular diastolic function in ischemic heart disease, hypertrophic cardiomyopathy, and the normal heart. Circulation 1990;81(suppl III):III-54–65.
16. Bacharach SL, Green MV, Borer JS. Instrumentation and data processing in cardiovascular nuclear medicine: evaluation of ventricular function. Semin Nucl Med 1979;9:257–74.
17. Bosquet A, Deconinck F, Lepoudre M, Jonckheer M. The temporal Fourier transform applied to functional isotopic imaging. In: DiPaola R, Kahn E, eds. Information Processing in Medical Imaging. Paris: INSERM 88, 1978:397–408.
18. Betocchi S, Bonow RO, Bacharach SL, Rosing DR, Maron BJ, Green MV. Isovolumetric relaxation period in hypertrophic cardiomyopathy: assessment by radionuclide angiography. J Am Coll Cardiol 1986;7:74–81.
19. Vitale DF, Green MV, Bacharach SL, et al. Assessment of regional left ventricular function by sector analysis: a method for objective evaluation of radionuclide blood pool studies. Am J Cardiol 1983;52:1112–9.
20. Holman BL, Wynne J, Idoine J, Neill J. Disruption in the temporal sequence of regional ventricular contraction. I. Characteristics and incidence in coronary artery disease. Circulation 1980;61:1075–83.
21. Hori M, Inoue M, Kitakaze M, et al. Ejection timing as a major determinant of left ventricular relaxation rate in isolated perfused canine heart. Circ Res 1984;55:31–8.
22. 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;38:1010–9.
23. Ludbrook PA, Byrne JD, Tiegenbrunn AJ. Association of asynchronous protodiastolic segmental wall motion with impaired left ventricular relaxation. Circulation 1981;64:1201–11.
24. Bing OHL, Keege JF, Wolk MJ, Finkelstein LJ, Levine HJ. Tension prolongation during recovery from hypoxia. J Clin Invest 1971;50:660–6.
25. Gilbert CG, Glantz SA. Determinants of left ventricular filling and the diastolic pressure-volume relation. Circ Res 1989;64:827–52.
26. Fioretti P, Brower RW, Meester GT, Serruys PW. Interaction of left ventricular filling and relaxation during early diastole in human subjects. Am J Cardiol 1980;46:197–203.
27. Green MV, Jones-Collins BA, Bacharach SL, Findley SL, Patterson RE, Larson SM. Scintigraphic quantification of asynchronous myocardial motion during the left ventricular isovolumetric relaxation period: a study in the dog during acute ischemia. J Am Coll Cardiol 1984;4:72–9.
28. Myreng Y, Smiseth OA. Assessment of left ventricular relaxation by Doppler echocardiography: comparison of isovolumic relaxation time and transmitral flow velocities with time constant of isovolumic relaxation. Circulation 1990;81:260–6.