A Clinical Study of Left Ventricular Relaxation

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SUMMARY Left ventricular (LV) relaxation was studied in patients with hypertrophic cardiomyopathy (HCM, n = 18), congestive cardiomyopathy (CCM, n = 11), hypertensive heart disease (HHD, n = 8), coronary artery disease (CAD) without left ventricular (LV) asynergy (n = 9) and with LV asynergy (n = 17), mitral stenosis (MS, n = 16), and mitral regurgitation (MR, n = 8). The time constant T and peak negative dP/dt were used as indexes of LV relaxation, and 18 normal subjects served as controls.

The time constant T was higher in elderly patients among normal controls (r = 0.652, p < 0.01), which suggests that prolongation of relaxation is a phenomenon of aging. The normal value of the time constant T was 33 ± 8 msec (mean ± SD), and that of peak negative dP/dt was 1864 ± 390 mm Hg/sec. The time constant T was significantly higher in HCM (64 ± 20 msec), CCM (56 ± 14 msec), CAD without asynergy (53 ± 16 msec), CAD with asynergy (57 ± 13 msec) and MS (47 ± 12 msec). Peak negative dP/dt was significantly lower in HCM (998 ± 303 mm Hg/sec), CCM (1060 ± 334 mm Hg/sec), CAD with asynergy (1370 ± 299 mm Hg/sec), MS (1367 ± 313 mm Hg/sec) and MR (1139 ± 305 mm Hg/sec).

Although the genesis of LV relaxation abnormality is not clear from this investigation, it seems to have multiple causes. Relaxation abnormality seems to be one of the earliest manifestations of mechanical dysfunction of the human left ventricle.

MYOCARDIAL RELAXATION is an energy-dependent process that consumes high-energy phosphate, and calcium released from the troponin is sequestered in the sarcoplasmic reticulum during this period. It has been shown in experimental animals and in the failing human ventricle that the process of calcium binding and uptake is disturbed in the failing myocardium. Studies in isolated muscle preparations elucidated prolonged relaxation in various conditions, such as recovery from hypoxia or ischemia, aging, hypertrophy and hypothyroidism. Shortening of relaxation has been reported with hyperthyroidism and after the administration of catecholamines. These observations suggest that myocardial relaxation is altered in various heart diseases.

Although impairment of left ventricular (LV) relaxation has been suggested in patients with congestive heart failure and during spontaneous or pacing-induced angina pectoris, using the maximal rate of LV pressure fall (peak negative dP/dt) as an index, these findings are inconclusive, because peak negative dP/dt is influenced by heart rate, systolic pressure, end-systolic volume and other factors. The time constant T of the LV pressure fall during isovolumic relaxation has been shown by Weiss et al. to be relatively independent of other determinants of cardiac performance and has been proposed as an index of LV relaxation. Mann and his co-workers reported relaxation abnormalities during angina pectoris induced by atrial pacing and showed a higher time constant T and lower peak negative dP/dt than under resting conditions.

During diagnostic cardiac catheterization, the positive deflection of the first derivative of LV pressure (peak positive dP/dt) always exceeded the negative deflection (peak negative dP/dt) in patients with hypertrophic cardiomyopathy (HCM), whereas peak negative dP/dt almost always exceeded peak positive dP/dt in patients with other heart diseases. Therefore, we initially thought that LV relaxation might be specifically impaired in HCM.

This investigation was performed to determine the normal value of the time constant T in the human left ventricle and to evaluate LV relaxation in various heart diseases, using the time constant T as the first index and peak negative dP/dt as the second index of LV relaxation.

Methods

Patients

The study population included 105 patients who underwent diagnostic cardiac catheterization between January 1976 and June 1979. They were consecutive cases whose LV pressure and its first derivative were obtained successfully with a catheter-tip manometer in each identified group. The catheterization diagnoses in the normal controls (group 1) were chest pain of unknown etiology (11 cases), athlete's heart (two cases), functional murmur (two cases), mild pulmonic stenosis (one case), idiopathic edema (one case) and dextroversion (one case).

The diagnoses of HCM (group 2) and congestive cardiomyopathy (CCM, group 3) were based not only on catheterization and coronary and LV cineangiographic findings but also on precise history and echocardiographic findings according to the criteria of the National Study Group of Idiopathic Cardiomyopathies of Japan after the modification of Goodwin's criteria. Twelve patients had asymmetric septal hypertrophy, and the interventricular septum and LV posterior wall were equally hypertrophied in...
five patients in group 2 by echocardiographic observation. Severe and localized hypertrophy was seen at the apex by two-dimensional echocardiography and LV cineangiography in one patient in this group (apical hypertrophy). A significant pressure gradient (30 mm Hg or more) was present in the left ventricle at rest or with isoproterenol infusion in five patients, and LV pressures were recorded beyond the obstruction.

One patient in group 3 was admitted because of cardiomegaly, chest pain, frequent ventricular premature complexes and electrocardiographic changes suggestive of myocardial ischemia in the left preordial leads. The echocardiogram on admission revealed an enlarged and poorly contracting left ventricle. After 2 weeks of bed rest, cardiomegaly subsided, LV pressures and volumes were normal at cardiac catheterization and right and left ventricular biopsy findings were almost normal. Therefore, this patient might have had acute myocarditis rather than CCM. The etiology was unknown in six patients, considered to be peripartum in one, alcoholic in two and due to progressive muscle dystrophy in one patient.

All patients with hypertensive heart disease (HHD, group 4) underwent cardiac catheterization for the evaluation of possible coronary artery disease (CAD) because of chest pain. They had at least 2 years of documented history of hypertension and electrocardiographic evidence of LV hypertrophy.

Patients with CAD were divided into two groups according to the absence (group 5) or presence (group 6) of LV asynery, which was identified by the cineangiographic finding of abnormal segmental wall motion. Three of nine patients in group 5 had a history of documented myocardial infarction, and all patients in group 6 had a history of at least one myocardial infarction. The catheterization was performed after successful medical treatment in patients with unstable angina, and at least 6 weeks after the acute attack in patients with myocardial infarction. No patient developed an acute ischemic attack before or during the measurement of LV pressures. All patients in groups 5 and 6 had significant stenosis at least in one of the three major coronary arteries, which was defined by the presence of lesions that resulted in 75% or greater narrowing of the intraluminal diameter of the vessels in multiple projections.

On admission, functional capacity was clinically evaluated according to the criteria of the New York Heart Association in patients with mitral stenosis (MS, group 7) and mitral regurgitation (MR, group 8). In group 7, two patients were in functional class I, three were in class II, 10 were in class III and one was in class IV; in group 8, two patients were in class I, two were in class II, three were in class III and one was in class IV. In group 7, the mitral valve area calculated by the Gorlin formula was 0.6 to 1.8 cm² (average 0.93 cm²). In group 8, mitral regurgitation evaluated by LV cineangiography was grade II in one patient, grade III in two patients and grade IV in five patients. Patients with aortic regurgitation by cineangiogram were excluded from the study because of the absence of isovolumic relaxation in this condition.

Methods

The catheterization was performed using the brachial approach with the patient in the fasting state after oral premedication with 2 mg of diazepam and 500 mg bromovalerylurea, and all medications except digitalis were withheld for 10–16 hours before the procedure. LV pressure was recorded in each patient with a high-fidelity micromanometer-tipped angiocatheter (Mikro-tip, Model PC-471 or 481, Millar Instruments) at high and low gain; an intracardiac phonocardiogram and the first derivative of LV pressure (mm Hg/sec) were recorded simultaneously. Zero level was calibrated electronically by a transducer control unit (Model TCB-100, Millar Instruments) before the insertion of the catheter, and zero shift was adjusted to the level of the mid-chest position via the water-filled system using a Statham P23Db pressure transducer. Photographic recordings were obtained at paper speeds of 50, 100, and 200 mm/sec in each patient, using an eight-channel optical recording system (Model 4588D, Hewlett-Packard), which included four bioelectric amplifiers (Model 8811A) for continuous electrocardiographic monitoring, high-fidelity LV pressure and intracardiac phonocardiographic recordings, a derivative computer (Model 8814A) for the continuous differentiation of LV pressure, and a pressure amplifier (Model 8805C) for the pressure recognition from the water-filled system. Five consecutive complexes in cases of normal sinus rhythm and 10 consecutive complexes in patients with atrial fibrillation were averaged for the determination of pressure, peak positive and negative dP/dt and the time constant T. Premature complexes and immediate post premature complexes were discarded. Two representative LV pressure tracings are shown in figure 1.

LV cineangiograms were performed after the recordings of the pressure with the same catheter in a 45° right anterior oblique projection. Thirty to 45 ml of contrast material (Angioconray) were injected in 3 seconds by a power injector (Contrac-4T, Siemens). Films were exposed at a rate of 60 frames/sec with a 35-mm cine camera (Arritechno 35, Arritechno) mounted on a 25-cm image intensifier (Cardoscope U, Siemens). The ECG, LV pressure and film numbers were simultaneously recorded on the cineangiographic film using a cathode ray tube, light-emitting diode, and optical assembly system (Cineangio Data Recorder, Model CDR 2000D, NAC Inc.) for the identification of the end-diastolic and end-systolic frames. Coronary cineangiograms were performed with the Sones technique in multiple projections, using a 17-cm image intensifier of the same system.

The first index of LV relaxation, the time constant T, was calculated from the high-speed (200 mm/sec or, occasionally, 100 mm/sec) recordings of LV pressure and dP/dt according to the method of Weiss et al. In brief, the LV pressure fall during isovolumic
TABLE 1. Comparisons of Left Ventricular Pressure, Volume and Indexes of Contractility and Relaxation in Various Heart Diseases

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Age (years)</th>
<th>HR (beats/min)</th>
<th>LV pressures (mm Hg)</th>
<th>LVEDVI (ml/m²)</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Systolic</td>
<td>End-diastolic</td>
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<tr>
<td>1 (Normal)</td>
<td>18</td>
<td>41 ± 18</td>
<td>73 ± 18</td>
<td>117 ± 12</td>
<td>8 ± 4</td>
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<tr>
<td>(n = 15)</td>
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<tr>
<td>2 (HCM)</td>
<td>18</td>
<td>38 ± 11</td>
<td>69 ± 13</td>
<td>115 ± 22</td>
<td>15 ± 8*</td>
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<td>(n = 16)</td>
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<tr>
<td>3 (CCM)</td>
<td>11</td>
<td>39 ± 9</td>
<td>77 ± 12</td>
<td>107 ± 16</td>
<td>11 ± 8</td>
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<td>(n = 9)</td>
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<tr>
<td>4 (HHD)</td>
<td>8</td>
<td>51 ± 11</td>
<td>71 ± 16</td>
<td>156 ± 9*</td>
<td>10 ± 3</td>
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<td>(n = 7)</td>
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<tr>
<td>5 (CAD without asynergy)</td>
<td>9</td>
<td>50 ± 12</td>
<td>65 ± 11</td>
<td>138 ± 20*</td>
<td>10 ± 5</td>
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<td>(n = 4)</td>
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<tr>
<td>6 (CAD with asynergy)</td>
<td>17</td>
<td>51 ± 10</td>
<td>73 ± 16</td>
<td>133 ± 18*</td>
<td>16 ± 6*</td>
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<tr>
<td>(n = 4)</td>
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<tr>
<td>7 (MR)</td>
<td>16</td>
<td>44 ± 6</td>
<td>76 ± 20</td>
<td>113 ± 14</td>
<td>8 ± 3</td>
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<td>(n = 9)</td>
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<tr>
<td>8 (MR)</td>
<td>8</td>
<td>29 ± 11</td>
<td>81 ± 17</td>
<td>108 ± 11</td>
<td>10 ± 4</td>
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Values are mean ± sd.
* p < 0.05 compared with the data of group 1 by the Dunnett method.
Abbreviations: LV = left ventricular; EDVI = end-diastolic volume index; EF = ejection fraction; HCM = hypertrophic cardiomyopathy; CCM = congestive cardiomyopathy; HHD = hypertensive heart disease; CAD = coronary artery disease; MS = mitral stenosis; MR = mitral regurgitation.

relaxation period is exponential,22, 23 and the following relationship can be obtained: P = e^At + B, dP/dt = A (e^At + B), where P is pressure, A is the slope of exponential pressure fall, t is the time after peak negative dP/dt, and B is the intercept. At t = 0, dP/dt = peak negative dP/dt = Ae^0 = APO, where PO is the LV pressure at peak negative dP/dt. Therefore, the time constant T, which is the negative reciprocal of A, can be obtained as: T = 1/-A = PO/peak negative dP/dt.

LV volumes were obtained by the area-length method of Dodge et al.24 by tracing the silhouette with a sonic pen using a semicomputerized system (combinations of the motion analyzer, sonic digitizer graph pen, microcomputer and graphic printer; Cardias GP 2000, NAC Inc.). Two or three of the earliest well-opacified complexes were averaged in each case, excluding premature and immediate post-patmature complexes. Ejection fraction (EF) was calculated as EF = EDV – ESV/EDV, where EDV is end-diastolic volume and ESV is end-systolic volume. Volumes and EF could not be obtained in several cases because of poor opacification of the cavity or because all complexes were premature and post-patmature.

FIGURE 1. Two representative tracings of left ventricular pressure (LVP) and its first derivative (dP/dt) from a patient with mild pulmonic stenosis (group 1) (A) and from a patient with hypertrophic cardiomyopathy (HCM, group 2) (B). Panel B shows a very prominent "a" wave, elevated left ventricular end-diastolic pressure, and very low peak negative dP/dt. The negative deflection of dP/dt is much less than the positive deflection, a characteristic finding in HCM. ICP CG = intracardiac phonocardiogram.
Table 1. (Continued)

<table>
<thead>
<tr>
<th>EF (%)</th>
<th>Peak dp/dt (mm Hg/sec)</th>
<th>Positive</th>
<th>Negative</th>
<th>Positive dp/dt</th>
<th>Time constant T (msec)</th>
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<tr>
<td>64 ± 7</td>
<td>1674 ± 421</td>
<td>1864 ± 390</td>
<td></td>
<td>0.90 ± 0.15</td>
<td>33 ± 8</td>
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<td>(n = 15)</td>
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<tr>
<td>68 ± 9</td>
<td>1398 ± 346</td>
<td>998 ± 303*</td>
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<td>1.43 ± 0.26*</td>
<td>64 ± 20*</td>
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<td>(n = 16)</td>
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<tr>
<td>43 ± 11*</td>
<td>1037 ± 318*</td>
<td>1060 ± 334*</td>
<td></td>
<td>1.00 ± 0.23</td>
<td>56 ± 14*</td>
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<tr>
<td>(n = 7)</td>
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<tr>
<td>67 ± 6</td>
<td>1983 ± 291</td>
<td>1983 ± 327</td>
<td></td>
<td>0.93 ± 0.19</td>
<td>49 ± 6</td>
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<td>(n = 7)</td>
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<tr>
<td>65 ± 5</td>
<td>1408 ± 125</td>
<td>1522 ± 148</td>
<td></td>
<td>0.93 ± 0.08</td>
<td>53 ± 16*</td>
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<tr>
<td>(n = 7)</td>
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<tr>
<td>39 ± 10*</td>
<td>1404 ± 344</td>
<td>1370 ± 299*</td>
<td></td>
<td>1.03 ± 0.13</td>
<td>57 ± 13*</td>
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<td>(n = 15)</td>
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<tr>
<td>58 ± 10</td>
<td>1322 ± 387*</td>
<td>1367 ± 313*</td>
<td></td>
<td>0.96 ± 0.14</td>
<td>47 ± 12*</td>
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<td>(n = 15)</td>
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<tr>
<td>57 ± 7</td>
<td>1243 ± 242*</td>
<td>1139 ± 305*</td>
<td></td>
<td>1.12 ± 0.18*</td>
<td>49 ± 11</td>
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<td>(n = 7)</td>
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The Dunnett method was used for the multiple comparison for normal control group; p < 0.05 was considered significant in comparisons between multiple groups of data. The unpaired t-test was also used.

Results

The mean results in each group are given in table 1. Peak negative dp/dt ranged from 1275-2772 mm Hg/sec (1864 ± 390 mm Hg/sec) in normal subjects (group 1), and the normal value of the time constant T was 22-46 msec (33 ± 8 msec). Peak negative dp/dt was high in patients with high LV systolic pressure (SP) in this group (r = 0.540, n = 18, p < 0.05) (fig. 2) but did not correlate with LVESV (r = 0.182, n = 15) or EF (r = 0.273, n = 15). The time constant T did not correlate with LVSP (r = 0.246, n = 18), ESV (r = 0.182, n = 15) or EF (r = 0.237, n = 15). The time constant T was higher in older patients and correlated positively with age in group 1 (r = 0.652, n = 18, p < 0.01) (fig. 3).

HCM was characterized by elevated LVEDP (15 ± 8 mm Hg) and normal LV volumes, SP and EF. A normal EDV with elevated EDP indicates that the left ventricle is stiff in HCM. Peak negative dp/dt was very low (998 ± 303 mm Hg/sec) and the time constant T was high (64 ± 20 msec). The ratio of peak positive to peak negative dp/dt was greater than 1 in all patients, which was significantly higher than in normal controls. These observations indicate that LV relaxation is abnormally prolonged in HCM.

A dilated and poorly contracting left ventricle is a defining feature of CCM. LVEDV index (131 ± 66 ml/m²) was significantly larger in this group, accompanied by lower EF (43 ± 11%) and peak positive dp/dt (1037 ± 318 mm Hg/sec). Abnormal LV relaxation was shown by lower peak negative dp/dt (1060 ± 334 mm Hg/sec) and higher time constant T (56 ± 14 msec) in this group. Significant positive correlations between EF and peak negative dp/dt (r = 0.776, n = 11, p < 0.01, fig. 4A) and the time constant T (r = 0.624, n = 11, p < 0.05, fig. 4B) suggest that

![Figure 2](http://circ.ahajournals.org/)

**Figure 2.** The correlation between left ventricular systolic pressure (LVSP) and peak negative dp/dt in normal subjects (p < 0.05). The significant correlation suggests that LVSP is one of the determinants of peak negative dp/dt in the human left ventricle.

![Figure 3](http://circ.ahajournals.org/)

**Figure 3.** The correlation between age and the time constant T in normal subjects (p < 0.01). Although the correlation coefficient is low, a significant correlation between age and the time constant T suggests that the human left ventricle becomes stiffer with advancing age.
the LV relaxation abnormality in CCM is partly due
to contractile failure.

The time constant \( T \) was slightly higher in HHD
(group 4, 49 ± 6 msec) but was not statistically
different from that in group 1 by the Dunnett method
of multiple comparison. LVSP was higher (156 ± 9
mm Hg) and peak negative \( dP/dt \) was identical (1863
± 327 mm Hg/sec) compared with group 1.

Elevation of LVSP in patients with CAD is a
natural finding because of the high incidence of this
disease among hypertensive patients. Four patients in
group 5 (CAD without asynergy) and six in group 6
(CAD with asynergy) had a history of mild hyperten-
sion. Although there were marked differences between
group 5 and group 6 in LVEDV index (66 ± 12 ml/m²
vs 121 ± 53 ml/m², \( p < 0.01 \)) and EF (65 ± 5% vs
group 6 39 ± 10%, \( p < 0.001 \)), peak negative \( dP/dt \)
(1522 ± 148 mm Hg/sec vs 1370 ± 299 mm Hg/sec,
NS) and the time constant \( T \) (53 ± 16 msec vs 57 ± 13
msec, NS) did not differ (unpaired \( t \) test). The time
constant \( T \) was significantly higher in groups 5 and 6
than in group 1. Although positive correlations were
present between peak negative \( dP/dt \) and LVSP (\( r =
0.544, n = 26, p < 0.01, \) fig. 5A), LVESV (\( r = 0.655, n =
26, p < 0.001, \) fig. 5B) and EF (\( r = 0.468, n = 26, p <
0.05, \) fig. 5C), the time constant \( T \) and EF did not
 correlate significantly in patients with CAD (\( r =
0.211, n = 26 \).

In patients with mitral valve disease, peak positive
\( dP/dt \) was lower than in normal subjects (MS 1367 ±
313 mm Hg/sec, MR 1243 ± 242 mm Hg/sec). LVEDV index
was larger in MR (140 ± 53 ml/m²) and EF was low-normal in both MS (58 ± 10%) and
MR (57 ± 7%). Peak negative \( dP/dt \) was lower in MS
(1369 ± 313 mm Hg/sec) with high time constant \( T \)
(47 ± 12 msec). In patients with MR, peak negative
\( dP/dt \) was significantly lower (1139 ± 305 mm
Hg/sec), but the time constant \( T \) (49 ± 11 msec) was
not significantly different by the Dunnett method.
Among these patients, there were no significant
correlations between these two indexes of LV relaxation
and LVSP, ESV, EF or the severity of symptoms.

Discussion

Relaxation of the heart is a major determinant of
early diastolic filling and atrial blood rushing into
the ventricle during the terminal stage of relaxation.24 At
the cellular and molecular levels, the calcium ion
released from the troponin is sequestered in the sar-
coplasmic reticulum against the ionic gradient.1 This
process is energy-dependent, and about 15% of the
total energy is consumed during this period.2, 4 A dis-
turbance of this process, calcium binding and uptake
of the sarcoplasmic reticulum, has been reported in
various experimental animal models of congestive heart failure4 and in the failing human ventricle.7, 8
In isolated muscle preparations, myocardial contract-
ion and relaxation have been modified separately by
pharmacologic interventions,18 and alterations of
relaxation have been observed in various conditions.
Tension prolongation is a well-known phenomenon in
aged myocardium11, 12 and during the recovery phase
from hypoxia or ischemia.9, 10 The calcium pump of the sarcoplasmic reticulum is affected by altered
thyroid state,26 and shortening or prolongation of the
relaxation period is seen in hyperthyroid or
hypothyroid cardiac muscles, respectively.24 Cardiac
hypertrophy has been reported to be the cause of lower
calcium binding24 and prolongation of relaxation.23
These observations of biochemical and muscle
mechanical studies suggest that relaxation can be
altered under various conditions in the intact heart.
Studies on LV relaxation in the intact heart have
focused mainly on myocardial ischemia or CAD, and
little is known about other conditions.

In the canine left ventricle, ligation of the left
anterior descending artery resulted in an immediate
fall of the maximal rate of LV relaxation (peak negative \( dP/dt \))7. A fall of peak negative \( dP/dt \) has been
observed in patients with CAD during sponta-
neous19 or pacing-induced angina pectoris.20 Low
peak negative \( dP/dt \) has been reported in patients with
congestive cardiomyopathy16, 17 and CAD with LV
dysfunction.18 These observations suggest that LV
relaxation is disturbed in congestive heart failure or
myocardial ischemia, but the results are inconclusive,
because peak negative \( dP/dt \) is influenced by heart
rate, SP, ESV and other factors.21 24 The time con-
tant \( T \) proposed by Weiss and his co-workers,22
however, is relatively independent of heart rate, SP
and ESV,22 24 and is therefore a better index of LV
relaxation.24 In a study of pacing-induced angina,
Mann et al. showed not only a decrease of peak
negative \( dP/dt \) but also a prolonged time constant \( T \),
indicating abnormal LV relaxation.

As is evident from this discussion and the recent
review by Brutsaert and Paulus,24 LV relaxation is in-
fluenced by various factors. In the present study, the
time constant \( T \) and age correlated significantly in
normal subjects. Although the study population was
small (\( n = 18 \)) and the correlation coefficient low (\( r =
0.652, p < 0.01 \)), aging seems to be one cause of relax-
ation abnormality. This observation coincides with
prolongation of relaxation in studies of isolated mus-
cle mechanics by Weisfeldt and his co-workers16, 17
and the observation by Harrison et al.25 that the
isovolumic relaxation period is longer in healthy per-
sons of advanced age.

A relaxation abnormality in HCM was suggested
by Sanderson et al.25 based on echocardiographic
observation. Significantly low peak negative \( dP/dt \)
and high time constant \( T \) in this group compared with
normal subjects indicate significant relaxation impair-
ment in HCM. An abnormally high ratio of peak
positive to peak negative \( dP/dt \) in HCM suggests that
relaxation abnormality is not associated with contrac-
tion abnormality. Therefore, it seems better not to
consider this ratio as an indicator of relaxation abnor-
mality. The genesis of relaxation impairment in HCM
cannot be evaluated from the present study, although
several possibilities may be considered. One factor is
low wall stress at the onset of relaxation. LV relaxa-
tion is influenced by the end-systolic pressure-volume
relation or the stress-strain relation, and because the LV wall is very thick with normal pressure at the onset of relaxation, passive stress to the myocardium must be lower than that in the normal left ventricle. We did not calculate wall stress in the present study, because wall thickness was not uniform in HCM. Different structural changes of the myocardium and the amount of fibrosis and degeneration must influence relaxation. The disarrangement of the myocardial fibers at cellular and subcellular levels is a common finding in these patients, and it may be difficult to restore the resting shape for these disarrayed muscle fibers. Hypertrophy itself may be a factor, because biochemical and muscle mechanical studies show abnormal relaxation in the hypertrophied heart. In the present study, peak negative dP/dt was the same in normal subjects and in patients with HHD. The time constant T was 49 ± 6 msec in HHD, which was not statistically different by the Dunnett method but significantly higher than the value for normal controls by the unpaired t test comparing these two groups only (p < 0.001). We could not conclude from this study whether relaxation abnormality exists in HHD, although the velocity of relaxation might be normalized in the presence of relaxation abnormality in HHD because of high SP, as peak negative dP/dt is dependent on this variable.

A relaxation abnormality in congestive heart failure is easily postulated from the biochemical changes discussed previously. Low peak negative dP/dt was reported in patients with CCM by Lewis and Gotsman, and Grossman et al. found not only reduced peak negative dP/dt but also low velocity of early diastolic circumferential fiber lengthening in this disease. We found low peak negative dP/dt and high time constant T in CCM. The main disorder of this disease is contractile or pump failure, and we found significant correlations between peak negative dP/dt and EF (fig. 4A) and between the time constant T and EF (fig. 4B). This observation suggests that the relaxation abnormality in CCM is partly mediated by contractile failure.

Papapietro et al. reported lower peak negative dP/dt in patients with CAD and impaired LV function and concluded that impairment of maximal rate of LV relaxation is due to the extension of LV wall asynergy and pump failure in CAD. Our results differ somewhat from theirs. Although there were significant differences in LVEDV, EDP and EF between the groups of CAD patients with (group 6) and without LV asynergy (group 5), peak negative dP/dt and the time constant T were similar. We found a significant correlation between peak negative dP/dt and EF in these two groups (fig. 5C), but our correlation is not as good as theirs and we found no relation between the time constant T and EF. The time constant T at rest in patients with CAD reported by Mann et al. (43 ± 11 msec, n = 14) is significantly higher than that in our normal subjects (33 ± 8 msec, n = 18, p < 0.005). In their study, patients with a history of hypertension were excluded. High time constant T in patients with CAD with or without LV dysfunction seen in our study suggests that the relaxation abnormality is not related to the degree of LV asynergy or pump failure in this disease. As none of our patients developed angina during LV pressure recordings, relaxation abnormality cannot be attributed to active ischemia. Cardiac hypertrophy due to hypertension, older age compared with normal subjects, and chronic subclinical ischemia and subsequent myocardial fibrosis may be contributory factors.

Ahmed and co-workers reported that the values of peak negative dP/dt normalized by LV pressure and end-systolic circumferential length in 10 patients with MS with reduced EF did not differ from the values obtained from 10 normal controls. They concluded that LV relaxation is normal in MS, even in the presence of reduced EF. Unfortunately, their data were based on a
water-filled system, and an error of 10–12% is inevitable with this system. Therefore, comparisons of dP/dt and data derived from dP/dt should be limited and are not suitable for interpatient comparisons if a water-filled system is used. We found low peak negative dP/dt and high time constant T in patients with MS with normal EF. We found no relation between the time constant T and LVSP, ESV, EF or the severity of symptoms in these patients. Therefore, the etiology of the relaxation abnormality in MS is unknown. Although the time constant T in MR was high (47 ± 11 msec), it was not statistically significant by the Dunnett method. This finding does not mean that relaxation is normal in this condition; the time constant T was significantly higher than normal by unpaired t test (p < 0.001), probably due to a small patient population in this group, as is the case of HHD. A study of large numbers of patients with MR is necessary to determine whether the relaxation abnormality is associated with MR.

In the present study, we found that the majority of patients with significant heart disease had a high time constant T. Because of a significant rise of LVEDP with a fall in peak negative dP/dt during myocardial ischemia in patients with CAD, many investigators have related relaxation abnormalities to changes in diastolic compliance. Although the current study does not examine diastolic compliance directly, relaxation abnormality and lower compliance seem to be concomitant findings, because most of the patients studied here had an abnormally high time constant T and a low peak negative dP/dt. Of particular clinical importance is the observation by Grossman et al. that early diastolic filling disturbance is present in CCM in association with relaxation abnormality. Rapid deterioration with the appearance of tachyarrhythmias is a common finding in patients with heart disease. Relaxation prolongation and diastolic filling disturbance might have a significant role for the pathogenesis of the deterioration. Although the genesis and clinical significance of LV relaxation abnormality in these heart diseases are not clear, this finding may be one of the earliest manifestations of mechanical abnormality of the diseased left ventricle.

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