Peak Negative dp/dt as an Index of Left Ventricular Relaxation

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The maximal rate of reduction of the left ventricular pressure (peak negative dp/dt) was studied in 25 cases with hypertrophic cardiomyopathy (HCM), 4 cases with congestive cardiomyopathy (COCM) and 10 control subjects. Peak negative dp/dt was significantly less in HCM (972±286 mmHg/sec) and COCM (1181±437 mmHg/sec) than that in control subjects (2140±266 mmHg/sec). A ratio of positive to negative peak dp/dt was increased in HCM alone, indicating a dissociation between positive and negative peak dp/dt. When the indices of distensibility and compliance were calculated by the method of Gaasch et al, significant correlations were observed between peak negative dp/dt and dV/dP (r=0.74, p>0.001) and between peak negative dp/dt-EDP and dV/dP-V (r=0.91, p<0.001) in HCM and control subjects. Thus, peak negative dp/dt seemed to be affected by alterations in the diastolic properties of the left ventricle and to be a valuable index of left ventricular relaxation.

Key Words: Hypertrophic cardiomyopathy, Congestive cardiomyopathy, Compliance, Distensibility

There appears recently to be an increased interest in the assessment of the diastolic properties of the left ventricle. The importance of the diastolic hemodynamics is emphasized in the clinical situation by the fact that several varieties of heart diseases, such as ischemic heart disease or cardiomyopathy, may produce symptoms caused more by abnormal diastolic properties of the left ventricle than through insufficient systolic performance. A variety of expressions have been used to characterize the diastolic properties, although attempts to evaluate them have encountered several serious difficulties.

In our previous study1), an analysis of left ventricular pressure and its first derivative relationship revealed the reduced rate of pressure fall during ventricular relaxation (negative dp/dt) in hypertrophic cardiomyopathy. The purpose of the present study was therefore to describe the usefulness of peak negative dp/dt in assessing the diastolic properties of the left ventricle.

MATERIALS AND METHODS

Twenty-nine subjects, 18 men and 11 women were studied. Their ages ranged from 12 to 55 years. They included 25 cases with hypertrophic cardiomyopathy (HCM) and 4 cases with congestive cardiomyopathy (COCM). Control subjects consisted of 10 cases, 4 men and 6 women, with mitral stenosis, atrial septal defect, patent ductus arteriosus and atrial fibrillation without organic heart disease. Their ages
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ranged from 16 to 49 years.

In all subjects, left ventricular catheterization was performed using 8F dacron catheter. Left ventricular pressure curve was recorded on a 8 channel jet writing recorder (Elema-Schönander) with EMT 3 transducer. Positive and negative peak dp/dt were measured from the first derivative curve of the left ventricular pressure computed continuously with a differentiating circuit. Five to ten consecutive beats were averaged for positive and negative peak dp/dt for each patient. Left ventriculogram was performed at a rate of 6 frames/sec. Left ventricular volumes were calculated using the area-length method of Dodge et al. An index of distensibility (dV/dP), stiffness (k) and compliance (dV/ dP×V) of the left ventricle was calculated according to the method of Gaasch et al as follows;

\[ P = be^{kV} \]
\[ \frac{dV}{dP} = \frac{1}{kP} \]

where P equals left ventricular end-diastolic pressure in mmHg, V equals left ventricular end-diastolic volume in ml/m², b equals the extrapolated left ventricular end-diastolic pressure at zero V, k is the slope of the log P-V relationship and e is the base of the natural logarithm. These variables were calculated using a constant pressure intercept (b=0.43 mmHg) which was obtained from the in vitro animal studies.

RESULTS

Table 1 shows the indices of pump function and contractility of the left ventricle.

The average end-systolic volume was 37±9 ml/m² in control subjects, 24±11 ml/m² in hypertrophic cardiomyopathy (HCM) group and 94±47 ml/m² in congestive cardiomyopathy (COCM) group. HCM group showed significantly reduced end-systolic volume (p<0.005). End diastolic volume in COCM group (170±49 ml/m²) was significantly greater (p<0.001) than that in control subjects (91±21 ml/m³) or in HCM group (80±30 ml/m³).

End-diastolic pressure averaged 9±2 mm Hg for control subjects, 22±7 mmHg for HCM group and 15±8 mmHg for COCM group. The average end-diastolic pressure was significantly higher in HCM group (p<0.001). Ejection fraction was 0.59±0.05 in control subjects, 0.69±0.09 in HCM group and 0.45±0.16 in COCM group, thus being significantly higher in HCM group (p<0.005) and lower in COCM group (p<0.05) than that in control subjects. Cardiac index did not differ significantly among the three groups.

Peak positive dp/dt averaged 2590±688 mmHg/sec for control subjects, 1727±348 mmHg/sec for HCM group and 1581±437 mmHg/sec for COCM group. The average Vpm was 0.97±0.25 ML/sec in control subjects, 0.78±0.21 ML/sec in HCM group and 0.79±0.13 ML/sec in COCM group. Both indices were significantly lower in HCM group than those in control subjects.

Table 2 shows the indices of the diastolic properties of the left ventricle.

The index of distensibility at end-diastole (dV/dP) in HCM group (1.1±0.6 ml/m²/}

### Table 1. Indices of pump function and contractility of the left ventricle.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Mean Age (years)</th>
<th>Sex</th>
<th>ESV ml/m²</th>
<th>EDV ml/m²</th>
<th>CI l/min/m²</th>
<th>EF</th>
<th>EDP mmHg</th>
<th>Vpm ML/sec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10</td>
<td>2</td>
<td>8</td>
<td>4</td>
<td>6</td>
<td>37±9</td>
<td>91±21</td>
<td>4.4±1.8</td>
</tr>
<tr>
<td>H C M 2 5</td>
<td>27</td>
<td>16</td>
<td>9</td>
<td>24±12**</td>
<td>80±30</td>
<td>3.5±1.3</td>
<td>0.69±0.09**</td>
<td>22±7</td>
</tr>
<tr>
<td>C O C M 4</td>
<td>35</td>
<td>2</td>
<td>2</td>
<td>94±47**</td>
<td>170±45*</td>
<td>3.2±0.5</td>
<td>0.45±0.16***</td>
<td>15±8***</td>
</tr>
</tbody>
</table>

* P<0.001 significantly differs from control
** P<0.005 significantly differs from control
*** P<0.05 significantly differs from control

Values shown are mean±standard deviation

Abbreviations: HCM=hypertrophic cardiomyopathy, COCM=congestive cardiomyopathy, ESV=end-systolic volume, CI=cardiac index, EF=ejection fraction, EDP=end-diastolic pressure.
Table 2. Indices of diastolic properties of the left ventricle

<table>
<thead>
<tr>
<th>No. of Cases</th>
<th>peak neg. dp/dt</th>
<th>peak pos. dp/dt</th>
<th>peak neg. dp/dt:EDP</th>
<th>k</th>
<th>dVdp/dP</th>
<th>dVdp/dP·V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.0</td>
<td>2140 ± 266</td>
<td>1.20 ± 0.27</td>
<td>252 ± 71</td>
<td>0.024 ± 0.011</td>
<td>3.6 ± 1.6</td>
</tr>
<tr>
<td>HCM</td>
<td>2.5</td>
<td>972 ± 286³</td>
<td>1.86 ± 0.47³</td>
<td>51 ± 27³</td>
<td>0.060 ± 0.038³</td>
<td>1.1 ± 0.6³</td>
</tr>
<tr>
<td>COCM</td>
<td>4.0</td>
<td>1181 ± 437³</td>
<td>1.42 ± 0.45³</td>
<td>50 ± 19³</td>
<td>0.023 ± 0.009³</td>
<td>4.1 ± 3.1</td>
</tr>
</tbody>
</table>

* P<0.001 significantly differs from control
*** P<0.05 significantly differs from control

Values shown are mean ± standard deviation

Abbreviations: HCM=hypertrophic cardiomyopathy, COCM=congestive cardiomyopathy, k=slope of the log P-V relationship, dVdp/dP=index of distensibility at end-diastole, dVdp/dP·V=index of compliance at end-diastole.

mmHg) was significantly lower (p<0.001) than that in control subjects (3.6±1.6 ml/m²/mmHg). The index was slightly higher in COCM group (4.1±3.1 ml/m²/mmHg) as shown in Fig. 1. The index of compliance (dVdp/dP·V) was significantly lower in HCM group (0.023±0.009/l/mmHg) and COCM group (0.022±0.006 l/mmHg) than that in control subjects (0.038±0.009 l/mmHg).

Fig. 2 shows representative first derivative curves (dp/dt) of the left ventricular pressure from patients with control, HCM, and COCM groups. The average peak negative dp/dt was 2140±266 mmHg/sec in control subjects, 972±286 mmHg/sec in HCM group and 1181±437 mmHg/sec in COCM group, thus significantly reduced (p<0.001) in HCM and COCM groups (Fig. 3). The average ratio of positive to negative peak dp/dt (peak pos. dp/dt/peak neg. dp/dt) was 1.20±0.27 in control subjects, 1.86±0.47 in HCM group and 1.42±0.45 in COCM group. The ratio was significantly greater in HCM group (p<0.001). When peak negative dp/dt was divided by end-diastolic pressure (peak neg. dp/dt/EDP), HCM group (51±27 l/sec) and COCM group (50±19 l/sec) showed significantly lower value (p<0.001) than control subjects (252±71 l/sec).

Correlations of peak negative dp/dt with the indices of distensibility and compliance

Fig. 1. Distensibility, dVdp/dP at end-diastole (A) and compliance, dVdp/dP·V at end-diastole (B) for control, hypertrophic cardiomyopathy (HCM) and congestive cardiomyopathy (COCM) groups. Shown for each group are means±SD.

Fig. 2. Representative first derivative (dp/dt) curves of the left ventricular pressure. A=control subject, B=hypertrophic cardiomyopathy, C=congestive cardiomyopathy.
were examined in control subjects and HCM group (Fig. 4 and Fig. 5). Peak negative dp/dt correlated significantly with distensibility at end-diastole (dV/dP) \((r=0.74, p<0.001)\). Compliance (dV/dP-V) showed significant correlation with peak neg. dp/dt*EDP \((r=0.91, p<0.001)\). A correlation between peak negative dp/dt and end-systolic volume was not significant.

Fig. 3. Peak negative dp/dt (A) and a ratio of positive to negative peak dp/dt (B) for control, hypertrophic cardiomyopathy (HCM) and congestive cardiomyopathy (COCM) groups. Shown for each group are means±SD.

Fig. 4. Relation between peak negative dp/dt and dV/dP at end-diastole in control subjects and hypertrophic cardiomyopathy (HCM).

Fig. 5. Relation between peak negative dp/dt-EDP and dV/dP-V at end-diastole in control subjects and hypertrophic cardiomyopathy (HCM).

of the myocardium may be responsible for substantial alterations in ventricular filling pressure, considerable interest has been paid to the diastolic properties of the ventricle. A number of investigators have developed varying methods to evaluate them. Bristow et al\(^6\) measured the volume change occurring during the last 0.2 sec of diastole and related this to the pressure difference produced by atrial systole. Diamond and Forrester\(^7\) determined total diastolic \(\frac{dP}{dV}\) by dividing the difference between end-diastolic and end-systolic pressure by stroke volume measured by dye-dilution technique.

In 1972, Gaasch et al\(^8\) described that the left ventricular pressure-volume relationship could be assumed exponential and the index of distensibility (dV/dP) could be represented as; \(p=ae^{bV}\), dV/dP=1/kP. In their method, it was assumed that the log P-V relationships at various end-diastolic volumes in a given ventricle are linear, the pressure intercept \(b\) varies little and that the slope can be estimated from a single coordinate of log P and V and a constant intercept \(b\) which was obtained from the in vitro animal studies. The method seems attractive for practical evaluation of the diastolic properties of the left ventricle, although it may have serious shortcomings. Our previous study\(^9\) also supported the usefulness of dV/dP and dV/dP-V in assessing the diastolic properties of the left ventricle.
In the present study, the indices of distensibility \((dV/dP)\) and compliance \((dV/dP \cdot V)\) were reduced significantly in HCM group. In COCM group, \(dV/dP \cdot V\) was significantly lower, while \(dV/dP\) was equal or slightly higher than control subjects. These findings imply that distensibility of the muscle per se is decreased both in HCM and COCM, while the distensibility of the entire ventricle is preserved in COCM.

Although intensive studies have centered on the rate of pressure development in the ventricle, little attention has been directed toward the rate of pressure fall during ventricular relaxation. In 1972, Cohn et al. documented that negative dp/dt is related both to the intrinsic contractility of the ventricle as well as to the end-systolic volume. Therefore, inotropic stimulation of the intact heart may lead to opposing effects on negative dp/dt; The first, direct effect, is to increase negative dp/dt and the second is that end-systolic volume declines, reducing negative dp/dt. Accordingly, the net result of inotropic stimulation may be a relatively constant negative dp/dt.

In the present study, peak negative dp/dt was reduced both in HCM and COCM, while a ratio of positive to negative peak dp/dt was increased in HCM only. These findings show that both negative and positive peak dp/dt were reduced in COCM, whereas in HCM peak negative dp/dt was predominantly reduced. Decrease of peak negative dp/dt in HCM might be interpreted as the consequence of their smaller end-systolic volume. However, no significant correlation was observed between these variables in HCM and control subjects. In addition, peak negative dp/dt correlated significantly with the indices of distensibility and compliance. Accordingly, alteration of the diastolic properties of the left ventricle could be also responsible for a decline in peak negative dp/dt.

In the dog experiment, Watanabe et al. observed a decrease in peak negative dp/dt after occlusion of coronary artery. McLaurin et al. reported the usefulness of peak negative dp/dt as an index of left ventricular relaxation rate, demonstrating a decrease in peak negative dp/dt during pacing induced ischemia. They described that during cardiac muscle relaxation, two basic process are believed to occur, dissociation of the bonds formed between the contractile proteins and elastic recoil of the tissues that have been stretched and put under tension by contraction, and that the former is the major factor governing the rate of relaxation. Disorderly arrangement of the muscle, myofibril and myofilament or incomplete ventricular relaxation would be alternative explanations for reduced peak negative dp/dt.

McLaurin et al. described a positive correlation between peak negative dp/dt and ventricular filling rate during rapid filling phase which was calculated using left ventricular echogram. It seems interesting that a good correlation was observed between indices during isovolumic relaxation and subsequent rapid filling phase.

Therefore, peak negative dp/dt would be a valuable index in assessing the diastolic properties of the left ventricle, especially during isovolumic relaxation. As the index can be obtained continuously with ease, it would be also useful for evaluation of the effects of drugs on the diastolic hemodynamics.

REFERENCES


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