LEFT VENTRICULAR DIASTOLIC PRESSURE-VOLUME AND STRESS-STRAIN RELATIONSHIP IN CHILDREN

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Diastolic pressure and volume (P-V) curves were approximately exponential and fitted the equation, \( \frac{dP}{dV} = aP + b \), where \( a \) was left ventricular volume elastic constant. Stress and strain (\( \sigma-\epsilon \)) curves were expressed by the equation, \( \frac{d\epsilon}{d\sigma} = k\sigma + c \), where \( k \) was wall stiffness constant. These exponential curves have been fitted over the whole diastole, but theoretically, the mid-diastole should reflect diastolic elastic properties best. In the present study, therefore, special attention was paid to the mid-diastole in each patient, and both P-V and \( \sigma-\epsilon \) relationships were analyzed by fitting the data to the above mentioned curves during this period of time. This analysis was made in two separate groups of patients. One was the control group consisting of 2 patients with normal hearts, 2 patients with mild pulmonary stenosis, and 25 patients with post mucocutaneous lymphnode syndrome. The other group consisted of patients with postoperative congenital heart disease, that is, 8 patients with atrial septal defect and 5 patients with tetralogy of Fallot. The elastic constant (\( a \)) could not be compared if the size of the hearts differed. The results of the present study, however, demonstrated that the size of the heart was closely related to the constant, \( a \). In the control group, the constant (\( a \)) was exponentially related to the size of the heart, and expressed as follows:

\[
a = 0.30e^{-0.037EDV} + 0.045 \quad (r = 0.94, \ p < 0.01)
\]

In contrast, the wall stiffness constant (\( k \)) was not related to the size of the heart. After surgical repair of congenital heart disease, the stiffness constant in the left ventricle was normal in patients with postoperative atrial septal defect, while it was significantly increased in patients with postoperative tetralogy of Fallot.

The diastolic behavior of the left ventricle is one of the most important parameters of cardiac function. Although it has been widely studied, there are still points to be clarified.\(^{1-13}\)

Key Words:
Pressure-volume relationship
Stress strain relationship
Exponential curve fitting
Chamber compliance
Muscle stiffness

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Fig. 1. Left ventricular pressure-volume (P-V) relationship on the semilog graph in case 14. The vertical axis is pressure ($\log_e P$) and the horizontal axis is volume. The linear portion of diastole was obtained during the mid-diastole.

LV = left ventricle; ED = end-diastole; A = start point of mid-diastole; B = end point of mid-diastole; $\log_e$ = natural logarithm.

Case 14

LV pressure (mmHg)

0 1 2 3 4
LV volume (ml)
0 20 30 40 50

Fig. 3. Left ventricular stress-strain ($\sigma$-$\varepsilon$) relationship on the semilog graph in case 14. The vertical axis is stress ($\log_e \sigma$) and the horizontal axis is strain. The linear portion of stress-strain relationship was obtained as same as P-V relationship during the mid-diastole.

abbreviations: same as Fig. 1.

Case 14

LV circumference (cm)
0 0.1 0.2

Fig. 4. Stress-strain ($\sigma$-$\varepsilon$) relationship for the exponential fit to data during the mid-diastole in case 14. The exponential portion of the P-V curve is expressed as $P = 0.107e^{0.104V} + 1.07$ ($r = 0.99$). The points of the rapid filling phase of the early-diastole and the slow filling phase of the late-diastole are below the exponential curve.

$e$ = base of the natural logarithm; $V$ = volume; $r$ = coefficient of correlation; other abbreviations: same as Fig. 1.

$\sigma = 8.51e^{8.17\varepsilon} + 2.06$ ($r = 0.99$).

$L_0$ is the minimum diastolic pressure point, other abbreviations: same as Fig. 2.

Fig. 2. Pressure-volume (P-V) relationship for the exponential fit to data during the mid-diastole in case 14. The exponential portion of the P-V curve is expressed as $P = 0.107e^{0.104V} + 1.07$ ($r = 0.99$). The points of the rapid filling phase of the early-diastole and the slow filling phase of the late-diastole are below the exponential curve.

$e$ = base of the natural logarithm; $V$ = volume; $r$ = coefficient of correlation; other abbreviations: same as Fig. 1.

Compliance of the left ventricle has been studied, but there are no reports on patients who have undergone surgical operation of congenital heart diseases.\textsuperscript{14--19} The purpose of the present study was to answer the following questions:

1. In which part of the diastolic phase should we fit the P-V and $\sigma$-$\varepsilon$ curves to the mathematical equations?
2. The volume elastic constant ($a$) should vary with the size of the heart. What is the...
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**TABLE I HEMODYNAMIC DATA AND ELASTIC CONSTANT OF CONTROL GROUP**

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**Abbreviations:** BSA = body surface area; P = pressure; V = chamber volume; h = equatorial free wall thickness; σ = midwall stress based on an ellipsoidal geometry; a = slope of the chamber stiffness and b = constant result from the equation dp/dV = aP + b; k = slope of the wall stiffness and c = constant result from the equation dp/dV = ka + c; dp/dt max = left ventricular maximum dp/dt; E.F. = left ventricular ejection fraction; RVPSP = right ventricular peak systolic pressure; RVEDP = right ventricular end diastolic pressure
patients suffered from mild pulmonary stenosis with a pressure gradient of 20 mmHg or less. 25 patients had mucocutaneous lymphnode syndrome (Kawasaki disease), which had occurred from 6 months to 5 years before, but they did not show cardiac enlargement or heart failure. In these patients with Kawasaki disease, cardiac catheterization did not demonstrate the presence of macroscopic cardiac lesions. The coronary arteries were normal and the contractility of the left ventricle and systemic blood pressure were normal. In others with Kawasaki disease some did demonstrate macroscopic lesions (i.e. coronary aneurysm, mitral regurgitation) and cardiac enlargement during acute phase, so were excluded from this study. The above patients, 29 cases total, were included in the control group. In the congenital heart disease group, 8 showed postoperative atrial septal defect (ASD), and 5 had postoperative tetralogy of Fallot (TOF). When catheterization was made postoperatively, it was conducted in patients 4 weeks after surgical correction. The research sample ranged in age from 1 year and 2 months to 14 years, and weighed 7.2 kg to 53 kg. Of these, 25 were boys, and 17 were girls. 

All patients were sedated with estazolam p.o. and pethidine HCL i.m., followed by diagnostic catheterization in the right and left heart by a routine method. Left ventricular pressure was simultaneously recorded by #4 or #5 Millar's micro-tip manometer, and a contrast medium was injected into the main pulmonary artery. Cineangiography was conducted at 90 or 120 frames per second by biplane simultaneous exposure. The high fidelity left ventricular pressure tracing plus the injector marker signal were recorded on an oscillographic photographic recorder (SAN-EI, VISIGRAPH-5L) at a paper speed of 200 mm per second during the main pulmonary arterial cineangiography. The starting point of the diastole was the notch of the rapidly declining ventricular pulse tracing. The volume of the left ventricle was measured in the diastolic phase, in which the left ventricle was first clearly presented in the levophase of main pulmonary arterial cineangiography. The left ventricular volume was calculated from bilateral projection by the biplane area length method of Dodge et al.\textsuperscript{20} Frame by frame analysis of volume and wall thickness was done and the corresponding pressure points were matched. Data between the start of diastole and end-diastole were analyzed by HP 5600M catheterization data analysis.
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Fig. 5. Relationship between left ventricular volume elastic constant, $a$, and end-diastolic volume was well correlated and was approximately curvilinear. The continuous line was obtained by exponential curve fitting to data and was fitted by the equation:
\[
a = 0.30e^{-0.037EDV} + 0.045
\]
where $a$ is volume elastic constant, $e$ is base of the natural logarithm and EDV is end-diastolic volume. Open squares represent normal in result, open triangles represent mild pulmonary stenosis and closed circles represent post mucocutaneous lymphnode syndrome (Kawasaki disease).

The left ventricular diastolic pressure-volume relationship was expressed as:
\[
dP/dV = aP + b ................................... (1)
\]
Integration and rearrangement gave:
\[
P = \frac{e^{aC} - e^b}{a} - \frac{b}{a} ................................... (2)
\]
where, $P$ = Pressure in mmHg
$V$ = Volume in ml
$a$, $b$, and $C$ = Constants
$e$ = The base of the natural logarithm
Since P-V curves are exponential, they are expressed by straight lines if $\log_e P$ is plotted on the vertical scale and volume on the horizontal scale. Based on the idea that the mid-diastole expressed diastolic elastic properties the best, we plotted the measured data on these scales, and regarded the interval, in which a straight line was obtained around the middle of diastole, as the mid-diastole. The starting point of this straight line was termed Point A, and end point was termed Point B. (See Fig. 1) Then, between Point A and Point B, exponential curve fitting was made (Fig. 2).

The stress-strain relationship can be expressed similarly to the P-V relationship as follows:
\[
d\sigma/de = k\sigma + c ............................ (3)
\]
where, $\sigma$ = Stress in g/cm² computed by the ellipsoid model
$e$ = Strain
$k$ = Stiffness constant
$c$ = Constant

As in P-V curves, the ordinate expressed $\log_e \sigma$, and the abscissa equatorial circumference, and data were plotted as shown in Fig. 3. A straight line was obtained for the $\sigma$-$e$ relationship during the same mid-diastole as in the P-V relationship. For this reason, exponential curve fitting was made during this interval (Fig. 4). In the present study, Lagrangian strain ($L_{\theta}/L_0$)
was used. The point of $L_0$ was the point in the early diastole, in which minimal diastolic pressure was recorded. The circumference at this point was selected as $L_0$.

**RESULTS**

Table I shows hemodynamic data, including the volume elastic constant (a) the stiffness constant (k) and other parameters in the control group consisting of patients with normal hearts (I), mild pulmonary stenosis (II) and post mucocutaneous lymphnode syndrome (III). Left ventricular end diastolic pressure (LVEDP) was $9.0 \pm 1.1$ mmHg (mean ± standard deviation). In the end diastole, the stress ($\sigma$) was $47 \pm 9$ g/cm². The end diastolic volume of individual patients ranged from 20 to 140 ml. Left ventricular ejection fraction was $72 \pm 3\%$ and maximum dp/dt was $1385 \pm 183$ mmHg/sec. Table II, III and IV show the hemodynamic data and stress in the patients of pre- and post-operative ASD and TOF. In patients with ASD, LVEDP* and stress** $\sigma$ were increased following operation (*$p < 0.05$, **$p < 0.01$). In patients with TOF, left ventricular ejection fraction was markedly decreased ($p < 0.01$), maximum dp/dt was decreased ($p < 0.05$) and right ventricular peak systolic and end diastolic pressure were elevated ($p < 0.01$) following operation.

**Pressure-volume relationship**

The P-V curve was constructed by curve fitting and it was fitted during the mid-diastole. Based on this relationship, the volume elastic constant, a, was computed using equation (2), and the results of this computation were then analyzed in relation to the size of the heart (i.e. end diastolic volume) (See Fig. 5). The volume elastic constant (a) was closely related to heart

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size in control group. It was fitted best to the exponential curve, and was expressed as follows:

$$a = 0.30e^{-0.037EDV + 0.045}$$

$$r = 0.94, p < 0.01$$

The results showed that the volume elastic constant ($a$) was exponentially increased with reduced heart size. On the other hand, results of three of eight postoperative ASD patients were beyond 2 standard deviations as were all postoperative TOF patients (Fig. 6).

**Stress-strain relationship**

The stress-strain relationship was also expressed by exponential curves. The best curve fitting was available in the same interval as that for P-V curves. The wall stiffness constant ($k$) was computed using equation (3), and then the results were analyzed in relation to the size of the heart. This constant for the control group was not significantly related to heart size, being $7.92 \pm 1.39$. Although the stiffness constant ($k$) probably expressed muscle stiffness, it was stable in the children, regardless of age and heart size (Fig. 7).

The stiffness constant ($k$) of postoperative ASD patients did not differ significantly from that of the control group. But the stiffness constant ($k$) of postoperative TOF patients was much higher, computed at $11.44 \pm 1.25$ g/cm², which contrasted to that of the control group and the patients having undergone ASD operation (Fig. 8). Left ventricular end diastolic volumes after surgical operation of ASD and TOF as a function of body surface area did not differ significantly from that in the control group (Fig. 9, 10).

**Diastolic period**

The duration of the early-, mid- and late-diastoles relative to the whole diastolic period were almost the same for each patient in the control group. The early-diastole accounted for about a half of the whole diastole. The mid-diastole was the shortest, and accounted for 19.6 ± 4.4% of the whole diastole. The mid-diastole started earlier after surgical operation of ASD and TOF (Table V).

The mean increase in volume in the control group for the early-diastole was 1.53 ml/kg, for the mid-diastole 0.43 ml/kg and the late-diastole 0.24 ml/kg.

**DISCUSSION**

The relationship between pressure and volume and that between stress and strain in the left ventricle can be expressed by exponential curves, which many investigators have reported. However, the results of these reports could not be accurately compared. An essential consideration is in which part of the diastolic phase should the curve be fitted. In the non-excised heart, the intervals between the early-diastole and the end-diastole cannot be expressed by the same exponential curve. Despite this fact, curve fitting has been done over the whole diastole. We agree with Noble's proposition that the relationship between pressure and volume is determined by the elastic properties of the left ventricle. As a result, when measuring elastic properties the exponential curve fitting should be made in the mid-diastole, since inertial, viscous and plastic properties which result from the sucking effect in the early-diastole and atrial kick in the late-diastole are not involved in the mid-diastole. For the purpose of determining the mid-diastole, data in the whole diastole was plotted on graph paper with $\log_{10}P$ on the ordinate and volume on the abscissa. The interval during which a straight line was obtained
around the middle of the whole diastole, was selected as the mid-diastole. In this interval, the
P-V relationship was very smooth as well as the a-e relationship, suggesting that the mid-diastole
was the most suitable interval for assessing the actual elastic properties of the left ventricle.
Neither early-diastole nor late-diastole is included in the exponential curve expressing the stress-
strain relationship. Thus it is inappropriate to use end-diastolic pressure or end-diastolic volume
as the indicator of diastolic properties. In the present study, left ventricular end-diastolic pressure
did not differ significantly between postoperative ASD and TOF. Notwithstanding, muscle elasticity
was much lower in postoperative TOF. These results suggest that it is impossible to estimate chamber compliance or muscle stiffness indirectly from end-diastolic pressure. As Diamond et al.² reported we used
the equation, \( P = \frac{e^{-\frac{ac}{a}} - e^{-\frac{b}{a}}}{a} \), in the fitting curves. The simplified equation, \( P = be^{KV} \),
involves some problems. Because the value of \( \frac{b}{a} \) is large, it cannot be ignored in the computation for fitting curves.

From an equation in which curves were fitted in the mid-diastole, values of the volume elastic constant (a), a factor of chamber compliance, were computed. The results were analyzed in relation to the size of the heart (i.e. EDV). In the control group, the volume elastic constant (a) was exponentially increased with reduced heart size. There has previously been no method for comparing chamber compliance of different sized hearts²³,²⁶ but now, the present study offers one method.

Changes in diastolic properties in the left ventricle were studied in patients after surgical operation for ASD and TOF. Four weeks after operation for ASD, three of the eight patients’ values for (a) were greater than 2 standard deviations from the mean, the stiffness constant (k) was similar to that of the control group, and the muscle stiffness was normal. Following operation for TOF, the volume elastic constant (a) and the stiffness constant (k) were significantly increased, resulting in reduced chamber and wall elasticity. Although chamber compliance decreased, wall elasticity did not always decrease, as in the case of postoperative ASD. Occasionally we encounter the patient who shows rather elevation of left ventricular end-diastolic pressure immediately after ASD closure. We suspect one

of the cause is decreased chamber compliance. The decreased chamber compliance of post-
operative ASD may be the effect of cardio-
pulmonary bypass, ischemia during the operation, pericardial change after pericardiotomy, and increased left ventricular end-diastolic volume and wall stress. The decreased chamber compliance and wall elasticity in the patients having undergone an operation for TOF has been attributed to several factors, including elevation of right ventricular peak systolic and end-diastolic pressure, right ventricular hypertrophy, the teflon patch used to close the ventricular septal defect, pericardial adhesion after pericardectomy and preoperative hypoxemia. The decreased wall elasticity following operation for TOF will influence the left ventricular function especially during exercise. As detailed above, the volume elastic constant (a) was not a good indicator of muscle stiffness. For this reason, both volume elastic constant (a) and wall stiffness constant (k) should be computed in order to obtain more accurate data on chamber and wall elasticity.

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