AN APPROACH TO THE ACCELERATIVE PHENOMENA OF LEFT VENTRICULAR PRESSURE GENERATION

DURING PRE-EJECTION PHASE:

A concept of "dominance index $t(dP/dt)/P$ "*

TOSHIAKI KUMADA

A relationship between the upstroke pattern of LV dP/dt and LV myocardial function was investigated in 37 patients with various cardiovascular diseases. A Millar's catheter-tip micromanometer was used to attain high fidelity of LV pressure pulse.

The parameter $t[(dP/dt)+(dP/dt)_0]/P$ was measured at each 5 mmHg increments of LV developed pressure (total pressure minus LV end-diastolic pressure). Where the $(dP/dt)_0$ is a value of dP/dt at the corresponding point to LVEDP and is usually zero. The values of $t[(dP/dt)+(dP/dt)_0]/P$ varied with time during the pre-ejection phase, having the tendency to increase to a maximum and then to decrease.

$D(t_{50})$, which is the value of $t[(dP/dt)+(dP/dt)_0]/P$ calculated at the LV developed pressure of 50 mmHg, correlated well with SV/mass ($r=-0.70$) and SW/mass ($r=0.69$). There was no significant relationship between $D(t_{50})$ and heart rate, LV peak systolic pressure, LV end-diastolic volume or LVEDP.

There were statistically significant differences of $D(t_{50})$ between the normal and the abnormal LV function groups (2.20 ± 0.21 , and 1.78 ± 0.10 , respectively: $p < 0.001$), and also between the normal and cardiomyopathy (CM) groups (1.76 ± 0.11 : $p < 0.001$). Two patients with CM whose LV biopsy findings showed severe myocardial fibrosis had low $D(t_{50})$ values of 1.58 and 1.66, respectively, while a patient diagnosed as having post-myocarditis had a significantly higher value of $D(t_{50})$, 2.25. He was shown to have a minimal myocardial damage on LV biopsy, and his clinical course was excellent. $D(t_{50})$ in a patient who had myocardial infarction was also significantly low. The theoretical base of $t[(dP/dt)+(dP/dt)_0]/P$ was also discussed.

From these, it is suggested that $t[(dP/dt)+(dP/dt)_0]/P$, termed as a "dominance index", which indicates the degree of dominance of the upward or downward convexes of the dP/dt curve, assesses the myocardial function and reflects the myocardial property. Hence, the importance of the accelerative phenomena of the LV pressure during the pre-ejection phase was stressed.

Key Words:

LV pre-ejection phase
Upstroke pattern of LV dP/dt
 $t(dP/dt)/P$
Accelerative phenomena

MANY investigators have evaluated the importance of the rate of rise of left ventricular pressure (dp/dt) as a measure of assessing the left ventricular (LV) myocardial function. Above all, many studies have been done on maxi-

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The 3rd Division, Department of Internal Medicine, Faculty of Medicine, Kyoto University, Kyoto, Japan

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mum dp/dt .¹⁻⁹

On the other hand, there are few descriptions concerning the upstroke pattern of the LV dp/dt . Mason et al.⁵ described that with the onset of isovolumic contraction the dp/dt rose slowly at first and then rapidly reached its peak. By using fiberoptic catheters, Letac and his coworkers¹⁰ showed that the second derivative (d^2P/dt^2) of LV pressure during the isovolumic phase had a positive and fairly smooth deflection. These observations suggest a smoothness of the upstroke pattern of LV dp/dt unless artifacts such as the flicking of the catheter or electrical noise affect the pressure tracing.

Concerning the effects of dp/dt of loading conditions, Wildenthal⁶ and Mason⁸ reported that an increase in preload caused an elevation of instantaneous dp/dt throughout the course of isovolumic contraction, as well as an increase of the peak dp/dt , whereas an elevation of arterial diastolic pressure elevated only peak dp/dt . Furthermore, when the loading of the heart is stable, dp/dt itself correlates with the contractile state of the left ventricle.^{4,5} It is possible from this that, since the dp/dt curve is the locus of the instantaneous dp/dt , the contour of the dp/dt upstroke itself also reflects myocardial contractile property. In spite of the importance of the dp/dt curve, there has been no report on the relationship between the upstroke pattern of LV dp/dt and the myocardial function.

Previously, we reported that $(dp/dt)/(P/t)$ or $t(dp/dt)/P$ derived from LV pressure was a quantitative expression of the upstroke pattern of dp/dt and a useful index in evaluating LV myocardial function among patients.¹¹ However, these data were obtained by using a fluid-filled catheter system which did not usually have sufficiently reliable frequency response to allow nonartefactual intraventricular pressure recordings.¹² Since it is necessary to get the precise ventricular pressure in order to analyze the dp/dt curve in detail, the validity of the previous results remained to be reexamined, at least by employing high-fidelity recording of intraventricular pressure. Thus, the present study was undertaken to reanalyze the upstroke pattern of LV dp/dt obtained by use of the catheter-tip micro-manometer and to reinvestigate the usefulness and the limitations of $t(dp/dt)/P$, as well as its theoretical base.

THEORETICAL CONSIDERATION

Consider a smoothly rising sigmoid curve: the

Fig. 1. The method for analyzing the degree of the "dominance" of the convexity (upward or downward) in a sigmoid curve illustrated schematically. Two points, shown as A(a, f(a)) and B(b, f(b)) here, were selected arbitrarily on the f(t) curve. Mu and Md are areas drawn by oblique lines, located above and below the line segment AB, respectively. (see text).

curve starts from the origin O, and is expressed as $f(t)$, a function of time (Fig. 1). Taking two arbitrary points A and B, on the curve with coordinates (a, f(a)) and (b, f(b)), respectively, the line segment AB joining points A and B can be expressed by the following equation:

$$Y(t) = \left[\frac{(f(b) - f(a))}{(b - a)} \right] t + \frac{(bf(a) - af(b))}{(b - a)} \quad (a \leq t \leq b), \dots \dots \dots (1)$$

where $(0 \leq f(a) < f(b), 0 \leq a < b)$

Let $Q(a, b)$ be the difference between the area M_u (above AB and below $f(t)$) and the area M_d (above $f(t)$ and below AB). Then

$$Q(a, b) = M_u - M_d$$

$$= \int_a^b [f(t) - [(f(b) - f(a))/(b - a)] \cdot t + (bf(a) - af(b))/(b - a)] dt$$

If we denote $F(t) = \int f(s) ds$, (where $F'(0) = f(0) = 0$) then $Q(a, b) = (F(b) - F(a)) - (b - a)(f(a) + f(b))/2$ (2)

We define here $D(a, b)$ by equation (3)

$$D(a, b) = (b - a)(f(a) + f(b)) / (F(b) - F(a)) \quad (0 \leq F(a) < F(b)) \quad \dots \dots \dots (3)$$

Then from equation 2, we obtain

$$2Q(a, b) = (F(b) - F(a))(2 - D(a, b)) \quad \dots \dots \dots (4)$$

From equation (4), and since $F(b) - F(a) > 0$, it is seen that when $Q(a, b) \leq 0$, $D(a, b) \geq 2$ and when $Q(a, b) > 0$, $D(a, b) < 2$.

Now, consider the areas M_u and M_d . If $M_u > M_d$, then $Q(a, b) > 0$ and therefore $D(a, b) < 2$; if $M_u < M_d$, then $Q(a, b) < 0$ and therefore $D(a, b) > 2$; and if $M_u = M_d$, then $Q(a, b) = 0$ and $D(a, b) = 2$. That is, the relative size of M_u and M_d determine whether $D(a, b)$ is greater or less than 2. M_d consists mainly of the area bounded by the

downward convex of $f(t)$ and M_u consists mainly of the area bounded by the upward convex of $f(t)$. Consequently, $Q(a, b)$ indicates which of the areas is greater, that is dominant. "Upward dominance" is obtained when $D(a, b) < 2$, namely, when the upward convex area is greater than the downward; "downward dominance" indicates the reverse situation, namely, $D(a, b) > 2$ (Fig. 2).

Definition of $D_a(t)$

Here, if we let $(b - a) = t$, $F(b) - F(a) = P_a(t)$ and $D(a, b) = D_a(t)$, then equation (4) is rewritten as

$$2Q_a(t) = P_a(t) \cdot (2 - D_a(t)) \quad \dots \dots \dots (5)$$

and from equation (3)

$$D_a(t) = t(f(t + a) + f(a)) / P_a(t) \quad \dots \dots \dots (6)$$

$D_a(t)$ is called the "dominance index at point A", and this indicates the degree of dominance of the upward and the downward convexes of the curve $f(t)$.

From equation (5), we obtain

$$D_a(t) = 2(1 - Q_a(t) / P_a(t)) \quad \dots \dots \dots (7)$$

Obviously, $D_a(t)$ is a continuous function of time. When the value of $D_a(t)$ decreases, the upward convex area increases in comparison with the downward. This is seen from equation (7). In fact, in order for $D_a(t)$ to decrease, the rate of increase of $Q_a(t)$ must be greater than that of $P_a(t)$. That is, the upward convex area must increase in comparison with the downward.

Clinical Applications of $D_a(t)$

Assume that the dP/dt upstroke curve is sigmoidal and the LVEDP point is taken as point A, then

$$f(t + a) = dP/dt$$

$$f(a) = (dP/dt)_0 = dP/dt \text{ at the LVEDP point}$$

$$P_a(t) = \text{LV developed pressure}$$

$$t = \text{the time interval from the LVEDP point to the time of measurement of the developed pressure.} \quad \dots \dots \dots (8)$$

In view of substitutions (8), equation (6) yields the dominance index $D(t)$ as follows.

$$D(t) = t \cdot [(dP/dt) + (dP/dt)_0] / P \quad \dots \dots \dots (9)$$

Since $(dP/dt)_0$ is usually zero at the LVEDP point, the dominance index takes a simpler form (10)

Fig.2. Diagrammatic representation of two typical, different patterns of the sigmoid curve: one is an upward dominance ($D(a, b) < 2$), and the other a downward dominance ($D(a, b) > 2$).

$$D(t)=t(dP/dt)/P \dots\dots\dots (10)$$

MATERIALS AND METHODS

Thirty seven patients aged 15 to 59 years, were studied during the diagnostic catheterization. Their diagnosis are listed in Table I–IV: Seven patients had mitral valvular disease, two aortic regurgitation, nine combined valvular disease, eight idiopathic cardiomyopathy, two aortitis syndrome, three coronary arterial disease, one myocardial infarction, and five other cardiovascular diseases. Seven patients had atrial fibrillation, and eight had regurgitation (mild to severe) during systole.

A routine right and left heart catheterization was carried out in the fasting state. The patients were premedicated with small, oral sedatives (Bromvaleryl Urea (0.5g), and Chlordiazepoxide (10 mg)), two hours before the beginning of the catheterization. Each patient was studied at rest in the supine position during catheterization. To permit the recording of high fidelity of LV pressure pulse, a Millar's catheter-tip micromanometer (5F or 7F) was inserted into LV through the brachial or the femoral artery by arterio-

tomy. This transducer unit has a frequency response of 20 KHz (Millar Mikrotip, Millar Instrument, Houston, Texas). The first derivative of LV pressure (dP/dt) was continuously determined with a R/C differentiating circuit. The time constant of this circuit is 1.0 msec, and it provides differentiation of linear amplitude within 5 percent to 65 Hz and has phase shift of 29° at 40 Hz. The differentiating circuit was calibrated by imposing a signal of a constant and known slope from an integrating amplifier and measuring the resulting response of the differentiator. The catheter-tip pressure sensor was calibrated with a mercury manometer before each study. A zero base line was established at the beginning of each study and confirmed at the end of each study. The other pressure were measured with a Statham strain gauge transducer (P23Db), and the zero reference pressure was set at midchest level. LV pressure, LV dP/dt , and electrocardiogram (lead II) were simultaneously recorded at 100–200 mm/sec on an Electronics for Medicine DR 12.

A left ventriculogram was obtained with a Schonander biplane film changer at six films per

Fig.3. A method of calculation of $t[(dP/dt)+(dP/dt)_0]/P$. First, the dP/dt at the LVEDP point ($= (dP/dt)_0$) was measured: usually, the value of $(dP/dt)_0=0$. Then, at each 5mmHg increments of LV developed pressure (total pressure-LVEDP) from LVEDP level, the time intervals (t) and dP/dt amplitude were measured, and $t[(dP/dt)+(dP/dt)_0]/P$ value at each point was calculated.

$t[(dP/dt)+(dP/dt)_0]/P$ was expressed as $D(t)$, a function of time. Especially, $D(t)$ at a developed pressure of 50mmHg was expressed as $D(t_{50})$. See text for further details.

Fig. 4. The gain (voltage), and the phase shift (degree) as a function of frequency, in the differentiating circuit.

second for five seconds. LV volume measurement was done by the area length method, and the LV mass weight was computed by the difference between the volume of the LV chamber plus wall and the volume of the LV chamber by 1.050. Premature ventricular contractions and post-extrasystolic beats were not analyzed. The cardiac output was determined by the Fick principle, and the stroke work in gram-meters was measured as $1.36 \times (\text{stroke volume} \times \text{mean aortic pressure})/100$.

LV end-diastolic pressure (LVEDP) was measured at the point after the A wave and where the slope of the LV pressure (dP/dt) was zero. When there was doubt as to the exact point, then a point immediately before the beginning of the abrupt rise of the dP/dt was chosen. The LVEDP point so obtained was found about midway between the Q wave and the R wave of lead II of the electrocardiogram

(ECG): the average time interval between the EDP point and the peak of the R wave in lead II was 20.4 ± 10.0 msec and the QR interval was 40.7 ± 8.1 msec. In cases in which the dP/dt was not zero at the LVEDP, the dP/dt value at this point ($= (dP/dt)_0$) was also measured.

To analyze the upstroke pattern of LV dP/dt on the basis of the theoretical consideration, the following techniques were used: at 50 mmHg of LV developed pressure (P), $t \cdot [(dP/dt) + (dP/dt)_0] / P$ was calculated (Fig. 3): where t = the time interval from the LVEDP point to the time of measurement of the developed pressure = 50 mmHg, dP/dt = the dP/dt value at the developed pressure of 50 mmHg, $(dP/dt)_0$ = the dP/dt value at the LVEDP point, and P = 50 mmHg of LV developed pressure. If the slope of the pressure at the LVEDP point is zero, then the equation becomes $t(dP/dt)/P$. This procedure was done for 5 consecutive beats in cases with sinus rhythm and the average value of 5 beats was taken as a $D(t_{50})$ value for each patient. In cases with atrial fibrillation, values of 5 to 10 beats were averaged. When LV developed pressure at peak dP/dt was less than 50 mmHg, a $t[(dP/dt) + (dP/dt)_0] / P$ value at the peak dP/dt was used instead of a $D(t_{50})$ value; 15 cases had such a low developed pressure (8 had mitral stenosis, 3 aortic regurgitation (combined), 2 cardiomyopathy, 1 aortopathy, and 1 myocardial infarction). In addition, t and dP/dt were measured at each 5 mmHg increments of LV developed pressure from LVEDP level up to the pressure point where the peak dP/dt occurs, and $t[(dP/dt) + (dP/dt)_0] / P$ value at each point was calculated and expressed as $D(t)$ (Fig. 3). The time course of these $D(t)$ values was obtained for each patient by plotting $D(t)$ against (t) time (Fig. 5A). The cases in which an upstroke curve of dP/dt had noise or vibration were excluded.

$V_{\max}$ was obtained from total pressure data by extrapolating the points between peak $(dP/dt / \text{total pressure})$ and peak $dP/dt / \text{total pressure}$ back to zero pressure by means of a linear least squares curvefitting, using the stiffness constant (K) = 32.

From conventionally established criteria, 15 patients without cardiomyopathy were divided into two groups. One consists of 7 patients who had an ejection fraction (EF) of more than 50%, an LVEDP of less than 12 mmHg, and a cardiac index (CI) of greater than 2.5 L/min/m^2 , and who had no clinical history of heart failure. The mean LV end-diastolic volume in this group was

133 ± 23 ml. They were regarded as having normal ventricular function. The other group consists of 8 patients who had an EF of less than 50% and who had one or more of the following: LVEDP in excess of 12 mmHg, CI of less than 2.5 L/min/m², or clinical history of heart failure. Their average LV end-diastolic volume was 246 ml (100 to 650 ml). The patients of this group were regarded as having an abnormal ventricular function. Besides these groups, an idiopathic cardiomyopathy (CM) group was prepared. This group consisted of 8 patients (6 with hypertrophic (obstructive) CM, and 2 with congestive CM).

A statistical analysis of the difference of $D(t_{50})$ or other parameters was performed between the normal, abnormal and other various groups by using the student's *t*-test.

Estimation of the differentiating circuit

The frequency response of the differentiating circuit was tested electrically by a sine wave generator. In response to sine wave changes in

the input voltage, the output of the differentiator showed 13° phase shift at 20 Hz and 29° at 40 Hz, and there was a linear relationship (± 5%) between the amplitude of the output and the frequency of the input signal up to 65 Hz (Fig. 4).

Since the Fourier analysis of LV pressure waves was not done in this study, we can not estimate exactly the spectrums of the harmonics. However, as stated by Gersh and Falsetti et al^{13,14} if beyond the 6th or 10th harmonics the amplitude is less than 1% of the fundamental and lies within the noise level of the system at heart rates ranging from 130 to 195 beats/min,¹³ there is a possibility that the mean phase shift introduced by the differentiator used here might be within a few milli seconds (theoretically within 2 msec): our study was done in the patients with a much lower fundamental frequency (1–2 Hz) compared with their dogs,¹³ and the main spectrums of the harmonics in the present study may be lower than the 10th harmonics.

Fig.5. Representative curves showing a relationship between $D(t)$ (or $t[(dP/dt)+(dP/dt)_0]/P$), measured at each 5mmHg increments of developed pressure throughout pre-ejection phase, and time (A in Fig.5). The time history of the $D(t)$ was named as a "dominance curve". Note that the "dominance curve" tends to increase to a maximum, and then to decrease.

B: Values of $t[(dP/dt)+(dP/dt)_0]/P$ were also plotted against LV developed pressure. A $D(t_{50})$ value was taken at 50mmHg of developed pressure, indicated by a dotted line.

The results of the close and repeated examinations concerning the phase shift of the dP/dt which was simultaneously recorded with LV pressure at 200 mm/sec suggested that the time delay was almost indistinguishable.

Though it would be desirable to eliminate this time delay, it is not expected that these errors would be significant. Hence, the time delay introduced by the differentiator was neglected here.

The error in measurement of $D(t_{20})$

The LVEDP point was located at 20.4 ± 10.0 msec before the R wave in lead II of ECG, as described above. The dP/dt value at the point ($=dP/dt_0$) averaged 11 ± 21 mmHg/sec in all cases.

When dP/dt and LV pressure were measured 5 msec after the original LVEDP point, dP/dt increased to 62 ± 42 mmHg/sec, LV pressure to 0.43 ± 0.48 mmHg, and, as a result, $D(t_{50})$ decreased by $2.3 \pm 3.4\%$.

When a point at 10 and 15 msec after the original EDP point was taken as a new EDP, then dP/dt increased to 117 ± 80 and 178 ± 118 mmHg/sec, respectively, and LV pressure to 1.14 ± 1.13 and 2.27 ± 2.0 mmHg, respectively. The decrease in $D(t_{50})$ averaged $4.9 \pm 4.9\%$ (with 10 msec delay) and $7.0 \pm 6.3\%$ (with 15 msec delay of the EDP point), respectively.

Double blind test was performed. Each $D(t_{50})$ was calculated by four independent examiners, and those interindividual variations were as follows: the coefficient of variables of the time interval between the EDP and the LV developed pressure of 50 mmHg (P_{50}) was $2.4 \pm 1.6\%$, that of dP/dt at P_{50} was 1.4 ± 0.5 mmHg/sec and that of $D(t_{50})$ was $3.6 \pm 1.3\%$, respectively.

Therefore, if the point of LVEDP was measured carefully, providing that the zero level of the dP/dt is determined exactly, the measuring error of $D(t_{50})$ can be less than 6%.

RESULTS

Tables I-IV list the diagnosis, age, sex and the routine hemodynamic data of all 37 patients. The dominance index $D(t_{50})$ is tabulated for each patient. The indices of LV pump function per unit of mass weight and the contractility indices ($SV/mass$, $SW/mass$, $\max dP/dt$ and V_{max}) are also listed.

$SW/mass$ and $SV/mass$

TABLE I NORMAL LV FUNCTION GROUP

Case	Sex	Age y.r.	Diagnosis	EF %	CI L/min/m ²	EDP mmHg	HF beats/min	HR ml	EDV mmHg	PP ml/G	$\frac{SV}{mass}$ ml/G	$\frac{SW}{mass}$ M	$D(t_{50})$ ML/sec	V_{max} mmHg/sec	$\max dP/dt$ mmHg/sec
1.	H.H.	f	32	MS, MR Cor. abn.	55.5	3.32	8	(-)	85.1	119	106	0.53	51.9	1.96	815
2.	N.S.	f	35	MS, AS, AF	56.2	2.70	10	(-)	80.0	105	140	0.38	45.9	2.21	2693
3.	S.C.	f	35	ASD, MR,	61.7	4.38	11	(-)	79.0	120	112	0.77	90.8	2.44	1588
4.	R.N.	f	15	AR	66.2	4.54	5	(-)	66.3	160	104	0.83	104.0	2.39	1264
5.	Y.A.	m	24	Post-M.	63.6	3.56	6	(-)	61.0	165	96	0.59	66.5	2.25	1556
6.	Y.K.	m	45	IHD	64.8	2.96	7	(-)	51.0	142	112	0.70	87.6	1.87	1200
7.	H.I.	m	29	NCA	70.8	...	6	(-)	76.9	120	112	0.88	128.7	2.26	1750
		mean	30.7		62.7	3.58	7.6		71.3	133	112	0.67	82.2	2.20	1538
		s.d.	9.5		5.4	0.81	2.2		12.2	22.9	13.8	0.18	29.5	0.21	559

MS=Mitral Stenosis, MR=Mitral Regurgitation, AR=Aortic Regurgitation, AS=Aortic Stenosis, Cor.abn.=Abnormalities of the coronary artery, AF=Atrial Fibrillation, ASD=Atrial Septal Defect, Post-M.=post-Myocarditis, IHD=Ischemic Heart Disease, NCA=Neurocirculatory Asthenia, HF=Heart Failure, PP=LV peak systolic pressure.

(B) CCM

1.	M.K.	m	34	CCM	39.5	3.73	8	(+)	82.0	185	119	0.34	42.4	1.80	0.87	964
2.	M.S.	m	49	CCM	19.9	2.92	19	(+)	101.0	266	130	0.26	26.2	1.58	0.97	1013
		mean	41.5		29.7	3.33	13.5		91.5	226	125	0.30	34.3	1.69	0.92	989

HCM=Hypertrophic Cardiomyopathy, HOCM=Hypertrophic Obstructive Cardiomyopathy, CCM=Congestive Cardiomyopathy.

TABLE IV OTHERS

Case	Sex	Age	Diagnosis	EF	CI	EDP	HF	HR	EDV	PP	SV	SW	D(t ₅₀)	V _{max}	max dP/dt
		y.r.		%	L/min/m ²	mmHg		beats/min	ml	mmHg	ml/G	mass		ML/sec	mmHg/sec
1.	T.M.	f	29	MS, AS, PH	...	2.86	10	(-)	108.7	...	...	...	1.77	1.45	1006
2.	C.O.	f	21	OTAP	57.7	4.39	12	(-)	78.0	130	0.58	100.0	2.18	1.48	1796
3.	T.Y.	f	36	OTAP	63.6	5.70	15	(-)	117.6	110	0.46	99.4	1.98	2.04	3558
4.	H.O.	m	36	IHD	62.5	...	16	(-)	91.6	112	0.44	63.9	2.07	1.33	2836
5.	M.M.	f	34	MS	67.1	2.36	4	(-)	79.6	85	0.49	39.0	2.02	2.08	969
6.	M.T.	f	50	ASD, MR, AF	59.0	3.50	8	(+)	94.9	122	0.49	45.6	1.81	0.97	1132
7.	T.T.	m	39	MS, AF	...	1.78	9	(-)	59.6	...	...	...	1.93	0.86	1152
8.	C.O.	m	26	Coarc.	54.0	4.85	14	(-)	96.0	161	0.39	71.0	2.07	1.69	2693
9.	H.S.	m	25	MR, AR	...	3.75	8	(-)	78.2	...	...	...	1.92	1.22	1360
10.	T.S.	m	37	Post-M.	39.4	2.62	7	(-)	78.2	137	0.44	51.3	2.09	1.64	1694
11.	T.T.	m	23	Chr.Th.	60.7	3.64	14	(-)	70.0	168	0.44	50.6	1.75	1.17	1022
12.	S.O.	m	34	AR	31.5	4.37	9	(-)	89.0	540	0.17	20.5	2.00	1.43	1299
13.	K.I.	f	30	MS	53.8	3.46	11	(-)	77.7	156	0.54	64.3	2.32	...	1307
14.	F.H.	f	59	CAD	52.4	...	16	(-)	76.8	103	0.44	62.2	1.93	0.84	1150
		mean	32.2		54.8	3.61	10.9		85.4	166	0.44	60.7	1.99	1.40	1641
		s.d.	10.4		11.8	0.64	3.7		15.3	123	0.11	23.8	0.16	0.40	810

PH=Pulmonary Hypertension, OTAP=Occlusive Thromboaropathy (aortitis syndrome), Coarc.=Coarctation of Aorta, Chr.Th.=Chronic Thyroiditis, CAD=Coronary Artery Disease.

Mean values for SV/mass and SW/mass are 0.67 ± 0.18 ml/g and 82.2 ± 29.5 meters for the normal function group; 0.31 ± 0.06 ml/g ($p < 0.001$) and 33.7 ± 9.3 meters ($p < 0.01$) for the abnormal function group; 0.31 ± 0.22 ml/g ($p < 0.01$) and 31.8 ± 21.7 meters ($p < 0.01$) for the patients with HCM; and 0.30 ± 0.05 ml/g ($p < 0.05$) and 34.3 ± 11.5 meters ($p = \text{NS}$) for the patients with CCM.

Contractility Indices ($\max dP/dt$ and $V_{\max}$)

Mean values for $\max dP/dt$ are 1538 ± 559 mmHg/sec for the normal function group; 1114 ± 320 mmHg/sec for the abnormal function group ($p = \text{NS}$); 1244 ± 448 mmHg/sec for the HCM group ($p = \text{NS}$), and 989 ± 35 mmHg/sec for the CCM group ($p = \text{NS}$). No significant differences from the normal group were found in these groups.

$V_{\max}$ averaged 1.49 ± 0.2 ML/sec in the normal function group. The mean value in the patients with the abnormal function was 1.02 ± 0.15 ML/sec. The differences from the normal group was significant ($p < 0.001$). Mean values in the patients with HCM and CCM were 1.09 ± 0.43 ML/sec and 0.92 ± 0.07 ML/sec, respectively. Although the mean values of $V_{\max}$ differed significantly from the normal group ($p < 0.05$ and $p < 0.01$, respectively), overlap occurred in 3 patients with HCM.

Dominance Index $D(t)$ or $D(t_{50})$

Fig. 5A demonstrates a time course of $D(t)$ during pre-ejection phase in three patients. $D(t)$, measured at each 5 mmHg increments of LV developed pressure, was not constant but varied with time during the pre-ejection phase and tended to increase to a maximum in the early phase of contraction and then to decrease. The time course of $D(t)$ was called a "dominance curve". It is clearly seen in Fig. 5A that the dominance curve in the patients with myocardial infarction or the congestive cardiomyopathy is located at a considerably lower level than the patient with NCA. In the present study, a comparison of the $D(t)$ value among all patients was done by employing the value of $D(t_{50})$ which was measured at the developed pressure of 50 mmHg, as seen representatively in Fig. 5B.

In 7 patients with the normal function $D(t_{50})$ averaged 2.20 ± 0.21 (dimensionless). This value differed significantly ($p < 0.001$) from that of 8 patients with the abnormal function in whom the $D(t_{50})$ value averaged 1.78 ± 0.10 . The mean

value in patients with cardiomyopathy was 1.76 ± 0.11 , which also differed significantly from the normal group ($p < 0.001$): (1.78 ± 0.12 in the HCM ($p < 0.01$), and 1.69 ± 0.31 in the CCM ($p < 0.02$)) (Fig. 6).

There are several patients who should be mentioned briefly. Case 2 and 3 (open circle in Fig. 6) in the normal group was a 32-year-old female and a 45-year-old male, respectively.

Fig. 6. $D(t_{50})$ in patients with normal, and abnormal ventricular function by conventional criteria, and in patients with cardiomyopathy. A significant separation between the patient group with the normal function and the other patient groups is apparent. The patients indicated by the number 1 to 5 were as follows: case 1 post-myocarditis, case 2 and 3 diagnosed as coronary arterial disease or the abnormalities by angiographically, case 4 with severe mitral stenosis who expired after valvular replacement, and case 5 with post-myocardial infarction and angina pectoris.

Note, case 2 and 3 who had the $D(t_{50})$ lower than the other patients with normal function, and case 5 with a significantly lower $D(t_{50})$ value, compared to case 1 showing a minimal myocardial damage on myocardial biopsy.

Fig.7. The relations of $D(t_{50})$ to heart rate (on the left), and to LV peak systolic pressure (on the right).

Fig.8. The relationship between $D(t_{50})$ and LV end-diastolic volume, (LVEDV), and between $D(t_{50})$ and LV end-diastolic pressure (LVEDP).

Angiographically, they were found to have a diffuse narrowing of the coronary arteries, but EF, LVEDP and CI in both patients were normal. Compared with the remaining patients of the

normal function group, both patients had a significantly lower $D(t_{50})$ value of 1.96 and 1.87, respectively. Case 4 (the triangle) in the abnormal function group was a 45-year-old

Fig.9. The relationship of $D(t_{50})$ to stroke volume (SV) per mass weight, and to stroke work (SW) per mass weight. $D(t_{50})$ tends to correlate well with SV/mass and SW/mass.

Fig.10. Three representative cases of the upstroke pattern of LV dP/dt , obtained by using a catheter-tip micromanometer. In the top figures, the initial, positive deflection of the dP/dt curve was demonstrated.

The convexity of the upstroke of the LV dP/dt curve can be characterized relatively easily by the pattern of the upstroke curve.

female with severe mitral stenosis and atrial fibrillation, and had congestive heart failure according to her history. She had $D(t_{50})$ of 1.69, and expired after mitral valve replacement. Another patient (case 5 in Fig. 6) had post-myocardial infarction and angina pectoris. He had an evidence of LV failure, and the angiograms showed the dyskinesia in the apical to basal portion of the left ventricle as well as the narrowing of the left coronary arteries. He had a significantly low $D(t_{50})$ value of 1.67. On the other hand, a 24-year-old male with signs of myocarditis in the past few months, showing the high $D(t_{50})$ (the double open circle, in Fig. 6), had a good prognosis. LV biopsy showed a minimal myocardial damage and in fact his recovery was excellent. The value for $D(t_{50})$ was 2.25. In contrast to this, two patients (F.K. and M.S. in Table III) with cardiomyopathy were proved to have severe myocardial fibrosis on LV biopsy and had a significantly lower $D(t_{50})$ value of 1.66 and 1.58, respectively.

There were no significant relationship between $D(t_{50})$ and the heart rate, LV peak systolic pressure, or LVEDV (Figs. 7 and 8). $D(t_{50})$ had a roughly inversed correlation with LVEDP, but the correlation coefficient was low ($r = -0.46$) (Fig. 8).

$D(t_{50})$ is compared with the stroke volume

per mass weight and the stroke work per mass weight in Fig. 9, with a correlation coefficient of 0.70, and 0.69, respectively. Of note was the close correlation with the pumping function per unit of mass.

Fig. 10 shows three representative cases of the upstroke pattern of LV dP/dt . Case 1 had mild aortic regurgitation (AR) with normal LV performance, in which the downward convexity is dominant in the dP/dt upstroke curve ($D(t_{50}) > 2$). Case 2 had congestive cardiomyopathy whose biopsy findings showed severe myocardial fibrosis, and had abnormal LV function. Case 3 had myocardial infarction, who was not included in the present data. In case 2 and 3, the upward convexity is dominant ($D(t_{50}) < 2$).

DISCUSSION

In an early study, the left ventricular pressure was approximated by the equation $P = At^k$ (P =LV developed pressure, A =constant of integration t =time, $K=(dP/dt)/(P/t)$ =constant) (11). However, this theory holds under the condition that K , that is $(dP/dt)/(P/t)$, is constant until LV developed pressure reaches at least 50 mmHg. In addition, ventricular pressure was measured with an external transducer system. The present results obtained by use of a micromanometer showed that $(dP/dt)/(P/t)$, or $t(dP/dt)/P$, is not constant in the pre-ejection phase, but varies with time (Fig. 5A). Thus, left ventricular pressure cannot be approximated by At^k . The apparent stability of $t(dP/dt)/P$ in the pre-ejection phase is thought to have arisen from distortion of the external manometer system.

Although there are no reports on the kind of upstroke pattern shown by the LV dP/dt curve, many papers carry recorded dP/dt curves. Close examination of their wave forms reveals that while notches may occur midway through the upstroke, or vibration or notches may be seen near the maximum dP/dt , the overall mode of the upstroke is sigmoidal. The report of Letac et al.¹⁰ who measured the second derivative of left ventricular pressure pulse (d^2P/dt^2) by use of a fiberoptic catheter, supports our idea. They stated that the d^2P/dt^2 of the LV isovolumic phase shows a smooth, positive deflection (sometimes with a small hump), and that the peak precedes that of the first derivative (dP/dt). These findings imply that the dP/dt upstroke curve is sigmoidal, because as d^2P/dt^2 increases with time the dP/dt curve must form a downward convex and as the second derivative

decreases the dP/dt curve must form an upward convex. And the peak of d^2P/dt^2 falls exactly at the point of inflection of the sigmoid dP/dt upstroke curve. Our recorded dP/dt curves also exhibited a sigmoidal shape, the downward convex in early systole transforming to an upward convex midway through the contraction. Although the overall upstroke curve was sigmoidal, not all curves were completely smooth: in some cases the curve showed a hump near the M component of the first sound, or notches or other irregularities.

In this study, the time course of $D(t)$ was obtained by plotting $D(t)$ values calculated for 5 mmHg increments of LV developed pressure against time, and showed a pattern of increase and subsequent decrease. As described earlier, the decrease of $D(t)$ with time implies that upward convex of the dP/dt upstroke curve is increasing relative to the downward convex. Thus, the findings in this study of increase and decrease in $D(t)$ are thought to support the validity of regarding the dP/dt upstroke curve as sigmoidal. This $D(t)$ curve shows the degree of dominance of the undulations of the dP/dt curve with time, and will be called the "dominance curve". In our results, the dominance curve of a dP/dt curve with a smooth upstroke was also smooth, and when the dP/dt upstroke curve showed humps or notches, corresponding deformations appeared in the dominance curve. This finding showed the dependence of $D(t)$ on the dP/dt pattern.

The "dominance theory" described previously is adaptable to curves other than sigmoids: for a curve exhibiting repeated undulations, the degree of dominance of the parts of the curve above and below a line segment joining two points on the curve may also be determined. Consider a dP/dt upstroke curve exhibiting some irregularities on the curve. If one takes $D(t)$ at a point on the upstroke curve near the maximum dP/dt (here, $D(t_{50})$ was taken, that is, $t[(dP/dt) + (dP/dt)_0]/P$ when developed pressure=50 mm-Hg), it is possible to assume a broad sigmoid character of the dP/dt upstroke curve and ignore the influence of few irregularities on the curve.

It is well known that dP/dt is influenced by loading conditions⁴⁻⁶. Thus, it is possible that the dP/dt upstroke curve is also influenced by these conditions. In the present study, subjects who had a chronic clinical course were chosen. No statistically significant correlations were found between $D(t_{50})$ and heart rate, peak

systolic pressure, LVEDV, or LVEDP in these patients with various cardiovascular lesions. Therefore, in the basal state, $D(t_{50})$ may be insusceptible to the influences of the loading conditions. Wildenthal et al.⁶ found a rise in maximum dP/dt with increased afterload, but this is thought to arise from a prolongation of the upward convex of the dP/dt curve (in fact, they showed this diagrammatically), and can be predicted to have no influence on the initial part of the dominance curve. The effects of an acute change of preload and heart rate on $D(t_{50})$ are unknown, but in this study $D(t_{50})$ was not necessarily elevated in patients with large volume overload or high heart rate.

The relation between $D(t_{50})$ and LV function can clearly be seen in Fig. 6 and 9. In a group with normal LV function, $D(t_{50})$ was above "2", in patients with abnormal LV function, $D(t_{50})$ was below "2". That is, if LV function declines, the upward convex of the dP/dt upstroke curve relatively increases. Further, in cardiomyopathy where severe fibrosis of the LV myocardium had been confirmed by left ventricular biopsy, and in myocardial infarction, $D(t_{50})$ was below 2; in contrast, in patients with post-myocarditis whose biopsied myocardial tissue showed virtually normal and whose subsequent clinical course was uneventful, $D(t_{50})$ was above 2. This finding suggests that as the myocardial damage progresses, the upward convex of the sigmoid dP/dt curve gradually becomes dominant over the downward convex. The significance of this change in the dP/dt curve becomes apparent when the second derivative is considered. As dP/dt follows the upward convex, d^2P/dt^2 decreases, indicating that the accelerative phenomena, which produce pressure, decline. This suggests that damage of the myocardial tissue is reflected by the accelerative phenomena of intraventricular pressure. Furthermore, $D(t_{50})$ tended to decrease with depressed LV pumping function per unit of mass weight. Hence, it is assumed that the myocardial shortening characteristics per muscle unit are also reflected by the accelerative phenomena during pre-ejection phase.

Several problems still remain concerning the use of the dominance index $D(t)$. First, there are cases where LVEDP cannot be determined precisely. In our measurements, LVEDP always occurred between the Q and R waves of lead II of the electrocardiogram, but the error in measuring $D(t)$ in this region must be considered. Second, the influence of loading conditions on $D(t)$ must

be examined further. Third, here we have calculated the value of $D(t)$ for a LV developed pressure of 50 mmHg, that is, $D(t_{50})$, but the dominance curve (Fig. 5A) itself must be further analyzed. Fourth, superimposition of noise arising from systolic regurgitation, such as mitral regurgitation, on the dP/dt upstroke curve often prevents analysis of the pattern. Fifth, the correlation of the dominance index with physiological conditions must be examined.

Despite the above problems, the dominance index is clinically valuable. Decrease in $D(t_{50})$ in patients with conventionally established LV abnormal function, and in patients with cardiomyopathy, myocardial infarction and other diseases, strongly suggests that the dominance index can act as an effective clinical indicator for evaluating cardiac function. Its greatest merit may be that LV function can be estimated merely by inspection of the dP/dt upstroke pattern (Fig. 10). Therefore, it must be stressed that the dominance index is superior to V_{max} in the simplicity of obtaining the $D(t_{50})$ value, though the V_{max} separated the abnormal function group from the normal in this series.

It is desirable to measure directly the second derivative (d^2P/dt^2) for the detailed analysis of the accelerative phenomena. However, because of the presence of artificial noises, the accurate measurement of the d^2P/dt^2 has frequently been made impossible without the introduction of special devices.¹⁰ This fact led us to attempt to devise the present method for approaching the accelerative phenomena without using d^2P/dt^2 curve itself. The $D(t)$ is not an absolute value of the d^2P/dt^2 but expresses the accelerative mode of LV pressure, suggesting the significance of measuring the time interval between the beginning of LV contraction and the point of the peak of the d^2P/dt^2 . Mirsky¹⁵ has proposed a similar parameter, $t(dP/dt)/P$, as an effective indicator of LV function. But he did not make further comment on this matter. The concept of "dominance" which we have proposed differs in its approach from recently criticized isovolumic phase indexes derived from dP/dt ¹⁶⁻¹⁸ by indicating a time factor (t) and in treating ventricular pressure as an accelerative phenomena. Thus, the importance of this accelerative nature must be stressed.

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