Influence of Acute Hemodynamic Changes on the Peak Velocity of Contractile Element Shortening and Maximum Velocity Obtained by the Calibrated Apex Cardiography in Dogs[†]

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SUMMARY

The effect of various alterations in preload, afterload and inotropic state of the left ventricle on the noninvasive peak velocity of contractile element shortening (V_{pm}) and maximum velocity of contractile element shortening (V_{max}) was studied in the anesthetized dogs in an attempt to test the methods and clarify some of the determinants of these parameters. Calibrated displacement left apex cardiogram obtained with time constant 3 sec and calibrated first derivative of apex cardiogram were recorded simultaneously with left ventricular pressure and its first derivative, electrocardiogram and phonocardiogram.

The values of V_{pm} obtained from catheterization and calibrated apex cardiography were similar in magnitude and standard deviations under various hemodynamic interventions. A highly significant relation was found between these invasive and noninvasive parameters of myocardial contractility. Both V_{pm} and V_{max} were elevated during the administrations of isoprenaline and strophanthin, where only V_{pm} showed a decrease after extreme volume or pressure load.

In conclusion, the results from this study suggest that V_{pm} and V_{max} of the calibrated apex cardiography are a reliable noninvasive tool for assessing left ventricular function; furthermore, V_{pm} is relatively load independent, whereas V_{max} is virtually unchanged over a broad range of loading conditions.

Additional Indexing Words:

Apex cardiogram First derivative Force-velocity relation

IN recent years, methods have been developed for calibration of the displacement left apex cardiogram (ACG) and its first derivative (dA/dt).¹⁻³⁾ By

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[†] Basic details of this study were presented at the ISM Conference, April 9-12, 1981.

Received for publication March 31, 1981.

using calibrated tracings, the dA/dt appeared to be related to left ventricular function, and its positive height has been shown to correlate significantly with positive peak dA/dt ,^{2),3)} furthermore, it was demonstrated the clinical value of index $dA/dt/A$.¹⁾⁻⁴⁾

In order to use noninvasively the informative values of peak velocity of contractile element shortening (V_{pm}) and maximum velocity of contractile element shortening (V_{max}), we proposed a new way of their estimation. The amount of V_{pm} and V_{max} was assessed by adapting the conventional catheterization method⁵⁾⁻⁹⁾ utilizing calibrated displacement ACG and its first derivative.

The present study was undertaken to examine noninvasively indices V_{pm} and V_{max} obtained by calibrated displacement apexcardiography in dogs, specifically with respect to pre- and afterload dependence.

MATERIALS AND METHODS

Experimental protocol

The experiments were carried out in 9 adult male and female mongrel dogs which weighed from 14 to 27 Kg (average 19 Kg). The animals were anesthetized with Thiopental (20 mg/Kg) infused intravenously with supplement as needed, 45 min after an injection of morphine sulphate (2 mg/Kg). Coagulation was prevented by an initial dose of sodium heparin 30 mg/Kg followed by 10 mg doses hourly. Artificial positive pressure respiration was instituted through a tracheal cannula. Dogs were in the left recumbent position and during recording of the left apex cardiogram the respirator was stopped for 20 to 120 sec.

Each dog was subjected to different procedures; short acting drugs or interventions were usually imposed first, and sufficient time was allowed for recovery. Changes primarily affecting afterload of the left ventricle were induced through balloon occlusion of descending aorta by means of rapid manual inflation of 30 to 40 ml air for 0.2–2 min into a rubber balloon mounted at the tip of a rigid catheter positioned in the aorta by way of right femoral artery. Effect of altering inotropic background were elicited by intravenous injection of isoprenaline (50 to 200 μ g) and strophanthine (1/32 to 1/16 mg). Changes in preload were provoked through balloon occlusion of the inferior vena cava at a level of the diaphragm via right femoral vein and by rapid intravenous infusion of 400 to 1600 ml 6% dextran at the end of experiment.

Recording equipment and measurements

In all experimental animals left ventricular pressure were recorded through well flushed 100 cm no 7 and 8 catheters with Statham P23D trans-

ducer balanced at the mid-chest level. The strain gauge and electromanometer Hellige (GBR) were calibrated before each experiment. The first derivative of left ventricular pressure (dp/dt) was obtained using an RC differentiating circuit with a 1 msec time constant and an output lineary proportional to the input, within 5%, up to a frequency of 75 cycles/sec. Catheters were flushed carefully with heparinized saline and only tracings free from obvious catheter artefacts were analyzed.

The derivation $dP/dt/24 \cdot P$ as an approximation of contractile element shortening velocity (VCE) during isovolumic systole has been discussed by Ross et al.¹⁰⁾ and Taylor et al.¹¹⁾ P was calculated using developed pressure measured with reference to the level of end-diastolic pressure (Fig. 1).¹²⁾ Details of measurements of V_{pm} and V_{max} have been described elsewhere.⁵⁾⁻⁹⁾

Used in this study fluid filled catheters are known to introduce distortion (change in wave form) and phase shift (time delay) in the transmitted signal.¹³⁾ Since no quantitative estimates of the error in V_{max} introduced by catheter response were available, the error was estimated in the following way. The observed left ventricular pressure was expressed as a Fourier series including 20 harmonics.¹³⁾ Typically the amplitude of the tenth harmonics was 1%. The addition of 10 more harmonics to the Fourier analysis did not change the results. The observed pressure was corrected for various values of catheter natural frequency and damping ratio. The corrected pressure was used to calculate V_{max} (based on pressure data alone). This was compared with the value from the original wave form.

Fig. 1. Simultaneous high-speed tracings (200 mm/sec) of electrocardiogram (ECG), phonocardiogram (PCG), left ventricular pressure (LVP), first derivative of left ventricular pressure (dp/dt), calibrated displacement left apex cardiogram (ACG), and its first derivative (dA/dt). P denotes developed LVP and A equals developed apex cardiographic isovolumic amplitude.

Fig. 2 summarize the results of the error estimate. The percent difference between the corrected and uncorrected values of V_{max} is plotted as a function of the natural frequency for two values of damping ratio, B . This error is caused by distortion only; phase shift does not affect the calculation since V_{max} is obtained from a plot of $dP/dt/k \cdot P$ versus P . Increased damping reduces the error for any given natural frequency. Except for very low natural frequencies, less than 10 cycles/sec, the fluid-filled catheter system overestimates the rate of pressure rise and, hence, V_{max} .

The transducer manufacturer estimates a natural frequency of 70 cycles/sec and a damping ratio of 0.3 for the catheter and transducer used in the present study.* These values are probably better than those obtained in actual application. It is estimated that the catheter system used here had a natural frequency above 20 cycles/sec, with damping ratios greater than 0.2. This would correspond to an expected error of less than 14% in the reported values of V_{max} .

The left apex cardiogram were recorded by means of a piezoelectric transducer (RFT, GDR) with an time constant 3 sec. The transducer was held manually at a point of maximal impulse of the beat of the heart. The first derivative of apex cardiogram was obtained by means of RC differentiating circuit with time constant of 1 msec and a flat response in a range of 0 to 70 cycles/sec.

For calibration of ACG and dA/dt , electric potential slope generated from the battery-resistance-capacitance circuit was used (Fig. 3). The ACG and dA/dt are expressed in relative units using calibration by triangular wave

Fig. 2. Estimated error in V_{max} caused by limited dynamic response of catheter system. The error is calculated from a Fourier analysis of the measured pressure corrected term-by-term for attenuation and phase shift. B = the fraction of critical damping.

* Statham Laboratories, Inc, Product Bulletin MP 109, September 1969.

Fig. 3. Method for calibration of apex cardiogram and its first derivative.

form with a slope of 4 V/sec and amplitude of 1 V. This ramp-signal passes through the same differentiating circuit as the pulse wave and both signals are recorded on paper. The height of the triangular signal in mm serves as a calibration factor (1X) and the height of the ACG is expressed as a factor of X. By using the time (t) from the nadir to the top of the ramp signal (in Fig. 3, t equals 92 msec), the calibration signal for the dA/dt can be expressed as a value of X/sec (in Fig. 3 the height of the calibration factor equals 10.8 X/sec). See also Fig. 1.

Adapting the catheterized formula for V_{CE} , we obtained non-invasively V_{CE} from calibrated dA/dt and its corresponding values of calibrated apex cardiographic amplitude A by the equation $V_{CE} = dA/dt/k \cdot A$, expressed in sec^{-1} . In a given formula k is the normalized modulus of series elasticity of the intact left ventricle and has been found experimentally to average 24.^{7),9)} When $dA/dt/k \cdot A$ measured during an ejection period (from the closure of the mitral valve to the point of the opening the semilunar valve) is plotted as the ordinate against A as the abscissa, a modified non-invasive force-velocity curve is obtained (Fig. 4). Our method is contributed by the statement of Wolk et al⁷⁾ for estimation of V_{max} , that it is not necessary to calculate absolute values for abscissa and ordinata as long as the first derivative is calibrated with reference to the primary curve. The closure of the mitral valve is determined by the first large, higher frequency vibrations of the first heart sound and the opening of the aortic valve—by the E point of ACG.^{14),15)} To obtain the force-velocity curve it is necessary to measure the value of each variables at 5 msec intervals, using recording at a paper speed of 200 mm/sec.

Determination of V_{max} from such phase plot was made as follows. With phase plots of $dA/dt/k \cdot A$ on the ordinate versus amplitude of A on the abscissa were in general inversely curvelinear after the inscription of peak velocity of contractile element shortening (V_{pm}) or peak V_{CE} , the shape of inverse curve between peak V_{CE} and aortic valve opening varied from a nearly linear inverse relation to a shallow concave-upward curve. For this reason, we have

Fig. 4. Example of a plot of noninvasive V_c against calibrated isovolumic apex cardiographic amplitude (A) and V_{ve} versus isovolumic pressure (B) from a representative beat. V_{pm} denotes the physiologic maximal velocity of shortening and V_{mx} (velocity shortening at zero load) is obtained by extrapolation on y axis with broken lines, drawn by eye.

followed the technique of Mason et al^(5),6) and Wolk et al,⁽⁷⁾ whereby extrapolation of the curve to the velocity axis intercept (V_{max}) was accomplished by hand and consisted of a smooth extension of the best line drawn through the inverse portion of the experimentally obtained phase plot. Although some authors perform the extrapolation to V_{max} mathematically, using the Hill equation, another experiments⁽¹⁶⁾ have cast doubt on the applicability of this equation to the heart muscle. Parameters A on the abscissa are calculated using developed amplitudes of isovolumic portion of ACG^(2),3) which is measured with the C point of ACG as a reference zero line (Fig. 1). The value of V_{pm} and V_{max} are expressed in circ/sec.

The electrocardiogram, was obtained by means of subcutaneous needles. Apical external phonocardiogram 140 cycles/sec were recorded with piezoelectric transducer (RFT, GDR).

The electrocardiogram, phonocardiogram, apex cardiogram, left ventricular pressure and their first time derivatives were recorded on an 6-channel carbon recorder 6 NEK-3 (GDR), simultaneously and continuously before, during and after various interventions. Paper speed was 200 mm/sec.

For each measurement the average of at least 5 separate cardiac cycles were used. After conversion of experimental data to digital form, all calculations were performed by an IBM 370 computer using standard statistical methods.

RESULTS

The ratio $dA/dt/k \cdot A$ was plotted against instantaneous isovolumic calibrated apex cardiographic amplitudes every 5 msec for each hemodynamic variation from the closure of the atrio-ventricular valve to the opening of the semilunar aortic valve. At the time of initial phase of isovolumic contraction, both values of A and V_{CE} progressively increased until a peak is attained approximately 30–35 msec from the onset of isovolumic systole. During latter stages of isovolumic systole non-invasive force-velocity curve progressively declines. Fig. 4 shows an example of a plot of V_{CE} obtained from calibrated apexcardiography versus developed isovolumic amplitude of ACG (A) and a plot of V_{CE} against developed left ventricular pressure (B). It can be seen

Fig. 5. Relation between invasive and noninvasive V_{pm} . $\square$ = control state; $\circ$ = occlusion dec. Ao subrange I; $\bullet$ = occlusion dec. Ao subrange II; $\blacksquare$ = isoprenalin; $\square$ = strophanthin; $\odot$ = vena caval occlusion; $\triangle$ = volume load subrange I; $\blacktriangle$ = volume load subrange II.

Fig. 6. Relation between invasive and noninvasive V_{max} . Symbols as in Fig. 5.

that the general course were similar in representative dog cardiac cycle. A close relation was found between Vpm derived from left ventricular pressure and dP/dt and those from calibrated apex cardiogram and its first derivative (Fig. 5). A nearly significant linear correlation was presented between catheterized and non-invasive Vmax (Fig. 6).

The combined results of different interventions on Vpm and Vmax derived from left ventricular catheterization and calibrated left apex cardiography are summarized in Table I. The total range of the left ventricular end-diastolic pressure (LVEDP) produced either by pressure or volume loading was divided into a two subranges (subrange I, 14–23 mmHg; subrange II 24–38 mmHg). In subrange I there were no significant decrease in both Vpm and Vmax, but at higher LVEDP (subrange II) Vpm were depressed significantly ($p < 0.05$).

Table I. Summary of Changes of Apex Cardiographic and Catheterized Peak Velocity of Contractile Element Shortening (Vpm) and Maximal Velocity Shortening (Vmax) in Dogs with Corresponding Changes in Heart Rate (HR), Left Ventricular End-Diastolic Pressure (LVEDP) and Mean Aortic Pressure (MAP)

	HR (beats/ min)	Apex cardiographic		Catheterized		LVEDP (mmHg)	MAP (mmHg)
		Vpm (circ/sec)	Vmax (circ/sec)	Vpm (circ/sec)	Vmax (circ/sec)		
Control state	107±12	1.76± 0.54	2.87± 0.92	1.38± 0.42	2.59± 0.85	9.4± 3.5	101±18
Occlusion des. Ao							
Subrange I	102±13	1.51± 0.62	2.45± 0.75	1.36± 0.45	2.32± 0.83	17.3± 5.2†	162±21*
Subrange II	86±10	1.33± 0.26	1.01± 0.80†	1.21± 0.62	1.27± 0.93†	28.1± 5.2*	190±23*
Isoprenalin	172±19*	2.80± 0.45*	4.05± 0.95*	2.75± 0.39*	3.26± 0.87*	5.0± 1.2	111±17
Strophanthin	105±10	2.35± 0.63†	3.92± 0.88†	2.70± 0.50†	3.70± 0.82*	7.3± 3.5	110±16
Vena caval occlusion	116±13	1.85± 0.60	3.02± 0.91	1.60± 0.43	2.73± 0.92	6.5± 4.5	106±18
Volume load							
Subrange I	106±12	1.42± 0.38	2.58± 0.68	1.63± 0.59	2.10± 0.70	16.1± 7.3†	133±16†
Subrange II	105±11	0.98± 0.27	1.98± 0.42†	0.98± 0.67	1.40± 0.35†	27.2± 5.8*	148±31*

Values are means±SD. * denotes $p < 0.01$ and † $p < 0.05$ when compared to control state.

DISCUSSION

As pointed by Frank,¹⁷⁾ there are basically two systems for recording pre-cordial vibrations, namely displacement and pressure (force) transducers, for

isometric and isotonic measurement respectively. A close relationship exists between two methods.¹⁸⁾ We have preferred to use calibrated displacement apexcardiography in view of its inherent simplicity and because it is more closely related to the findings obtained during clinical examination.

A marked similarity in time course and contour (especially in isometric phases of cardiac cycle) between left ventricular pressure and dP/dt , on one hand, and left apex cardiogram and dA/dt , on other hand, has been repeatedly observed in dog^{15),18)-21)} and man.^{1)-4),15)} By normalizing the first derivative of apical displacement ($dA/dt/A$) and first derivative of left ventricular pressure ($dP/dt/P$), many authors¹⁾⁻⁴⁾ obtained an excellent correlation between them. Denef et al²²⁾ using force transducer for calibrated left apex cardiogram and its first derivative investigated peak velocity of contractile element shortening (peak VCE). Under various hemodynamic conditions, they found a highly significant correlations between invasively and noninvasively obtained peak VCE.

This study makes evident for the first time the applicability of displacement calibrated ACG and its first derivative to the quantitative study of the force-velocity properties of the heart muscle. Thus, the determinations of VCE, construction of the isovolumic noninvasive pressure-velocity curve and extrapolation to Vmax provided a sensitive index of contractility. In this study, it was observed that Vpm were elevated during the administration of isoprenalin and strophanthin. With moderate varying afterload or volume load in both subranges I there were no significant changes in Vpm and Vmax. At extreme elevation of aortic pressure and preload (subranges II), however, only the index Vmax tended to diverge significantly. The reason for this decline of Vmax is not clear. It may, however, represent reflex withdrawal of sympathetic activity to the intact ventricle consequent to stimulation of baroreceptors in the systemic arterioles and in the low pressure vascular compartments within the chest.²³⁾ It has been shown in experimental and clinical studies^{5),7),9)} that Vmax is independent of variation in LVEDP and aortic pressure; Nejad et al²⁴⁾ reported loading dependence of Vmax. Only Mechmel and co-workers²⁵⁾ found changes in Vpm with varying in pressure load in dog experiments.

In conclusion, the results from this study suggest that myocardial contractility can be assessed noninvasively from calibrated displacement apexcardiography by indexes Vpm and Vmax, furthermore Vpm is relatively load independent, whereas Vmax is virtually changed over a broad range of loading conditions.

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