Isovolemic Intraventricular Pressure Change:

An Index of Myocardial Contractility during Anesthesia

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Maximal intrinsic velocity (V_{max}) can be used as a simple and reliable method for determining changes in myocardial contractility in intact subjects during anesthesia. Extrapolation of the isovolemic force–velocity curve, constructed by plotting the ratio of the first derivative of the left ventricular pressure (dP/dt) to isovolemic force (KP) against corresponding intraventricular pressure (P) to zero pressure, allows estimation of V_{max}. The method is independent of changes in preload and afterload, and requires only insertion of a cardiac catheter within the left ventricle, not thoracotomy or implantation of an electromagnetic flowmeter. Cyclopropane anesthesia (arterial concentration: 19 ± 1 mg/100 ml) resulted in unchanged V_{max} ($P > 0.2$), whereas methoxyflurane caused a significant decrease in V_{max} ($P < 0.01$) in intact dogs. (Key words: Contractility; Force-velocity relations; Anesthetics; Intact heart.)

THE CONCEPT of force–velocity relations has *been shown to be a reliable and accurate in*dex for the evaluation of changes in myocardial contractility during anesthesia.[1-3] However, calculation of force–velocity relations of the intact heart requires both measurement of instantaneous changes in left ventricular pressure and geometric measurement depending upon the assessment of instantaneous ventricular radius by means of either an electromagnetic blood flowmeter, which requires thoracotomy, or biplane cineangiocardiography.[1, 4-6]

The purpose of this communication is to describe a method for determining maximal intrinsic velocity (V_{max}), an index of myocardial contractility, in the intact heart without measurement of ventricular geometry. The method requires only placement of a cardiac catheter within the left ventricle for a high-fidelity recording of intraventricular pressure and the first time derivative (dP/dt) during the isovolemic portion of contraction, when there is no change in ventricular radius. Data relative to effects of anesthetic agents on V_{max} measured by this method will be presented.

Methods

Unpremedicated dogs were anesthetized by intravenous injection of a 1:5 chloralose–urethan solution (chloralose, 150 mg/kg; urethan, 750 mg/kg). Left ventricular and aortic pressures were measured with catheter-tip micromanometers (Statham Model SF 1). Testing of this pressure-recording system revealed a uniform (±5 per cent) amplitude response to 300 cycles/sec. The first time derivative of left ventricular pressure, dP/dt, was determined with an R-C differentiating circuit (time constant: 300 μsec). Left ventricular and aortic pressures and left ventricular dP/dt were recorded simultaneously together with the electrocardiogram, on a multichannel oscillograph (Sanborn 560 series).

Measurements of the maximal intrinsic velocity (V_{max}) were made before and during administration of cyclopropane and methoxyflurane. Data were analyzed by means of Fisher's t test and average values expressed as the mean value ±SE. In addition, effects on V_{max} of changing the preload (left ventricular end-diastolic pressure) and the afterload (mean aortic pressure) were studied in dogs anesthetized with chloralose-urethane alone.

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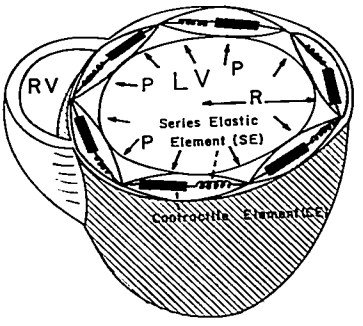


$$\text{Wall Stress} = \frac{P\,R}{2\,h}$$

FIG. 1. Graphic representation of left ventricle with a thin-walled spherical configuration. The equation expresses the average wall stress (contractile tension per unit of circumference) calculated in accordance with Laplace's Law. (P = intraventricular pressure; R = instantaneous radius; h = wall thickness.) In a thin-walled spherical system, the wall thickness (h) may be negligible, and the contractile tension may equal PR/2.

Calculations

The model for cardiac muscle used in the calculation of force–velocity relations is that of A. V. Hill,[7] in which muscle is conceptually described as a contractile element (CE) connected to an undamped nonlinear spring, a series elastic component (SE). In calculating the maximal velocity of shortening of CE, the left ventricle is considered to be a thin-walled sphere (fig. 1). Assuming force to be distributed evenly across the ventricular wall, it can be shown mathematically that the average stress (T), or the force per unit of length of circumference at the equator, is equal to PR/2, where P = intraventricular pressure and R = the instantaneous ventricular radius which remains constant during the isovolemic portion of contraction.[8]

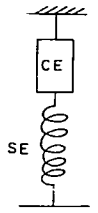
Isovolemic contraction of the intact heart is analogous to the isometric contraction of isolated heart muscle. Since both ends of the muscle are fixed by external constraints, there is no apparent fiber shortening and no ejection of blood (fig. 2). Force will be developed when the contractile element (CE) starts to shorten against the series elastic component (SE). Thus, velocity of shortening of the contractile element (V_{ce}) is equal to the rate of stretching of the series elastic component (V_{se}). V_{se} is directly proportional to the rate of stress development (dT/dt) and inversely related to the modulus of elasticity of the SE (dT/dl), which is the linear function of stress (T). Since there is no ejection of blood and the ventricular radius remains relatively constant during isovolemic contraction, the isovolemic tension is related by a constant (k) to isovolemic ventricular pressure (P). Stress development (dT/dl) may be expressed as the derivative of the wall stress equation, T = PR/2, with respect to time. Thus, the velocity of shortening of the contractile element (V_{ce}) may be calculated as the ratio of the first time derivative of left ventricular pressure (dP/dt) to corresponding isovolemic stress (T).

Figure 3 is a representative record of left ventricular and aortic pressures and dP/dt obtained simultaneously in an intact dog. Isovolemic contraction takes place before aortic valve opening, at which time intraventricular pressure exceeds aortic pressure. Left ventricular pressure (P) and corresponding dP/dt at a given instant were analyzed at ten-msec intervals throughout the isovolemic portion of ventricular systole. The isovolemic force–velocity curve was constructed by plotting V_{ce}, that is, (dP/dt)/kP, on the ordinate against force per unit of area or intraventricular pressure on the abscissa (fig. 4). Extrapolation of the curve to zero pressure allows estimation of V_{max}.

Results

Effect of Preload

The effect of preload on V_{max} was studied in five dogs. Left ventricular end-diastolic volume (LVEDV) was varied by rapid infusion and/or withdrawal of blood. For one dog in which left ventricular end-diastolic volume, measured seven times, varied from 32 ml to 73 ml, the mean value of V_{max} was 0.76 ± 0.004 sec^{-1}. The average value of V_{max} for all experiments is shown in table 1.



$$V_{CE} = V_{SE} = \frac{dl}{dt} = \frac{dF/dt}{dF/dl}$$
$$= \frac{dp/dt}{k\,P}$$

FIG. 2. Hill's model of muscle used for calculation of velocity of shortening of the contractile element (CE) during the isovolemic phase of contraction (no ejection of blood). P = pressure (stress: force/area); CE = contractile element; SE = series elastic component; V_{ce} = velocity of shortening of the contractile element; V_{se} = rate of lengthening of the series elastic component; k = coefficient of modulus of elasticity of the series elastic component; the value of 24.7 is used in this study.

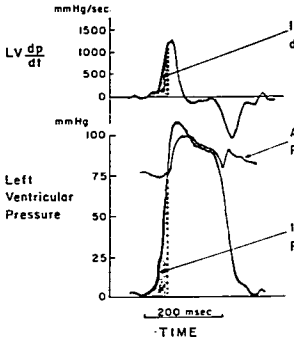


FIG. 3. Simultaneous recordings of left ventricular and aortic pressures and the first time derivative of left ventricular pressure. The shaded areas are related to the isovolemic portions of intraventricular pressure (bottom) and isovolemic dP/dt (top).

EFFECT OF AFTERLOAD

Variations in aortic impedance were obtained in each of five dogs by inflating a balloon placed near the tip of a metal cannula to produce partial obstruction of the proximal aorta. For one animal in which mean aortic pressure, measured 11 times, varied from 80 to 120 mm Hg, the mean value of V_{max} was 0.80 ± 0.01 sec^{-1}. No significant changes in V_{max} occurred with changes in mean aortic pressure (range 80 to 140 mm Hg) in any experiment ($P > 0.1$) (table 1).

EFFECT OF CYCLOPROPANE ANESTHESIA

Figure 5 illustrates the effect of cyclopropane on V_{max} in one dog. Values of V_{max} were unchanged from the control value during anesthesia with two different arterial concentrations (19 and 23 mg/100 ml). Values of V_{max} in nine dogs before and during anesthesia are shown in table 2. Average values of V_{max} before and during anesthesia in nine dogs are shown in figure 6. Values of V_{max} obtained during cyclopropane anesthesia (mean arterial blood concentration 19 ± 2

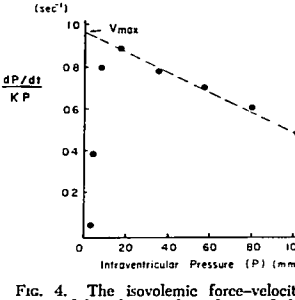


FIG. 4. The isovolemic force–velocity curve constructed by plotting the velocity of shortening of the CE, that is (dP/dt)/kP, on the y axis. Extrapolation of the curve to zero pressure permits estimation of V_{max}.

TABLE 1. Effect of Preload (LVED–Volume) and Afterload (Mean Aortic Pressure) on Mean Value of Maximal Intrinsic Velocity (V_{max})

Number of Conditions	V_{max} (sec^{-1})	LVED-Volume (ml)	Mean Aortic Pressure (mm Hg)
29	0.80 ± 0.01	47 ± 35 ($P > 0.5$)	114 ± 14 ($P > 0.1$)

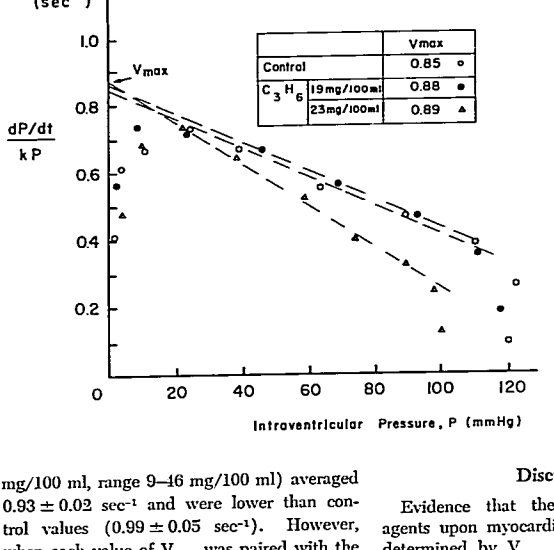


FIG. 5. V_{max} before (open circles), and during cyclopropane anesthesia (closed circles and triangles).

mg/100 ml, range 9–46 mg/100 ml) averaged 0.93 ± 0.02 sec^{-1} and were lower than control values (0.99 ± 0.05 sec^{-1}). However, when each value of V_{max} was paired with the control value for the same animal, changes in V_{max} during cyclopropane anesthesia were not significant ($P > 0.2$).

Effect of Methoxyflurane Anesthesia

Figure 7 represents isovolemic force–velocity relations in one dog before and during methoxyflurane anesthesia (arterial blood concentration 24.1 mg/100 ml). Values of V_{max} before and during anesthesia were 0.97 and 0.83 sec^{-1}, respectively. Values of V_{max} in seven dogs before and during anesthesia are shown in table 3. On nine occasions in seven dogs the mean values of V_{max} before and during anesthesia (mean arterial blood concentration: 18 ± 1 mg/100 ml, range 13.0–24.0 mg/100 ml) were 1.18 ± 0.06 and 0.89 ± 0.05, respectively (fig. 8). Paired t test revealed that changes in V_{max} during methoxyflurane anesthesia were significant ($P < 0.01$).

Discussion

Evidence that the effects of anesthetic agents upon myocardial contractility may be determined by V_{max}, derived from intraventricular pressure and dP/dt, is presented. The method is independent of changes in preload and afterload. It requires only insertion of a cardiac catheter into the left ventricle to obtain a high-fidelity recording of ventricular pressure and its instantaneous slopes (dP/dt). The values are obtained without resorting to thoracotomy for either placement of an electromagnetic flowmeter probe or implantation of radiopaque marks.

It should be pointed out that the velocity of shortening probably never reaches a maximal value in the intact heart because of the early onset of isotonic shortening.[9] For this reason, V_{max}, which is the theoretical velocity of shortening of unloaded contractile element, has been approximated by extrapolating the force–velocity curve mathematically to zero force or stress.[1-2, 4, 9] The isovolemic force–velocity curve described in the present study also shows that the values of velocity of shortening of the contractile element in early systole (10–15 msec from onset of ventricular

contraction) are lower than ensuing values, indicating delayed onset of the maximal active state of the intact heart (fig. 4). The ratio of maximal dP/dt to the instantaneous pressure (IP) has been suggested as the index of myocardial contractility [10] and used to evaluate myocardial performance during anesthesia.[11] In heart muscle, the maximal active state develops slowly. Therefore, dP/dt does not reach its maximal value during the isovolemic portion of contraction, and the value of the ratio (maximal dP/dt)/IP is always lower than the true maximal intrinsic velocity. Thus, studies relating to the use of the ratio for assessment of changes in contractility during anesthesia [11] may not reflect true changes in the intrinsic contractile state. It should also be noted that the contractile element velocity declines sharply once the aortic valve opens and isotonic contraction begins. This is illustrated by the points of the isovolemic force–velocity curve, which are no longer on a straight line (fig. 4).

Another interesting finding in the present study is that changes in dP/dt are related to changes in velocity of shortening of the contractile element. This finding is the result of the advantage of evaluating contractility of the intact heart during the isovolemic portion of contraction, when the radius of the ventricle remains constant and the ventricle has not seen the afterload level, since the aortic valve has not opened.

TABLE 2. V_{max} before and during Cyclopropane Anesthesia in Nine Dogs

Dog	C_3H_6* (mg/100 ml)	V_{max} (sec^{-1})
1	0	0.80
	12	0.76
	20	0.75
	20	0.79
	19	0.78
	18	0.75
	19	0.83
2	0	1.00
	9	0.90
	9	0.90
3	0	1.04
	12	1.07
	11	1.04
	11	1.06
4	0	0.90
	11	0.91
	11	0.93
	19	0.92
5	0	0.85
	14	0.85
	14	0.84
	11	0.91
	19	0.86
	19	0.88
	23	0.89
6	0	0.89
	10	0.85
	17	0.86
	20	0.80
7	0	1.15
	13	1.03
	20	1.02
	10	1.05
8	0	1.19
	31	1.14
	31	1.15
	46	1.11
	46	1.09
	46	1.06
9	0	1.09
	16	1.10

* Mean arterial blood C_3H_6 concentration: 19 ± 2 mg/100 ml.

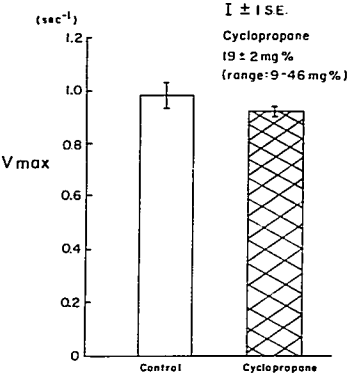


FIG. 6. Mean values of V_{max} before (open bar) and during (hatched bar) cyclopropane anesthesia in seven dogs ($n = 32$) ($P > 0.2$).

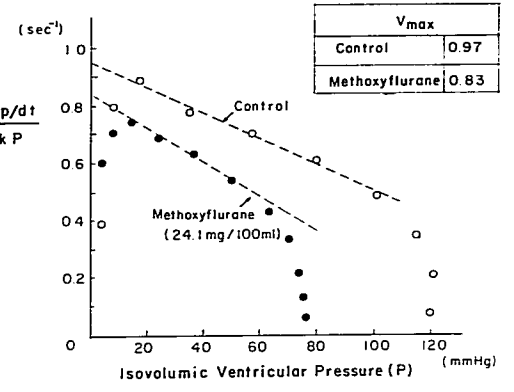


FIG. 7. Isovolemic force–velocity curves obtained before (open circles) and during (dots) methoxyflurane anesthesia.

Our findings of unaltered myocardial contractility in intact dogs during cyclopropane anesthesia and decreased contractility during methoxyflurane anesthesia are in accordance with those reported previously.[1] The reproducibility of the method, together with high accuracy in assessing changes in contractility in intact subjects during anesthesia may justify the use of V_{max} as an index of myocardial contractility in man during anesthesia. We have used the method for several patients who required general anesthesia during diagnostic cardiac catheterization, and it is also applicable in the clinic.

TABLE 3. V_{max} before and during Methoxyflurane Anesthesia in Seven Dogs

Dog	Methoxyflurane* (mg/100 ml)	V_{max} (sec^{-1})
10	0	0.97
	24	0.83
11	0	1.01
	20	0.75
	23	0.75
12	0	1.37
	13	0.94
13	0	1.26
	17	1.08
14	0	1.31
	13	1.04
15	0	1.24
	15	0.98
16	0	1.08
	16	0.97
	23	0.69

* Mean arterial blood methoxyflurane concentration: 18 ± 1 mg/100 ml.

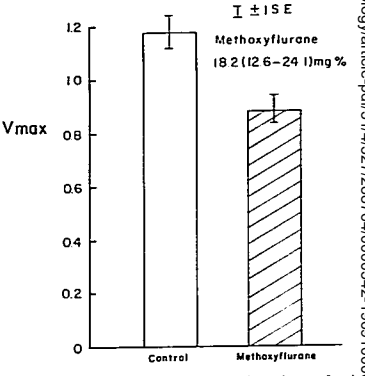


FIG. 8. Mean values of V_{max} before (open bar) and during (hatched bar) methoxyflurane anesthesia in seven dogs ($n = 9$) ($P < 0.01$).

The author is indebted to Professor Benjamin E. Etsten for his enthusiastic support and guidance.

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Pediatric Anesthesia

DIAPHRAGMATIC HERNIA The diagnosis of congenital diaphragmatic hernia should be considered in any newborn with signs of repiratory distress. The affected hemithorax usually has decreased respiratory excursions and the abdomen, being devoid of its normal contents, is scaphoid. The affected side of the chest may be dull to percussion, or it may be resonant if obstructed, air-dilated viscera are in the pleural space. The mediastinum usually is shifted away from the hernia. Cardiac sounds usually are heard best to the right of the sternum because most diaphragmatic hernias occur on the left side. In older patients, gastrointestinal, rather than respiratory, symptoms may predominate. A nasogastric tube must be passed promptly to remove gas and secretions from the stomach. This should be performed prior to roentgenographic study, transportation of the infant, or institution of assisted ventilation by face mask. The marked acidosis resulting from hypoxemia must be treated at once and ventilatory support with oxygen through an endotracheal tube is urgently required if there is evidence of respiratory insufficiency. Overinflation of the lungs must be avoided assiduously to prevent production of a pneumothorax. The infant should be placed in a head-up position on the affected side to aid the return of the mediastinum to the midline and compress the herniated viscera rather than the functioning lung. (*Whittaker, L. D., Jr., and others: Hernias of the Foramen of Bochdalek in Children, Proc. Mayo Clin. 43: 580* (Aug.) *1968.*)