Species Differences in Intrinsic Myocardial Contractility[1] (34913)

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Hill's model for skeletal muscle is also applicable to cardiac muscle so that myocardial contractility may be described in terms of contractile element behavior (1). Any given contractile state is characterized by a unique inverse relationship between the velocity of shortening of the contractile element and stress. The extrapolation of contractile element velocity to its theoretical maximum (V_{max}) at zero stress may be used as a measure of contractility which is independent of diastolic fiber length but susceptible to inotropic influcences (1), and which is, moreover, closely linked to the energetics of contraction (2). Intrinsic myocardial contractility has not been measured in previous comparative studies of circulatory function (3). In the present study, recently developed methods of measuring contractile element velocity in the intract ventricle (4) were used to show that myocardial contractility appears to differ between different mammalian species.

Methods. Dogs, cats, rabbits, guinea pigs, and rats were anesthetized with sodium pentobarbital (20–30 mg/kg) and ventilated with room air. Following thoracotomy, left ventricular pressure tracings were obtained through apical puncture, and single isovolumic contractions were induced by occlusion of the aortic root during diastole (5). The pressure–volume relationship of each heart was subsequently obtained after potassium-arrest. Circumferential wall stress was calculated assuming the heart to be a moderately thick-walled sphere (4). Since contractile element shortening equals series elastic lengthening during isometric contraction, contractile element velocity (V_{ce}) may then be calculated from the rate of rise in wall stress ($d\sigma/dt$) and the modulus of elasticity ($d\sigma/dl$) of the series elastic element.

$$V_{ce} = \frac{d\sigma/dt}{d\sigma/dl} = \frac{d\sigma/dt}{k\sigma + c}.$$

The modulus of series elasticity is similar in cat, rat, and dog myocardium (6) and was assumed to be so in all the species studied. Isovolumic contraction approximates adequately to isometric conditions so that contractile element force–velocity relations may be derived from single isovolumic beats or from the isovolumic portion of ejecting beats (4). An analogue computer (EAI-TR 48) was used to calculate instantaneous contractile element velocity against total wall stress throughout isovolumic contraction and to display this force–velocity curve on an oscilloscope (Fig. 1).

Results. V_{max} was found to differ between different species (Table I, Fig. 2). Moreover it appeared to be generally related to natural heart rate ($r = 0.9$) by a factor similar to that observed in dog hearts paced at different rates (7). However, attempts to pace hearts from larger species at unnaturally fast rates resulted only in incomplete relaxation without further augmentation of V_{max}.

Discussion. If smaller mammals are compared with larger mammals, their metabolic rate and cardiac output are increased relative to their left ventricular volume and stroke output (3). The increase in cardiac output is necessarily met by a faster heart rate, and this in turn requires a shorter duration of contraction which is in accord with the inverse relationship ($r = 0.95$) between heart rate and time to peak isovolumic pressure

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TABLE I.[a]

Species (n)	Body wt (kg)	LV wt (g)	Heart rate[b] (per min)	LVP (mm Hg)		LV σ (g/cm^2)	End diastolic		Isovolumic		V_{max}[b] (ML/sec)
				Ejecting	Isovolumic	isovolumic	Pressure (mm Hg)	Vol (ml)	TPT[b] (msecs)	dP/dt (g/sec)	
Dog (5)	22 ± 2	108 ± 10	128 ± 10	128 ± 4	251 ± 14[c] ($n = 15$)	232 ± 19[c] ($n = 15$)	4.3 ± 0.7	29.4 ± 1	161 ± 3	1877 ± 167	3.1 ± 0.1 ($n = 12$)
Cat (10)	2.6 ± 0.1	6.4 ± 0.3	183 ± 11.6	104 ± 14	213 ± 18	184 ± 22	4.8 ± 0.5	2.1 ± 0.4	127 ± 13	3861 ± 485	3.9 ± 0.3
Rabbit (5)	3.3 ± 0.4	4.1 ± 0.3	227 ± 6.9	75 ± 4	191 ± 4	266 ± 13	3.2 ± 0.4	2.3 ± 0.3	97 ± 2	3960 ± 495	3.3 ± 0.1
Guinea pig (6)	0.32 ± 0.01	0.64 ± 0.03	277 ± 14	52 ± 3	146 ± 9	120 ± 7	2.8 ± 0.3	0.2 ± 0.01	85 ± 6	3039 ± 263	4.6 ± 0.3
Rat (6)	0.38 ± 0.02	0.79 ± 0.05	443 ± 6	104 ± 6	205 ± 12	186 ± 11	3.8 ± 0.5	0.26 ± 0.03	50 ± 2	8850 ± 833	6.5 ± 0.5

[a] All values given as mean ± standard error.

[b] Differences significant (t test, $p < 0.05$) between following nearest pairs in respective series: V_{max} in dog/cat, cat/rat, rabbit/guinea pig, guinea pig/rat; TPT in dog/cat, cat/rabbit, rabbit/rat, guinea pig/rat; heart rate in dog/cat, cat/rabbit, rabbit/guinea pig, guinea pig/rat.

[c] Data from different group of dogs, after Taylor *et al.* (5). (Their values for stress have been reduced by 30% to correct for their use of a different formula.)

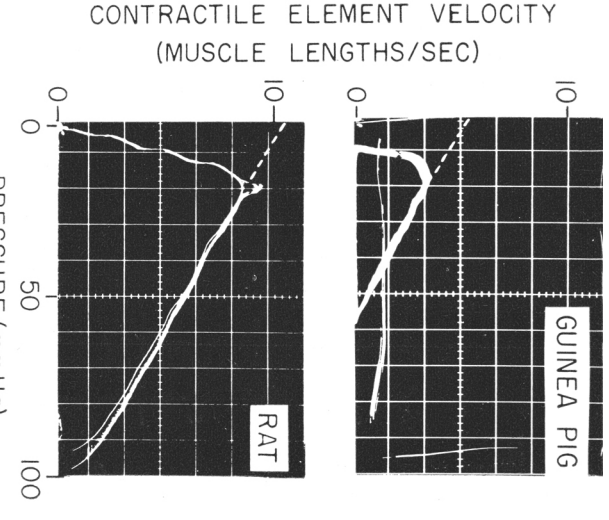

FIG. 1. Representative contractile element force velocity curves in guinea pig and rat left ventricle. Data obtained from ejecting beats. The portion of the descending curve used to extrapolate backwards to its intercept (V_{max}) at zero force precedes ejection. The factor by which pressure is multiplied to give wall stress remains constant during the isovolumic phase. Pressure is therefore conveniently displayed along the abscissa instead of stress, since it may be shown mathematically that V_{max} is unaltered by multiplying the abscissa values by any constant, whether the curve be hyperbolic, exponential, or linear.

demonstrated in this study. Left ventricular pressure and stress in ejecting and in isovolumic contractions differed somewhat between different species, but these parameters are sensitive to changes in diastolic fiber length, and no consistent relationship to natural heart rate is apparent. Arterial pressures have been reported to differ little between different mammals (8), and the relationship between left ventricular pressure and wall stress was shown to be generally constant in the different species studied. It is therefore probable that left ventricular stress under physiological conditions is approximately the same in most mammals. A previous study has shown that V_{max} differs in papillary muscle preparations from the cat and from the rat at

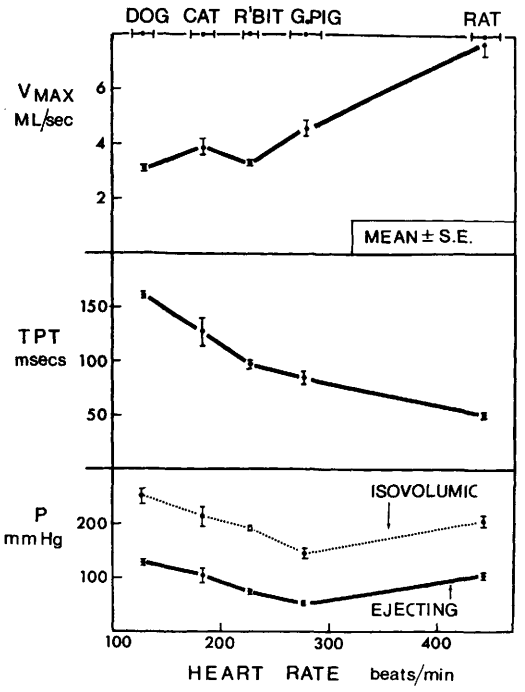

FIG. 2. Extrapolated maximum contractile element velocity (V_{max}) in muscle lengths (ML) per sec., time to isovolumic peak pressure (TPT), and peak pressure (P) of ejecting and isovolumic beats, in the left ventricles of anesthetized dogs, cats, rabbits, guinea pigs, and rats, related to heart rate in each species. Mean ± standard error indicated.

the same frequency of contraction (9). Moreover the findings in guinea pig and rat hearts, which are of similar size, suggest also that the observed differences in V_{max} reflect intrinsic differences in myocardial performance and are not simply due to varied synchrony of fiber contraction consequent upon heart size. Thus the higher contractility found in smaller species represents an appropriate adaptation to the maintenance of blood pressure at the faster heart rates needed to match the demands of higher metabolic rates. A difference in contractility implies a difference either in intracellular calcium kinetics, or in myosin ATPase activity such as has been demonstrated between ATPase from fast and from slow skeletal muscle.

Summary. Left ventricular myocardial contractility has been estimated in terms of contractile element force–velocity relations in five mammalian species. Contractility appeared to differ in different species and to be related to natural heart rate.

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