Relation of \( V_{max} \) to Different Models of Cardiac Muscle

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ABSTRACT

The present study was undertaken to reevaluate the effects of preload on maximum velocity of shortening at zero load, \( V_{max} \), relative to the length-tension curve. Force-velocity relations were measured from afterloaded isotonic contractions and were calculated from isometric contractions of isolated cat papillary muscles. Results were interpreted in the light of three alternative mechanical models of muscle. \( V_{max} \) was obtained by mathematical extrapolation of each force-velocity relation to zero load using a hyperbolic least-squares analysis performed on an IBM 360 computer. With the application of all three muscle models to isotonic force-velocity relations, \( V_{max} \) was relatively constant at low preloads but was reduced substantially as muscle length approached \( L_{max} \) (the length at the peak of the active length-tension curve). In force-velocity relations from isometric contractions, similar results were obtained with the two-element and Voigt models of muscle. With the Maxwell model, \( V_{max} \) remained more nearly constant near \( L_{max} \). Peak developed force (isometric contraction), maximum \( dP/dt \), peak calculated velocity of the contractile element (\( V_{CE} \)), and \( V_{max} \) were compared in terms of their dependence on preload and length over the entire length-tension curve (using the Maxwell model). Peak \( V_{CE} \) and \( V_{max} \) were similar and were less dependent on preload than maximum \( dP/dt \) or developed force.

KEY WORDS contractile element series elastic element
parallel elastic element Frank-Starling mechanism Voigt model
Maxwell model cat papillary muscle preload contractile state

The classic studies of A. V. Hill (1) identified the hyperbolic relation between the velocity of shortening and force development as the most fundamental mechanical relation of skeletal muscle. The extension of this force-velocity relation to cardiac muscle (2, 3) provided a precise means for quantifying the mechanical behavior of the myocardium. In particular, the extrapolated maximum velocity of shortening at zero load, \( V_{max} \), was proposed as an index of cardiac contractile state, since it was apparently unchanged by changes in preload but was altered by changes in contractile state (4).

Over the years, however, there have been several theoretical criticisms of the use of \( V_{max} \) as an index of contractile state in heart muscle. First, the active state in cardiac muscle is not constant, so that measurements obtained at different times in the contraction cycle may be made at different intensities of active state (5, 6). Second, there is difficulty in extrapolating to \( V_{max} \) since the force-velocity relation may be nonhyperbolic, particularly at higher loads (7). Third, the measurements of force and velocity of muscle shortening do not necessarily coincide with the force and velocity of the contractile element when the muscle is considered in terms of a three-element model (8). Fourth,
there are quantitative differences between the magnitudes of V_max calculated from isotonic force-velocity relations and from isometric force-velocity relations (9). The present study of isolated heart muscle was therefore undertaken to evaluate V_max relative to changes in preload in terms of alternative models.

**Methods**

After cats had been anesthetized with pentobarbital (40 mg/kg, i.p.), papillary muscles were rapidly removed from the right ventricles and suspended in Krebs-bicarbonate solution at 30°C (Na⁺ 148, K⁺ 4.0, Ca²⁺ 5.0, Mg²⁺ 2.5, Cl⁻ 128, and HCO₃⁻ 25 mEq/liter; phosphate 1.2, and glucose 5.0 mM; pH 7.4). Muscles were aerated with 95% O₂-5% CO₂ and stimulated at 12/min by mass electrodes placed parallel to the muscle in the bath. The voltage was maintained 10–15% above threshold. One end of each muscle was attached to a force transducer, and the other end was attached to the tip of an isotonic lever system (equivalent mass 100 mg) by a small length of 4-0 silk (10). The average cross-sectional area of all 15 muscles studied was 1.1 ± 0.1 (SE) mm². Average muscle length was 8.4 ± 0.5 mm. Developed force was 7.2 ± 0.6 g/mm² and resting force was 1.1 ± 0.2 g/mm² at L_max.

Force-velocity relations were measured at different preloads, which corresponded to muscle lengths between 10–12% less than L_max (the length at the peak of the length-tension curve) and 1–2% more than L_max. At each preload, isotonic force-velocity relations were obtained by measuring peak isotonic velocity of muscle shortening as afterload was progressively increased from zero to isometric force (3).

Isometric force-velocity relations were calculated from isometric contractions with a small online analog computer employing the formula V_CE = (dP/dt)/(KP + C) which is the formula for series elastic shortening (9). V_CE is the velocity of shortening of the contractile element; K and C are constants describing the length-tension relation of the series elastic element, which was obtained by isotonic quick-release techniques (11).

The design and construction of the analog computer was carried out by the Computer Science Facility at Cedars-Sinai Medical Center. The dP/dt differentiator circuit uses a Fairchild 741C amplifier. The 1/K and the C generator are controlled by a high-accuracy voltage divider (±1%). The linear amplifier section is temperature-compensated and has a temperature coefficient of 40 ppm/°C. The linear differentiator is a two-stage element that permits continuous adjustment of the output voltage, which is proportional to (dP/dt)/(KP + C).

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**Figure 1**

*Three proposed mechanical models of heart muscle. CE = contractile element, SE = series elastic element, PE = parallel elastic element.*

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**Figure 2**

*Length-tension relations of the elastic elements of a representative cat papillary muscle. The passive length-tension relation is the parallel elastic element (PE) in the Maxwell model. The series elastic element (SE) was obtained by isotonic quick-release techniques. The differences between these two curves represents the parallel elastic element of the Voigt model.*
Results were interpreted in the light of three different mechanical models of muscle illustrated in Figure 1. The two-element model consists of a contractile element and a series elastic element. In this model, the contractile element is not freely extensible at rest but can bear resting force. During isotonic contraction, both the velocity of shortening and force of the muscle are identical to the force and velocity of the contractile element. Two three-element models were also evaluated. A parallel elastic element is in parallel with both the contractile and the series elastic elements in the Maxwell model and with the contractile element only in the Voigt model. As the contractile element shortens in these two models, the parallel elastic element moves down its length-tension curve, and force is shifted from the parallel elastic element to the contractile element in an isotonic contraction (12).

Extrapolated $V_{\text{max}}$ was calculated by a least-squares computer program on an IBM 360-91 digital computer, with the assumption that the force-velocity relation was hyperbolic up to two-thirds of developed force. $V_{\text{max}}$ was then normalized for the specific length of the muscle at that preload. No attempt was made to measure force-velocity relations at a constant length or intensity of active state. Rather, the present study was restricted to the measurement of force-velocity relations obtained from after-loaded isotonic contractions (3) or calculated from isometric contractions (9).

Results

LENGTH-TENSION RELATIONS OF THE ELASTIC ELEMENTS

Length-tension relations of the elastic elements in the different muscle models are illustrated for a representative muscle in Figure 2. The passive length-tension relation was obtained by lengthening the muscle 0.1 mm every 10 seconds. The passive length-tension curve of the muscle represents the parallel elastic element in the Maxwell model, since the contractile element is presumed to be freely extensible at rest. The series elastic element extension curve obtained by quick-release techniques at a low preload is the same in all three models. In the Voigt model, the parallel elastic element is defined as the

![Graph](https://example.com/graph.png)

**Figure 3**

Force-velocity relations in a representative cat papillary muscle obtained from a series of afterloaded isotonic contractions at different preloads. $L_{\text{max}}$ corresponds to a preload of 2.0 g. Extrapolation to $V_{\text{max}}$ (solid symbols) was obtained by a least-squares hyperbolic fit of the velocity points at lower loads. The extrapolation with a preload of 3.0 g was estimated.

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\( V_{\text{max}} \) AND MUSCLE MODELS

\( \text{FORCE} \) \( \text{gm} \)

\( \text{MUSCLE LENGTH} \) \( \text{mm} \)

\( \text{VELOCITY} \) \( \text{mm/sec} \)

**FIGURE 4**

Representative afterloaded isotonic contraction in a cat papillary muscle. The preload is 0.8 g with an afterload of 3.0 g. The heavy vertical lines indicate the time at which peak velocity of muscle shortening occurred.

\( V_{\text{max}} \) was further reduced to 0.95 muscle lengths/sec. In some muscles, \( V_{\text{max}} \) could not be calculated at muscle lengths greater than \( L_{\text{max}} \), because the first portion of the curve was no longer hyperbolic.

Reinterpretation of the data of Figure 3 in terms of the Voigt model is complicated because peak velocity of muscle shortening does not occur until the muscle has already shortened somewhat, as illustrated in Figure 4. In this representative afterloaded isotonic contraction, peak velocity of muscle shortening does not occur until 70 msec after the muscle has begun to shorten, during which time it has shortened 0.2 mm (2% of muscle length). Since the parallel elastic element in the Voigt model is a very stiff spring (Fig. 2), the unloading of the parallel elastic element is essentially complete by the time peak muscle velocity is attained. Thus, the appropriate force across the contractile element at the time peak muscle velocity is reached is also total force in the Voigt model, exactly as it is in the arithmetic difference between the passive length-tension relation of the muscle and the series elastic element. As seen in Figure 2, the parallel elastic element in the Voigt model is typically a stiffer spring than the series or the parallel elastic elements of the Maxwell model.

**ISOTONIC FORCE-VELOCITY RELATIONS**

Figure 3 illustrates the data obtained from a series of afterloaded isotonic contractions in a representative cat papillary muscle. At each afterload, velocity of muscle shortening is plotted as a function of the total force. Thus, the direct experimental data conform to the two-element model of muscle, since the force and velocity of muscle shortening are identical to the force and velocity of shortening of the contractile element during afterloaded isotonic contractions. As illustrated in Figure 3, extrapolated \( V_{\text{max}} \) was 1.72 muscle lengths/sec with a 0.2-g preload, rose to a plateau of 2 muscle lengths/sec, and then fell to 1.3 muscle lengths/sec at \( L_{\text{max}} \) (2.0-g preload). At a muscle length greater than \( L_{\text{max}} \) (3.0-g preload), \( V_{\text{max}} \) was further reduced to 0.95 muscle lengths/sec. In some muscles, \( V_{\text{max}} \) could not be calculated at muscle lengths greater than \( L_{\text{max}} \), because the first portion of the curve was no longer hyperbolic.

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**FIGURE 5**

Cumulative results in ten cat papillary muscles illustrating the dependence on preload of extrapolated \( V_{\text{max}} \), obtained from isotonic force-velocity relations with the three different muscle models. \( V_{\text{max}} \) is plotted as a percent of its value at a muscle length of 92% of \( L_{\text{max}} \). The preload appropriate to each muscle length is plotted as a percent of the preload at \( L_{\text{max}} \). Results are means ± se.
FIGURE 6

Representative isometric contraction of a cat papillary muscle. The preload equals 0.05 g. Contractile element velocity ($V_{CE}$) was computed on-line by a small analog computer. Force has been normalized for cross-sectional area and velocity has been normalized for muscle length (ML/sec).

two-element model. The velocity of the contractile element in the Voigt model also equals the velocity of muscle shortening since the length of the series elastic element does not change during isotonic contraction. Thus, reinterpretation of the data of Figure 3 in terms of the Voigt model does not measurably alter the results.

Reinterpretation of the data in terms of the Maxwell model is slightly more complex. The distance the muscle has shortened at the point of peak muscle velocity unloads the parallel elastic element according to the length-tension relation of the muscle (Fig. 2). Thus, the force across the contractile element at that moment equals the total force minus the residual force across the parallel elastic element. The velocity of shortening of the contractile element is the sum of the velocity of shortening of the muscle plus the additional velocity of lengthening of the series elastic element, which is stretched during isotonic contraction as force is shifted from the parallel elastic element. This additional component was calculated according to previous analyses (8, 12) and was relatively negligible when compared to the velocity of muscle shortening.

FIGURE 7

Force-velocity relations in a representative cat papillary muscle calculated from isometric contractions at different preloads for the two-element model. Extrapolated $V_{max}$ (solid symbols) was obtained from a least-squares hyperbolic fit of the velocity points at loads up to two-thirds of developed force.

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A summary of the calculated isotonic $V_{\text{max}}$ data for all three muscle models is seen in Figure 5. $V_{\text{max}}$ is plotted in percent on the vertical axis with the 100% reference point arbitrarily selected as that muscle length which is 92% of $L_{\text{max}}$. Both muscle length and preload are plotted on the horizontal axis as a percent of $L_{\text{max}}$. For all three muscle models, $V_{\text{max}}$ was relatively constant at muscle lengths between 92 and 97% of $L_{\text{max}}$, but was reduced as muscle length approached and exceeded $L_{\text{max}}$. The $V_{\text{max}}$ data of Figure 5 were normalized for the individual muscle length at each preload. If all the data were normalized for the muscle length at $L_{\text{max}}$, then the $V_{\text{max}}$ points at shorter lengths would be reduced relative to $V_{\text{max}}$ at $L_{\text{max}}$ by a percent approximately equal to the percent difference between that length and $L_{\text{max}}$. Thus, in Figure 5 the relative reduction in $V_{\text{max}}$ at $L_{\text{max}}$ would be 5-8% less if this method of normalization was employed. Thus, no matter which mechanical model of muscle or method of normalization was selected, $V_{\text{max}}$ was dependent on preload near $L_{\text{max}}$, although it was relatively independent of preload at shorter muscle lengths.

**FIGURE 8**

Force-velocity relations in a representative cat papillary muscle calculated from isometric contractions at different preloads for the Maxwell three-element model. Extrapolated $V_{\text{max}}$ (solid symbols) was obtained as in Figure 7.

**FIGURE 9**

Cumulative results obtained from isometric force-velocity relations in 14 cat papillary muscles illustrating relative changes in extrapolated $V_{\text{max}}$ as a function of muscle length and preload for the three muscle models. $V_{\text{max}}$ is plotted as a percent of maximum, and muscle length and preload are plotted as a percent of their values at $L_{\text{max}}$. Results are means ± se.
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had a hyperbolic portion, and $V_{\text{max}}$ could not be calculated.

In the Maxwell model, the appropriate input to the computer to calculate $V_{\text{CE}}$ is developed force, since resting force is borne entirely by the parallel elastic element throughout isometric contraction. Data appropriate to the Maxwell model for the same muscle seen in Figure 7 are illustrated in Figure 8. As shown, $V_{\text{max}}$ was lowest with zero preload and a very high preload (3.3 g), but was relatively constant at intermediate preloads.

Calculations of $V_{\text{CB}}$ for the Voigt model are slightly more complex. As the contractile element shortens in that model, force is shifted from the parallel elastic element to the contractile element. By the time peak $V_{\text{CE}}$ is
reached, the shift of force from the parallel elastic element to the contractile element is virtually complete, because the parallel elastic element is such a stiff spring. Thus, the force across the contractile element becomes total force by the time peak $V_{CE}$ is reached. The velocity of the contractile element in the Voigt model is calculated by using total force as the input to the computer, since $V_{CE}$ is identical to the lengthening velocity of the series elastic element, which has total force across it throughout contraction. Thus, calculation of $V_{max}$ in terms of the Voigt model yields results virtually indistinguishable from those of the two-element model as seen in Figure 7.

A summary of the calculations of isometric $V_{max}$ as a function of muscle length and preload is seen in Figure 9. $V_{max}$, as a percent of its maximum value, is plotted as a function of muscle length and preload. With the two-element and Voigt models, $V_{max}$ was relatively constant at lower preloads and shorter muscle lengths but was substantially reduced (60%) as the muscle reached $L_{max}$. With the Maxwell model, $V_{max}$ was relatively constant over the intermediate range, although there was a gradual rise and fall in each muscle.

Because of the potential difficulties of extrapolating accurately to $V_{max}$, measurements of peak $V_{CE}$ alone were also evaluated during isometric contractions at different muscle lengths. Figure 10 illustrates representative measurements of peak $V_{CE}$ using the input to the computer as total force (two-element model) and developed force (Maxwell model). The same relative changes were seen in peak $V_{CE}$ in Figure 10 as in $V_{max}$ in Figure 9. Thus, with the two-element model, peak $V_{CE}$ was relatively constant at low preloads and shorter muscle lengths but was progressively reduced as the muscle was stretched to $L_{max}$ and beyond. With the Maxwell model, there was a gradual rise and fall of peak $V_{CE}$ similar to the $V_{max}$ results of Figure 9.

The relative sensitivity of $V_{max}$ and peak $V_{CE}$ to changes in muscle length were next compared with developed force and maximum $dP/dt$ over the physiologic range of the length-tension curve. In Figure 11, each of the four parameters is expressed as a percent of its maximum value. Peak $V_{CE}$ and $V_{max}$ were calculated from developed force according to the Maxwell model. As illustrated, all four indexes of contractile performance have the same general rise and fall as a function of muscle length, although peak force and maximum $dP/dt$ were maximum at $L_{max}$, and $V_{CE}$ and $V_{max}$ were maximum at a muscle length 2% less than $L_{max}$. Maximum $dP/dt$ and developed force were indistinguishable, since there was no significant change in time to peak force. Peak $V_{CE}$ and $V_{max}$ were also similar, but they were less dependent on muscle length than maximum $dP/dt$ or developed force.

Discussion

The application of force-velocity relations to cardiac muscle provided a quantitative means of describing the mechanical performance of the myocardium (2-4). In particular, the use of $V_{max}$ as an index of contractile state was particularly attractive, because of its apparent independence of preload and initial muscle length (4). The earlier studies, however, were generally restricted to lower preloads and to isotonic force-velocity relations. Because such measurements were made at different times after the onset of contraction and because of the changing intensity of active state in a cardiac twitch, however, such measurements have been criticized (5, 6). Further studies, however, have suggested that time may not be a limiting factor at least during those portions of the contraction where the measurements were made (13).

The present study has purposely avoided any attempt to evaluate the separate effects of instantaneous length, time, and active state on the force-velocity relations of the contractile element. Rather, the experiments were designed to quantify isotonic force-velocity relations obtained in a standard fashion from afterloaded contractions (2-4) and to calculate force-velocity relations from standard isometric contractions. Although such measurements retain the problem of time, they deal with the
actual course of contraction and thus are applicable to attempts to measure contractile state in the intact heart (14, 15).

Recently, Pollack (8) analyzed force-velocity data in terms of different muscle models and concluded that \( V_{\text{max}} \) was dependent on preload. His calculations, however, were made on the assumption that peak isotonic muscle velocity was achieved immediately after the muscle began to shorten. That this is not the case is evident in Figure 4 and previous studies (1, 10). Furthermore, Pollack analyzed only isotonic and not isometric force-velocity relations, although there are considerable differences between them both in terms of calculated velocity (9) and appropriate interpretation according to different muscle models (16).

The analysis of the present study has taken into account these additional factors. Calculations of \( V_{\text{max}} \) from isotonic contractions were similar in all three models and demonstrated a relatively constant \( V_{\text{max}} \) at low preloads, although \( V_{\text{max}} \) was reduced as muscle length approached \( L_{\text{max}} \). Because the velocity measurements near zero load are critical in the determination of extrapolated \( V_{\text{max}} \), it is not surprising that \( V_{\text{max}} \) falls with higher preloads (Fig. 3) since the shape of the force-velocity curve is necessarily altered by a lack of experimental velocity points at loads less than the preload. In this regard, recent experiments with continuous unloading of the preload during isotonic contraction have demonstrated that the maximum measured velocity of shortening is similar at muscle lengths from \( L_{\text{max}} \) to 12\% less than \( L_{\text{max}} \) (17). Furthermore, this measured velocity of maximum shortening was similar to the \( V_{\text{max}} \) calculated from afterloaded isotonic contractions as it was in the present study (17).

With isometric contractions, \( V_{\text{max}} \) was also relatively constant at low preloads with the two-element and Voigt models but fell as muscle length approached \( L_{\text{max}} \). With the Maxwell model, however, there were lesser changes in \( V_{\text{max}} \) on isometric contraction at muscle lengths of \( L_{\text{max}} \) and greater. During isometric contraction, the magnitude of calculated peak \( V_{\text{CE}} \) (or \( V_{\text{max}} \)) is determined by at least two opposing factors. Thus the early increase in active state (5) tends to increase the velocity of the contractile element, while rising force tends to decrease velocity. The former effect predominates in the first 40 msec of contraction (up to peak \( V_{\text{CE}} \)), but the latter effect is dominant thereafter. The decrease in \( V_{\text{CE}} \) produced by rising force is probably the major factor responsible for the lower magnitude of isometric \( V_{\text{max}} \) as compared to isotonic \( V_{\text{max}} \) (9).

Previous studies have suggested that no one muscle model is adequate to account for all of the experimental data (6, 10, 12, 18). In a similar fashion, in the present study, \( V_{\text{max}} \) was more constant with the two-element and Voigt models at low preloads and with the Maxwell model (isometric \( V_{\text{max}} \)) at higher preloads. Although a constancy of \( V_{\text{max}} \) is not necessarily a determining factor of an appropriate muscle model, it is important relative to the use of \( V_{\text{max}} \) as an index of contractile state, particularly in the intact heart (14, 15, 19).

Of great interest was the comparison of extrapolated \( V_{\text{max}} \), peak \( V_{\text{CE}} \), maximum \( \frac{dP}{dt} \), and developed force over the physiologic length-tension curve appropriate to the Maxwell model (Fig. 11). Percent changes in force and maximum \( \frac{dP}{dt} \) were indistinguishable, since there were negligible changes in time to peak force. Furthermore, the relative magnitudes of peak \( V_{\text{CE}} \) and extrapolated \( V_{\text{max}} \) were similar up to 98\% of \( L_{\text{max}} \), which would recommend the use of peak \( V_{\text{CE}} \) as an index of contractile state since it can be directly measured and does not require mathematical extrapolation. Neither \( V_{\text{max}} \) nor peak \( V_{\text{CE}} \), however, was totally independent of preload in the Maxwell model, which is the ideal requirement for an index of contractile state responding only to changes in inotropic state.

In studies of force-velocity relations in the intact heart, both the two-element and Maxwell models have been used (14, 15, 19). The number of assumptions required and the difficulties of calculations, however, do not readily lend themselves to the routine use of
force-velocity relations as a measure of contractile state. Thus, because of these difficulties, it may be that some other more simply derived index or combination of indexes will be more practical as descriptors of contractile state (20).

References
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