Reconsideration of the Ultrastructural Basis of Cardiac Length-Tension Relations

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A fundamental property of vertebrate striated muscle is the dependence of developed tension and extent of shortening on initial muscle length. In both cardiac and skeletal muscle, the tension developed during an isometric contraction decreases as the length of the muscle is altered in either direction from an optimal value. The importance of this phenomenon in the intact heart was recognized more than 50 years ago by Frank (1) and Starling (2) and became the basis for Starling’s law of the heart, which states that ventricular stroke volume varies directly with changes in end-diastolic ventricular volume. Stroke volume can also be increased by interventions such as catecholamines which enhance contractility, or it can be decreased when ventricular performance is depressed as it is in congestive heart failure. The constant interplay of the Frank-Starling mechanism (changing diastolic volume) and changing contractility determines the manner in which the heart varies its output relative to its input on a beat-to-beat basis and thus permits widely varying demands to be met (3).

The mechanism whereby changes in initial length alter tension development in striated muscle has been largely defined by studies correlating muscle ultrastructure with function (3-5). The fundamental structural and functional unit of contraction in both cardiac and skeletal muscle is the sarcomere, the basic repeating unit in the longitudinally oriented myofibril (6). Sarcomeres have a distinctive detailed structure that is best perceived with the electron microscope (Fig. 1). Each sarcomere is delineated by a pair of Z lines. The bandlike appearance of the sarcomere results from the disposition of two sets of filaments which are arranged in a partially overlapping, interdigitating array. The thick myosin filaments are 100-120 Å in diameter and 1.65μ in length, and the thin actin filaments are 50-70 Å in diameter and 1.0μ in length. In the cross-banded pattern, the length of the darker A band is determined by the length of the myosin filaments and is constant. Two sets of actin filaments, which are also constant in length, are connected end to end at the Z line, and their opposite ends interdigitate to a varying degree with the myosin filaments in the A band. The width of the lighter I band corresponds to that portion of the actin filaments which does not extend into the adjacent A band. Therefore, the width of the I band varies with the length of the sarcomere. The lighter central region of the A band between the ends of the interdigitating sets of actin filaments constitutes the H zone. In the center of this band, a thin, dark strip known as the M line which probably represents fixed structural cross-connections between myosin filaments.

Present evidence indicates that shortening and force generation in striated muscle are related to the interaction between cross-bridges on the myosin filaments and sites on the actin filaments (5-7). When the fiber is at rest, troponin located periodically along each actin filament in association with tropomyosin inhibits cross-bridge interaction (8). However, when excitation of the fiber occurs, calcium is released from the sarcoplasmic reticulum and interacts with troponin, thereby removing its inhibition of the interaction of actin and myosin. During excitation in cardiac muscle, calcium also enters the intracellular space from the extracellular space and possibly from sarcolemmal storage sites (9). In association with activation of an actomyosin adenosinetriphosphatase, the myosin cross-bridges undergo a conformational change.
Schematic representation of the arrangement of filaments within a sarcomere. The sarcomere is delimited by the Z lines. The H zone, a region of variable width determined by the relative position of the thin filaments in the A band, should be distinguished from the pseudo H zone, a region of fixed width corresponding to the portion of the thick filaments devoid of cross-bridges. The relative positions of the thick and thin filaments in this illustration provide for an overall sarcomere length of approximately 2.5\(\mu\).

which produces a directional force, and the actin filaments are drawn inward toward the center of the A band. By means of a repetitive making and breaking of cross-links, force is generated and muscle shortening occurs. Despite changes in sarcomere length, there is no perceptible change in the length of either the actin or the myosin filaments; this observation provides the basis for the sliding filament theory of muscle contraction (5–7).

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According to the sliding filament theory of muscle contraction (5–7), the total force on any one filament is the sum of the forces contributed by each cross-bridge interaction with actin (cross-link), which in turn is proportional to the number of cross-links formed and, therefore, to the width of the overlap zone between actin filaments and portions of the myosin filaments containing force-generating cross-bridges. The area of overlap between actin filaments and portions of the myosin filaments containing force-generating cross-bridges remains constant between 2.0\(\mu\) and 2.2\(\mu\) and decreases linearly at lengths beyond 2.2\(\mu\).

At shorter skeletal muscle lengths, the direct relation between isometric tension development and the number of myosin cross-bridges overlapped by actin filaments no longer holds. When sarcomere length is decreased from 2.00\(\mu\) to 1.65\(\mu\), there is a progressive decline in developed tension without a change in the number of myosin cross-bridges overlapped by actin filaments (Figs. 2 and 3). The explanation for this decline in active tension is uncertain, but it may be related to a passive resistance to force generation and shortening resulting from the meeting of actin filaments at the center of the sarcomere and their subsequent passage into the opposite half of the sarcomere (11, 12). In addition, if the actin filaments are able to interact with active sites on the opposite half of the myosin filament, an active resistance to contrac-
Relation between actively developed isometric tension and resting sarcomere length for frog skeletal muscle fibers and cat right ventricular papillary muscles. The curve for skeletal muscle fibers is derived from the data of Gordon et al. (10). In both tissues, peak developed tension is attained at a sarcomere length of 2.2µ. At a sarcomere length of 2.0µ, tension development is substantially decreased in cardiac muscle but remains maximal in skeletal muscle. At sarcomere lengths less than 2.0µ, developed force falls in both types of muscle, but it falls more precipitously in cardiac tissue. At sarcomere lengths longer than 2.0µ, cardiac muscle is resistant to further extension and its developed force declines precipitously compared with the linear fall determined for skeletal muscle. In cardiac muscle, this decrease in force cannot be entirely explained by sarcomere elongation and a decrease in myofilament overlap.

At skeletal muscle sarcomere lengths shorter than 1.65µ, the slope of the decline in developed tension increases markedly (Fig. 3), and tension reaches zero at a sarcomere length of approximately 1.30µ (10). This corner in the skeletal muscle length-tension relation occurs at a sarcomere length (1.65µ) corresponding to the point at which myosin filaments collide with Z lines. Such a collision should oppose force generation, and folding or crumpling of the myosin filaments with further shortening should reduce the number of cross-bridge sites available for tension generation. Another factor which may further reduce tension generation at these short muscle lengths has been suggested by the work of Taylor and Rudel (14), who have found that electrically stimulated muscle fibers shortening below a sarcomere length of 1.6µ develop a central waviness which they have attributed to inactivation of contraction. This phenomenon has not been observed in fibers shortening to a similar degree in the presence of caffeine (15), a drug believed to improve the effectiveness of membrane depolarization during activation. Furthermore, in skinned frog muscle fibers activated directly by calcium, the decline in tension development at sarcomere lengths shorter than 1.7µ is significantly less than that observed in electrically stimulated fibers (16). These findings suggest that the deactivation observed when electrically stimulated fibers shorten to sarcomere lengths below 1.6µ results from an interruption of the inward spread of the activating signal or perhaps from an uncoupling of the transverse tubular system and the sarcoplasmic reticulum. The close similarity of skeletal muscle sarcomere length-tension relations for electrically stimulated, intact fibers and calcium-activated, skinned fibers at sarcomere lengths of 1.7-3.6µ (10, 16) suggests that deactivation of contraction becomes an important determinant of force generation only at sarcomere lengths shorter than 1.7µ.
Attempts to define the ultrastructural basis of the length-tension relation in cardiac muscle have been hampered by the lack of a suitable in vitro preparation comparable to the isolated single-fiber preparations used in skeletal muscle studies. Most of the information currently available concerning cardiac sarcomere length-tension relations has been obtained from studies using isolated papillary muscles fixed for electron microscopic study at various resting muscle lengths corresponding to different points on the muscle length-tension curve. Such studies have established a general relation between muscle length, sarcomere length, and developed tension similar in many respects to that found in skeletal muscle (17-20). However, certain critical differences between these two types of striated muscle raise fundamental questions as to the basis for the observed length-tension relation in cardiac muscle.

In an attempt to resolve some of these differences, we recently reexamined the sarcomere length-tension relation in isolated cat papillary muscles using an improved isometric myograph which allowed direct, continuous measurements of length and force in muscles mounted between rigid metal clips (21). Active and resting length-tension curves were determined; each muscle was then fixed in glutaraldehyde while it was resting at a preselected length along either the ascending or the descending portion of the length-active tension diagram. Average sarcomere lengths at Lmax, the muscle length at which active tension is maximal, measured 2.18 ± 0.02μ (SE) (range 2.12μ to 2.26μ). This result is virtually identical to the values of 2.15μ to 2.25μ reported in previous studies (17, 19, 20). Sections along the entire length of muscles fixed at Lmax showed little variation in sarcomere length and no evidence of fiber buckling. The ascending limb of the developed tension curve extended from 70% to 100% of optimal length (Lmax) (Fig. 4). However, resting tension was not measurable until muscle lengths of 85% of Lmax were reached. Thereafter resting tension increased exponentially, accounting for 15% of the total tension developed at Lmax (total tension = active tension + resting tension). In this respect cardiac muscle differs markedly from skeletal muscle in which resting tension is negligible at the optimal length for active tension development. Sarcomere lengths in cardiac muscle were directly related to resting muscle length at lengths greater than 85% of Lmax. At muscle lengths between 70% and 85% of Lmax, myofibrillar curling and buckling were noted in association with a fairly constant sarcomere length of 1.75-1.85μ. These results agree with those previously reported by Grim et al. (20) in rat papillary muscles and suggest the presence of a restoring force in cardiac muscle similar to that seen in skeletal muscle (22) which tends to reextend sarcomeres to a minimum rest length of about 85% of Lmax.

Another striking difference between skeletal and cardiac muscle length-tension relations becomes apparent when developed tension is compared in the two tissues at sarcomere lengths between 2.00μ and 2.20μ (Fig. 3). At these sarcomere lengths, myofilament overlap is optimal and, because the central 0.15-0.20μ region of the myosin filament is devoid of cross-bridges, the number of active force-generating sites should be constant. As predicted...
by the sliding filament theory, there is a plateau of maximal tension development between sarcomere lengths of 2.00\(\mu\) and 2.20\(\mu\) in skeletal muscle (10, 16). However, no plateau of actively developed tension is observed in cardiac muscle; instead, active tension decreases rapidly at sarcomere lengths both above and below 2.20\(\mu\) (Fig. 4). A 10\% reduction in sarcomere length from 2.20\(\mu\) to 2.00\(\mu\) results in a 30\% decrease in developed tension (Fig. 4). At sarcomere lengths below 1.90\(\mu\), developed tension declines extremely rapidly, approaching zero at 1.65-1.75\(\mu\). At these short lengths, considerable buckling in the papillary muscles results in wide variations in sarcomere length between adjacent sections of muscle. Thus, sarcomere length-tension relations cannot be well defined in papillary muscles at resting lengths shorter than 80-85\% of Lmax.

Other discrepancies between cardiac and skeletal muscle are observed when length-tension relations beyond Lmax are examined. Resting cardiac muscle is very stiff compared with skeletal muscle; cardiac muscle resting tension rises exponentially at lengths greater than 85\% of Lmax. At Lmax, resting tension is quite substantial and rises precipitously with further elongation of the muscle (Fig. 4). In contrast, resting tension is negligible in skeletal muscle until the muscle is stretched to lengths 20\% or more beyond Lmax. Once resting tension appears, further lengthening of skeletal muscle results in an exponential increase in resting tension as it does in cardiac muscle. In skeletal muscle, active tension decreases at lengths beyond Lmax in accordance with the decreasing filament overlap, as predicted by the sliding filament theory (10, 16). However, a simple relation between tension development and filament overlap does not hold for cardiac muscle at lengths beyond Lmax. Sarcomeres in cardiac muscle resist overstretching. An extension of papillary muscle to a length 20\% beyond Lmax results in an average sarcomere length of only 2.35\(\mu\), which is considerably less than that expected based on a one-to-one relation between muscle and sarcomere length. The basis for the discontinuity between sarcomere and muscle length measurements beyond Lmax has not been explained, but it may be related to internal fiber rearrangements or slippage (18, 23). At papillary muscle lengths 20\% beyond Lmax, actively developed tension is decreased to 40\% of that at Lmax, while resting tension rises to an exceedingly high level. Thus, unlike skeletal muscle, the fall in actively developed tension in heart muscle stretched beyond the optimal length for force development is much greater than that expected from a decrease in myofilament overlap alone and a reduction in the number of force-generating cross-bridges (Fig. 2).

Recent studies of sarcomere length-tension relations (24, 25) using live right ventricular papillary muscles or trabeculae carneae from rats have largely confirmed the findings obtained using tissue fixed for light or electron microscopy (17, 21, 23). When sarcomere length is measured directly using the light microscope and laser techniques in muscles at rest and during isometric contraction, maximal active tension development is generally observed at sarcomere lengths of 2.29–2.32\(\mu\). These values are almost identical to those found in muscles fixed in glutaraldehyde after corrections are made for the known 3–5\% shrinkage that occurs during fixation. Below Lmax, resting sarcomere length decreases as a direct function of muscle length down to approximately 2.00\(\mu\). There is no plateau of active tension development between sarcomere lengths of 2.00\(\mu\) and 2.30\(\mu\); tension increases approximately 75\% over this length range. Isometric contractions initiated at sarcomere lengths from 2.30\(\mu\) to 2.00\(\mu\) result in considerable sarcomere shortening of approximately 10\% despite the fact that overall muscle length is constant. This internal sarcomere shortening during isometric contraction cannot be entirely explained by stray compliances in the equipment and may be related to the large internal series elastic compliance found in cardiac muscle. The possible importance of internal sarcomere shortening during isometric contraction in determining the length dependency of force development in heart muscle has been pointed out previously (26-28) and will be discussed in detail later in this review.

A different interpretation of the ultrastructural basis for the cardiac length-tension relation has been suggested by Gay and Johnson (29). Using direct microscopic techniques, these investigators studied the relation between muscle length and sarcomere length in unstimulated strands of cardiac muscle obtained from right ventricular trabeculae carnea of rabbits. They found considerable fiber buckling and a wide dispersion of sarcomere lengths ranging from approximately 1.7\(\mu\) to 2.0\(\mu\) at muscle lengths at which the strand was just taut. Considerable further extension of the strand was required (about 40–60\% of its overall length) before the fibers became straightened and aligned with the long axis of the strand. At this length most of the sarcomeres measured between 2.0\(\mu\) and 2.2\(\mu\) and closely approximated the sarcomere length previously observed at the apex of both the skeletal and the cardiac muscle length-tension relation.
With extension beyond the point at which all fibers appeared straightened, the length of sarcomeres did not increase uniformly. Generally, no predictable relation was found between the overall length of the muscle strand and the length of sarcomeres within it. Furthermore, no strand length was identified at which the majority of the sarcomeres did not increase during an isometric contraction induced by electrical stimulation. These authors attributed length-dependent increases in cardiac tension development not to a uniform increase in contractile sites arranged in parallel but to a wide dispersion of sarcomere lengths: more fibers straighten as the muscle is stretched, thereby increasing the number of sarcomeres at a resting length of 2.0-2.4μ. However, because neither resting nor active tension was measured in these preparations, it is impossible to correlate the sarcomere length measurements with known portions of the length-tension curve. However, the extensive curling of the fibers in their preparation suggests that Gay and Johnson (29) were studying sarcomeres at muscle lengths at which restoring forces become important and there is no direct relation between muscle and sarcomere lengths, i.e., below 85% of Lmax in resting muscle (20, 21). Furthermore, the right ventricular trabeculae carneae used in their study may not be representative of ventricular myocardium in general because of the presence of relatively large amounts of connective tissue and variable numbers of noncontractile Purkinje fibers. Therefore, the true significance of these findings remains to be determined.

More recently, preliminary reports from Dr. Johnson’s laboratory (30, 31) have appeared in which the technique of light diffraction was used to measure sarcomere spacing in frog atrial trabeculae at rest and during isometric contraction. Unlike the situation with ventricular muscle sarcomeres, which are extremely resistant to overstretching, sarcomere lengths up to 3.5μ could be produced in these atrial trabeculae by an appropriate stretch. An anatomical basis for this marked difference between atrial and ventricular myocardium in the capacity to resist passive stretch has not been defined. At such long sarcomere lengths, atrial muscles could still generate significant amounts of active tension. During isometric contractions, internal sarcomere shortening of up to 35% of resting sarcomere length was uniformly observed despite no change in overall muscle length. Although a complete description of the sarcomere length-active tension curve was not given, the results suggest that actively developed tension was more closely related to the final sarcomere length reached after internal shortening than it was to the initial resting sarcomere length. These results again suggest the role of an internal elastic compliance in the determination of cardiac length-active tension relations.

Ultrastructural Basis for Cardiac Muscle Length-Tension Relations.—In skeletal muscle, the relation between muscle length and active tension development can be reasonably well explained at lengths greater than Lmax by the degree of myofilament overlap which in turn determines the number of force-generating cross-bridge attachments (10, 16). Below Lmax other factors in addition to myofilament overlap become important determinants of measured force; these factors include internal resistive forces (11, 12), restoring forces (13), and deactivation induced by shortening (14). Although the basic mechanisms determining cardiac length-tension relations are probably similar to those acting in skeletal muscle, certain critical observations mentioned previously raise important questions concerning the fundamental nature of this process in cardiac muscle. (1) Resting cardiac muscle is relatively stiff; tension rises exponentially as the muscle is stretched over a sarcomere length range for which resting tension is minimal in skeletal muscle. At lengths beyond Lmax, resting tension rises extremely rapidly; a disparity develops between sarcomere length and muscle length with muscle length increasing more than sarcomere length. (2) The decline in active tension development at cardiac muscle lengths beyond Lmax is much greater than that expected from a simple decrease in myofilament overlap. (3) There is no plateau of constant tension development in cardiac muscle between sarcomere lengths of 2.00μ to 2.20μ where myofilament overlap is optimal. (4) During isometric contraction, there is substantial internal sarcomere shortening in cardiac muscle which may be attributed to a large internal compliance effectively in series with the contractile components of the sarcomere.

Resting Elastic Properties.—The locale of the increased resting stiffness in cardiac muscle has been the subject of much speculation. In skeletal muscle, resting tension has classically been attributed to the passive elastic characteristics of the sarcolemma and other collagenous supporting tissues (22, 32). However, the sarcolemma does not contribute appreciably to resting tension in skeletal muscle until sarcomere lengths greater than 3.3μ are reached (22, 33); this length is considerably greater than that at which resting tension becomes prominent in cardiac muscle. However, because cardiac muscle fibers are considerably smaller than skeletal muscle fibers, they have a
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relatively greater proportion of sarcomemal material. Therefore, differences in the absolute amount or in the elastic properties of cardiac sarcolemma may contribute to the increased passive stiffness of this tissue. Furthermore, despite contradictory reports (34), it seems likely that cardiac muscle contains considerably more collagenous connective tissue than does skeletal muscle. Gay and Johnson found seven times more collagen in the ventricle than they found in the psoas muscle of rabbits (29). Thus, the resting elastic properties of cardiac muscle may be largely due to the presence of increased amounts of extracellular collagen in a nonaligned matrix.

Another possible source of resting tension in cardiac muscle has been suggested by Hill (35). He found evidence that a certain number of myosin cross-bridges remain attached to actin filaments in resting skeletal muscle, thus accounting for a small portion of the resting muscle tension. Recently, Matsubara and Millman (36) have reported that cross-links between myosin and actin filaments may be present in resting papillary and trabecular muscles from several mammalian species. The presence of cross-links in resting cardiac muscle has also been suggested by the finding that resting tension can be altered upward or downward at the same overall muscle length by various positive inotropic interventions (37, 38). However, a possible explanation for this altered diastolic compliance other than residual actomyosin cross-links has been provided (39) by the finding that a decrease in resting tension related to paired pulse stimulation is not present under isotonic conditions although it is prominent under isometric conditions. The appearance of an apparent compliance change only under isometric conditions may be attributed to increased stress on viscoelastic elements of the muscle resulting in stress relaxation. Furthermore, Feigl (40) has shown that paired pulse stimulation is on occasion associated with aftercontractions which are slow in onset and can be easily confused with altered diastolic compliance. Thus, the role of residual cross-links in the determination of resting length-tension relations in cardiac muscle remains unresolved and awaits further critical experimentation.

Additional structures have been proposed to explain the increased passive stiffness of cardiac muscle, in particular the extremely steep increase in resting tension at lengths beyond Lmax and the inability to lengthen ventricular muscle sarcomeres beyond 2.45-2.50μ without their disruption. On the basis of selective extraction studies performed in rat papillary muscles, Grimm and Whitehorn (41) have suggested that a large part of resting tension in cardiac muscle is borne by intracellular structures that do not involve myosin but are critically dependent on actin. A linkage between actin filaments across the H zone—the so-called S filaments of Hanson and Huxley (42)—has been proposed to account for these findings. Another alternative explanation for the stiffness of resting cardiac muscle is a connection between myosin filaments and the Z line. Such so-called C filaments have been tentatively identified in dipteran and bee flight muscle (43). Finally, it is also possible that cardiac muscle contains ultrathin filaments separate from myosin and actin which extend the length of the sarcomere from Z line to Z line similar to those described in certain crustacean muscles (43). Although the existence of these filaments in cardiac muscle is strictly conjectural at this time, attempts to identify such structures should provide a fruitful area for future research.

Elastic Properties during Contraction.—Since there is no plateau of constant tension development in cardiac muscle between sarcomere lengths of 2.00μ and 2.20μ, we are left with the apparent dilemma that active tension is length dependent in a range of resting sarcomere lengths for which myofilament overlap is optimal and the number of available sites for cross-bridge linking is constant. Furthermore, the decline in active tension at muscle lengths beyond Lmax is much greater than that expected from a simple decrease in myofilament overlap. From these considerations it is clear that cardiac length-active tension relations cannot be entirely explained by ultrastructural findings in accordance with the sliding-filament theory for muscle contraction. How then do muscle length changes modulate active tension development in cardiac muscle as required by Starling’s law of the heart? The answer may relate in part to the properties of the series elastic element in heart muscle (26-28).

According to the classic concepts of Hill (44), active muscle can be represented by three functionally discrete elements: (1) an active contractile element which generates force and shortening, (2) a passive series elastic element which transmits the force generated by the contractile element to the exterior, and (3) a passive parallel elastic element which supports resting tension. The exact structural arrangement of these elements has been the subject of much speculation. No single configuration has been uniformly successful in accounting for the mechanical properties of cardiac muscle. The most commonly used models differ only in the relation of the parallel elastic element to the other
elements. In the Maxwell configuration, the parallel elastic element is in parallel with both the contractile element and the series elastic element. The Voigt model is similar except that the parallel elastic element is in parallel with only the contractile element. In both models, the activated contractile element shortens and stretches the series elastic element during isometric contraction, and force develops in accordance with the stress-strain properties of the series elastic element.

The compliance of the series elastic element is substantially greater in cardiac muscle (5-8%) (45, 46) than it is in skeletal muscle (1-2%) (47). The stiffness of the series elastic element in skeletal muscle permits little change in sarcomere length during isometric contraction. However, the 5-8% extension of the series elastic element of heart muscle during an isometric contraction allows significant internal translation of myofilaments within the sarcomere despite a constant overall muscle length. Figure 4 illustrates the effect that this internal sarcomere shortening has on the measured length-active tension relation of cardiac muscle. In Figure 4A, resting and actively developed tension are plotted versus resting or diastolic sarcomere length; in Figure 4B, developed tension is replotted as a function of the predicted systolic sarcomere lengths which would result from stretching the series elastic element during isometric contraction. The dots on the resting tension curve show the resting sarcomere lengths for three muscle lengths. The dots on the active tension curve define the sarcomere length reached during the course of isometric contraction, as predicted by the stress-strain characteristics of the series elastic element. For example, a muscle with a resting sarcomere length of 2.10μm would shorten internally during isometric contraction to a sarcomere length of approximately 1.95μm based on a series elastic extension of 8%. In this instance, despite initiation of contraction at a sarcomere length at which developed tension should be maximal, the actual tension developed is 30% below maximal (Fig. 4). Thus, although resting sarcomere lengths in cardiac muscle may correspond to the plateau region of optimal myofilament overlap, no plateau of tension development is seen because the substantial shortening of sarcomeres which occurs during isometric contraction places the sarcomeres at shorter lengths that correspond to the ascending portion of the length-active tension curve. At systolic sarcomere lengths below 2.00μm, developed tension may be reduced by factors similar to those acting in skeletal muscle such as internal loads (11, 12), restoring forces (10, 13), and length-dependent inactivation of contraction (14, 15).

Considering the internal sarcomere shortening that occurs during contraction in cardiac muscle, it would be expected that a plateau region of maximal tension development would be present if contractions were initiated at appropriate sarcomere lengths beyond 2.20μm. However, this phenomenon has not proved to be the case. Papillary muscles stretched to lengths 5-10% beyond Lmax show a rapid decline in actively developed tension, accompanied by a steep rise in resting tension (Fig. 4). The reason for this rapid decline in active tension is not known, but it may be related to the properties of the stiff parallel elastic element of cardiac muscle. If the parallel elastic element is arranged in parallel with the contractile element but not the series elastic element as in the Voigt configuration, contractile element or sarcomere shortening during isometric contraction at the expense of the compliant series elastic element should also result in shortening of the parallel elastic element. This shortening would partially discharge the tension supported by the parallel elastic element and transfer some of its load to the contractile element. Under these circumstances, only a portion of the actual tension generated by the contractile element would be expressed in the muscle as actively developed tension and the remainder would support resting tension. Thus, at cardiac muscle lengths beyond Lmax at which resting tension rises to exceedingly high levels, it seems possible that a significant portion of the tension generated by the contractile element may be diverted into supporting the resting tension discharged by the parallel elastic element as a result of internal shortening. Such an effect could contribute to the observed rapid decline in actively developed tension at cardiac muscle lengths beyond Lmax. However, this explanation does not apply if the true structural model of cardiac muscle more closely resembles the Maxwell model rather than the Voigt model. In the Maxwell model, no transfer of resting tension from the parallel elastic element to the contractile element would occur during isometric contraction because, in this instance, internal sarcomere shortening would have no effect on the length of the parallel elastic element.

An additional factor that may contribute to the rapid decline in actively developed tension at muscle lengths beyond Lmax is a change in membrane electrical properties induced by stretch which possibly interferes with the process of excita-

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tion-contraction coupling. Furthermore, at papillary muscle lengths 20% beyond Lmax, actual structural damage is manifested by occasional disruption of sarcomeres and Z line obliteration (23). Such structural changes undoubtedly contribute to the marked decline in active tension at longer lengths, but the paucity of such changes makes it unlikely that they constitute the primary reason for the observed functional deterioration.

Conceptually, the contribution of a passive series elastic element to the sarcomere length-active tension relation in cardiac muscle is complicated by the lack of knowledge concerning the precise structural identity of such compliant elements. The highly branched histological structure of this tissue suggests one possible source (48). This branching appears to result from the ability of a single cardiac Z line to serve as a center for attachment of two groups of thin actin filaments. The longitudinal axes of the individual branch chains of sarcomeres are necessarily at an angle with respect to the long axis of the muscle as a whole. Stress applied to the muscle, whether generated internally or externally, would result in a change in the mean fiber branching angle which would tend to lengthen the muscle. Since muscle length is constant during isometric contraction, internal sarcomere shortening would result. Such changes in the angle of fiber branching with stress could account for a significant portion of the increased series elastic compliance seen in cardiac muscle.

Other possible sites for the series elastic compliance include the Z lines, intercalated discs, and cross-bridge links between actin and myosin. Indeed, Huxley and Simmons (49) have suggested that the series elastic properties of skeletal muscle can be largely attributed to the force-generating cross-bridges. Noble and Else (50) and Pollack et al. (51) have recently reported that the compliance of the series elastic element in cardiac muscle varies with time after activation, suggesting that cross-bridge elasticity may be important to the series elastic compliance measured by quick-release techniques. Their inability to define a unique series elastic compliance with the properties of a passive nonlinear spring suggests that the traditional Hill model for cardiac muscle may not be useful for quantitative characterization of contractile element properties. These findings disagree with earlier reports (45, 46) as well as with more recent studies from our laboratory (52, 53) in which the series elastic compliance of cardiac muscle varied in a linear fashion with force and was independent of time. The reasons for the differences between these studies probably relates to differences in experimental technique and to the extrapolation procedure used to obtain data in the studies by Noble and Else (50) and Pollack et al. (51). Such extrapolations were avoided in our laboratory (52, 53) by directly measuring muscle force and length continuously throughout the release interval. Because of the exponential shape of the stress-strain relation for cardiac muscle series elasticity derived from real-time measurements, it was not possible to exclude appreciable series elastic compliance residing in attached myofilament cross-bridges. However, in assessing these data concerning cardiac series elastic properties, it should be remembered that activated cardiac muscle has an approximately three- to fourfold greater series elastic compliance than does skeletal muscle (45-47). Since the motion of a force-generating cross-bridge is thought to be approximately 80-100 Å or less than 1% of overall muscle length, it does not seem possible that all or even a majority of the measured series elastic compliance in cardiac muscle can reside in the cross-bridge links. Thus, we believe that the traditional Hill model for cardiac muscle should not be abandoned at the present time.

Although speculations concerning the source of the increased series elastic compliance in cardiac muscle are very interesting, this problem needs to be resolved by direct experimental methods. Refinements of the techniques currently being used to measure sarcomere lengths in living cardiac muscle (24, 25) may allow active tension development to be measured while the central sarcomeres are maintained at a desired length with controlled stretch. This approach should help to further define the true nature of the series elastic compliance in cardiac muscle as well as its influence on cardiac length-tension relations.

References


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