Studies on Starling's Law of the Heart

VIII. Mechanical Properties of Human Myocardium Studied in Vivo

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During the last century the investigations of Fick, von Kries, and Blix,1-4 on the strength of contraction of skeletal muscle led to the concept that the length and tension of the muscle at the time of stimulation determined the magnitude of its contractile response. Frank5 and later Starling6 as well as other investigators7-10 extended these observations to the heart, but the complex anatomy of this organ has made analogies to skeletal muscle difficult. Thus, Patterson, Piper, and Starling7 appreciated that they did not actually measure the length of the myocardial fibers in their experiments, but used measurements of ventricular end-diastolic volume to indicate changes in the fiber length. Similarly, these investigators utilized the mechanical activity of the ventricle, as reflected in the stroke volume and systolic pressure, to provide an index of the force of contraction. Many investigators have subsequently contributed to an understanding of the manner in which Starling’s law is integrated into the regulation of the circulation, and have correlated ventricular end-diastolic volume (or an index thereof) and end-diastolic pressure with the cardiac output, stroke work, or a similar index.8-12

Following Wohlish and Claman’s observations13 on the resting length-tension relationships of excised muscle strips, Lundin14 carried out extensive experiments on the mechanical properties of resting and contracting threads of frog ventricle. Length-tension relationships of isolated strips of myocardium were defined by Abbott and Mommaerts,15 and by Sonnenblick,16 utilizing cat papillary muscle preparations, and by Blinks,17 working with rabbit atrium. Cotton and Maling,18 employing a Cushey lever system, were the first to analyze the length-tension relationships of the dog’s ventricle in situ, while Monroe and Franch19 defined left ventricular pressure-volume relationships in an isolated dog heart preparation. The purpose of the present investigation was to examine the mechanical properties of functioning human myocardium during isometric contraction. Particular attention was directed toward (1) determining the applicability of Starling’s law to segments of human heart muscle, i.e., ascertaining whether the length of a segment of myocardium modifies its force of contraction; (2) studying the relationship between the length of a given segment of myocardium and the rate of development of tension; and (3) investigating some of the viscoelastic properties of the human myocardium.

Methods

Eleven patients (eight female and three male), ranging in age from 5 to 43 years, with an average age of 22 years, were studied at the time of cardiac operation. Among them were five patients with atrial septal defects, four of the ostium secundum variety and one of the ostium primum type. Four of these patients with atrial septal defects had normal pulmonary artery and right ventricular pressures, while the fifth had moderate pulmonary hypertension (48/23 mm. Hg). Two patients had ventricular septal defects with associated pulmonary hypertension (pulmonary artery pressures = 41/22 mm. Hg and 105/40 mm. Hg). Two patients with congenital aortic stenosis and left ventriculo-systemic arterial pressure gradients of 57 and 60 mm. Hg were studied. One patient had mitral stenosis with a left atrioventricular end-diastolic gradient of 15 mm. Hg. None of these 10 patients had experienced congestive heart failure and none had elevations of the ventricular end-diastolic pressures recorded at the time of the preoperative cardiac catheterization. The eleventh patient, a 13-year-old boy with severe pulmonic stenosis and a right ventricular pressure of 142/72 mm. Hg, gave...
a history of congestive heart failure and had a right-to-left shunt across a patent foramen ovale.

All patients were on maintenance digoxin at the time of operation. Pre-anesthetic medication consisted of meperidine (25 to 75 mg.), scopolamine (0.1 to 0.4 mg.), and promethazine (15 to 50 mg.). After induction with intravenous thiopental, light general anesthesia was maintained with nitrous oxide-oxygen; a muscle relaxant, either succinylcholine or d-tubocurarine was also used. The chest was opened through a median sternotomy in all patients except the patient with mitral stenosis in whom a left lateral thoracotomy was performed. The pericardium was opened widely, and the observations reported below were carried out during the period when the surgical team was directing its attention to exposing the femoral artery, prior to establishing cardiopulmonary bypass.

A Walton-Brodie strain-gauge arch\(^1\) was modified in such a manner that the distance between the legs could be altered by means of a micrometer screw (fig. 1); each revolution of the screw increased the distance between the legs by 0.50 mm. This modified arch was sewn to the right ventricle of the 10 patients with congenital heart disease, and to the left ventricle of the patient with mitral stenosis. An attempt was made to align the axis of the arch with the longitudinal axis of the ventricle (fig. 2). Considerable care was taken to avoid the inclusion of any visible coronary vessels within the sutures during attachment of the arch to the ventricle. In addition, the blood supply reaching the myocardial segment from its large lateral surfaces was not compromised.

Since the viscoelastic properties of tissue are by definition time-dependent, in any given experiment, changes in the length of the myocardial segment were induced at equal time intervals and, in any given patient, measurements of tension were carried out at constant time intervals after each change in length of the muscle. These intervals ranging from 10 to 15 seconds. The output of the strain-gauge arch was recorded simultaneously with the systemic arterial pressure or the electrocardiogram on a multichannel photographic re-

corder (fig. 3). No changes in systemic arterial pressure, electrocardiographic configuration, heart rate, or temperature occurred during the studies on any patient.

At the completion of each experiment the strain-gauge arch was calibrated so that the tension could be expressed in grams of force. The active or developed tension was calculated by subtracting the end-diastatic or resting tension from the peak or maximal systolic tension. The baseline length of the myocardial segment under study was taken as that length at which the strain gauge recorded a barely detectable end-diastatic tension. The rate of change of tension in grams per second was calculated by dividing the developed tension by the time required for its development. This rate was calculated for the initial 0.08 second of systole as well as for the total ascending limb of the time-tension curve.

Results

Myocardial Length-Resting Tension Relationships

The relationship of the length of the myocardial segment between the points of attachment of the gauge to the end-diastatic or resting tension (T\(_r\)) was determined in each patient. The baseline length ranged from 20
to 30 mm. The maximum by which length was increased varied among the different patients, and ranged from 18 to 97 per cent above baseline. Although the magnitude of the increase in $T_r$ with any given increase in length varied considerably among the different patients, the general pattern was similar, i.e., the relationship between length and $T_r$ was a curvilinear one, convex to the length axis (fig. 4). As length was increased, there was at first only a very slight elevation of $T_r$, but with progressive stretching $T_r$ increased more strikingly.

**Myocardial Length-Maximal Tension Relationships**

The relationships between myocardial segment length and the peak systolic tension ($T_m$) for the 11 patients studied are plotted in figure 5. The curves depicting this relationship were, in general, similar in shape to those relating length and $T_r$, except for the higher levels of tension resulting from the addition of active tension ($T_a$) to $T_r$. As might be expected, in no instance did $T_m$ decline as length was increased, i.e., a descending limb of the curve relating length and $T_m$ was not observed.

**Myocardial Length-Active Tension Relationships**

As the myocardial segment was stretched, $T_m$ tended to increase more rapidly than $T_r$. 

Myocardial tension recorded from the right ventricle of patient N.B., with a ventricular septal defect, at increasing degrees of stretching. $T_r =$ resting tension, $T_m =$ peak systolic tension.

![Figure 3](image-url)
Relationships between myocardial segment length and maximal tension in the 11 patients studied.

![Figure 5](image1)

Figure 5

Relationships between myocardial segment length and active tension in the 11 patients studied.

![Figure 6](image2)

Figure 6

Relationships among myocardial segment length, resting tension (Tr), maximal tension (Tm), and active tension (Ta) in patient N.B. The tracings from this patient are reproduced in figure 3, and other data are shown in figures 9 and 11.

![Figure 7](image3)

Figure 7

Duration of Active Tension and Rate of Tension Development

Although Ta increased with progressive elongation of the myocardial segment, the duration of active tension did not change appreciably (fig. 8) and the time interval required to reach Tm also remained almost constant. Consequently, the relationship between length and Ta per second, i.e., the rate of development of tension (fig. 9), was similar to the relationship between length and Tm (fig. 7). Since most of the rise of tension occurred during the first portion of systole, the rate of development of tension during the first 0.08 second of contraction was also calculated. The relationships between length and Ta per second for this interval were qualitatively similar to those obtained when the entire ascending limb was considered. However, the absolute values for Ta per second were greater when the first 0.08 second of contraction was considered (fig. 9).

Resting Tension-Active Tension Relationships

The curves relating Tr to Ta exhibited a very steep rise of Ta as Tr was initially increased. However, with progressive elevations of Tr, Ta reached a plateau and in some instances declined (figs. 10 and 11). The curves relating Tr to the mean rate of development of Ta were similar in shape to the curves relating Tr to Ta (fig. 11).

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Stress-Relaxation and Hysteresis

When the myocardial segment was rapidly stretched, the resultant increases of $T_r$, $T_m$, and $T_a$ were greatest during the first cardiac cycle, and then tended to decline. Since the relationships between myocardial length and tension were time-dependent, all the observations reported herein were carried out at a constant time interval following each change of myocardial segment length.

In six patients, the myocardial segment was stretched by given increments as already described, and the segment was then shortened in the opposite manner. This sequence of progressive lengthening followed by shortening of the muscle was repeated several times. It was observed consistently that for any given values of length, $T_r$ and $T_m$ were always higher when the segment was being lengthened than when it was being shortened. The curves relating myocardial length to tension during stretch and release constituted "hysteresis loops" (fig. 12). When the sequence of lengthening and shortening was repeated it was observed that although the ascending limb of the second hysteresis loop was lower than the first, the descending limb of the second loop showed little change from that of the first (fig. 13). With each successive lengthening and shortening the hysteresis loop became progressively thinner.

Discussion

A potential limitation of the strain-gauge arch for investigating the mechanical properties of ventricular muscle is that the muscle segment under study is probably not functionally independent of the remainder of the heart and may therefore be influenced by the activity of the adjacent myocardium. However, the electrical and mechanical activity of the entire heart remained constant while the length of the small segment of myocardium under study was altered. The response of the myocardial segment was undoubtedly influenced by the absolute quantity of myocardium to which the strain-gauge arch was attached.
STARLING'S LAW OF THE HEART

The modulus of elasticity of resting cardiac muscle in vitro was determined for the first time by Bohnenkampf and Ernst.21 These investigators, working with frogs' ventricle, reported that cardiac muscle obeyed Hooke's

Relationship between resting and active tension in the 11 patients studied.

law, i.e., they observed a linear relationship between the stress and strain of the muscle. Wohlish and Clamann,13 in experiments on strips of excised frog myocardium, found that the modulus of elasticity varied as the degree of stretch was altered. The resting length-tension diagrams of segments of human myocardium (figs. 4 and 7) revealed an upwardly concave curve, resembling the resting length-tension diagrams obtained from preparations of cat papillary muscle.15,16 As the myocardial segment was initially stretched beyond the baseline length, the length-T relationship exhibited little curvature and the increment of tension was usually relatively small. With greater elongations, however, T, tended to rise more steeply (fig. 4). Lundin14 also found that when the frog myocardial fibers were on the steep portion of their length-tension curve a given increase in length required approximately 10 times as much tension as when the fibers were on the flat portion of the curve. Our observations are also consonant with the pressure-volume diagrams on the frog heart, observed by Frank,22 and the left ventricle of the dog, studied by Monroe and French.19

Figure 10

Relationship among resting tension, active tension, and rate of development of tension in patient N.B.
Relationships among length-tension during progressive stretching (solid lines) followed by release (broken lines).

The relative flatness of human myocardial resting length-tension curves with small degrees of stretching is of importance in limiting the elevation of ventricular end-diastolic pressure, and therefore of atrial and venous pressures, for any given augmentation of myocardial length.

In the experiments described, the myocardial segment was stretched to relatively high levels of resting tension in an attempt to characterize the entire length-tension relationship (fig. 4). Relatively little data are available to permit an estimation of the changes in linear dimensions of the ventricle that actually occur in the intact organism. In earlier experiments performed in this laboratory on open-chest dogs it was observed that when the end-diastolic circumference of the left ventricle was rapidly increased, with blood transfusions, by 15 per cent of control, the left ventricular end-diastolic pressure rose to values in the neighborhood of 35 mm. Hg. It seems unlikely that the linear dimensions of the mammalian heart in situ could increase by more than 15 to 20 per cent, and it is suggested that only the initial portion of the length-tension curves obtained in the present study describes the relationships that exist in most physiologic circumstances.

The peak systolic tension developed by the portion of myocardium studied was also found to be a function of its length, and increased progressively as the segment was stretched (figs. 5 and 7). The active tension was also found to increase as the segment was initially elongated. As observed by Sonnenblick in the cat papillary muscle preparation, an increase in segment length did not alter the time interval during which active tension was maintained, and accordingly the increase in active tension as the muscle was stretched was accompanied by an increase in the rate of development of tension. In the majority of patients who were studied a plateau of the length-active tension relationship was reached when the segments had been stretched to approximately 115 to 150 per cent of their baseline lengths; descending limbs were apparent in several instances, and it is likely that they would have been noted in all of the experiments if the muscle had been stretched further. These findings on the human heart, studied in vivo, are thus qualitatively similar to those obtained from a variety of isolated myocardial preparations, and show that a descending limb of the length-active tension curve for human myocardium definitely exists (figs. 6 and 7).

Stress relaxation and hysteresis loops have previously been demonstrated to occur in a variety of tissues including smooth and skele-
tal muscle, the tortoise ventricle, as well as the aorta and other major arteries.\textsuperscript{26-30} The present investigation extends these observations to the human heart, studied in situ. As in other investigations, it was observed that the magnitude of the relaxation and the width of the hysteresis loops increased with the degree of stretch. It is interesting to note that the hysteresis loops of the length-maximal tension curves circumscribed larger areas than the loops of the length-resting tension curves (fig. 12). Thus, at any given myocardial segment length the active tension was higher when the segment was being lengthened than when it was being shortened. This mechanism may play a role in modifying the resting tension in situations in which significant and rapid changes in heart size occur.

Summary

This investigation was designed to study the mechanical properties of human myocardium in vivo, and to ascertain whether Starling’s law applies to the human ventricle by determining whether the length of a segment of myocardium influences its force of contraction. A modified Walton-Brodie strain-gauge arch was sewn to the right ventricle of 10 patients and to the left ventricle of one patient at the time of operation. This instrument permitted the controlled alteration of the length of the myocardial segment to which it was attached, as well as the measurement of the tension exerted by this segment of myocardium throughout the cardiac cycle. In all 11 patients studied it was noted that as myocardial length was increased, the end-diastolic tension tended to rise slightly at first, but with further stretching the end-diastolic tension increased more strikingly. As the segment was stretched the maximal systolic tension, which it developed, increased more than did its resting tension. Thus, within limits, the active or developed tension rose as the myocardial segment increased in length. In five patients the active tension declined after the myocardial segment had been stretched to values ranging between 15 and 50 per cent above baseline length, i.e., a descending limb of the length-active tension relationship was evident. No change in duration of active tension occurred with progressive stretching of the myocardial segment, and changes in the rate of development of tension paralleled the changes in the active tension. In six patients the segment of myocardium was stretched progressively and was then permitted to shorten in the opposite direction. Hysteresis of the myocardium was demonstrated, since, at any given myocardial segment length, the resting and the maximal tensions were higher when the segment was being lengthened than when it was being shortened. These observations provide a description of the mechanical properties of functioning human myocardium and indicate that this tissue behaves in accordance with the Frank-Starling principle.

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References


The Environment

The world of our senses is a world of matter and energy, space and time. After centuries of philosophical and scientific study, these, the very logical elements of science, are still without a final description.—Lawrence J. Henderson. The Fitness of the Environment. New York, The Macmillan Co., 1924, p. 8.
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