PHYSIOLOGIC LOADING OF ISOLATED HEART MUSCLE

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Summary: An electromechanical system with computer control has been developed which permits the simulation of physiologic loading for isolated cardiac muscle. In contrast to conventional loading techniques, where relaxation occurs at the same load as shortening, the new system allows isometric relaxation at peak shortening prior to isotonic relaxation at reduced load.

Efforts to relate data obtained in studies of isolated heart muscle to indices of ventricular performance have been limited in part by the experimental apparatus available for providing a load. The use of purely mechanical loading systems, such as a lever and weight in the conventional 'afterloaded isotonic' contraction, results in the following loading sequence:

a) Isometric contraction
b) Isotonic contraction
c) Isotonic relaxation
d) Isometric relaxation

The principal non-physiologic aspect of the above sequence is that isotonic relaxation immediately follows isotonic contraction. Thus, during the initial phase of relaxation

the muscle is abruptly lengthened by the same load that it has just lifted. The present experiment demonstrates for the first time the contraction of isolated cardiac muscle during a physiologic loading sequence.

Methods

To overcome limitations of purely mechanical methods of loading, an electromechanical system with computer control was developed. The system loads the muscle by means of a low-inertia d.c. motor with integral displacement transducer. Tension is sensed at the opposite end of the muscle with a low compliance semiconductor strain gage transducer. Electronic servo circuits allow control of muscle length with an effective compliance of 1 micron/gram, and a response time of 1 msec; or control of tension to an accuracy of 20 mg/mm of muscle shortening. A small general purpose computer (DGC Nova 800) is programmed to control the sequencing of loading conditions, provide input for the controlled parameter, and process the resulting data. The system is designed to provide flexibility in supplying a variety of physiologic and non-physiologic loading conditions to the muscle preparation.

As a first approximation to physiologic loading, the system was programmed to simulate the sequence of the normal cardiac cycle. Phases (c) and (d) of the conventional after-loaded isotonic sequence were interchanged to allow isometric relaxation at peak shortening prior to isotonic relaxation at resting tension, thus simulating aortic valve closure and mitral valve opening respectively. The following experimental procedure was followed:

Papillary and trabecular carneae muscles were dissected from the left ventricles of freshly decapitated rats and

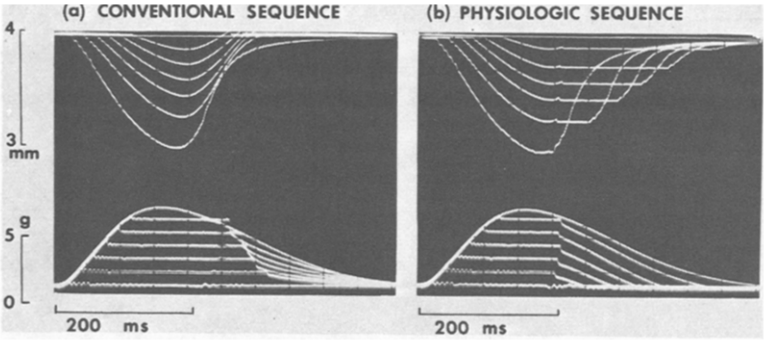

Figure 1: Rat left ventricular papillary muscle. A series of 7 conventionally (a) and physiologically (b) sequenced contractions with one gram increments in afterload. In each photograph, displacement curves are displayed on the top while tension is simultaneously depicted on the bottom. An inverse relation between tension and displacement is seen. Both series were loaded by the electromechanical load regulation unit under computer control. In the physiologically loaded series, isometric relaxation at peak shortening precedes isotonic relaxation at resting tension. Muscle length 4.03 mm, cross sectional area 0.97mm^2, preload 1.50 gms.

mounted vertically in a muscle chamber containing Krebs-Henseleit solution (1) bubbled through with 95 percent O_2 and 5 percent CO_2. Glucose (5mM) was present in the bath solution, kept at a constant temperature of 28°C. Muscles were stimulated 12 times per minute by parallel platinum electrodes delivering 5-msec pulses at currents 10 percent greater than the threshold for maximum mechanical response.

The upper end of the muscle was attached via a spring clip and gold chain to the motor lever arm. The lower end of the preparation was connected to the force transducer via a similar clip and a section of stainless steel tubing which extended through a small mercury-sealed opening in the bottom of the muscle chamber. Following a 30-minute equilibration period, the muscle was carefully stretched to the apex of its length-active tension curve and studied.

Results and Discussion

At the resting tension corresponding to muscle length at peak active tension, two series of loading sequences were applied under computer control. Resulting shortening and tension waveforms were displayed on an oscilloscope and a cumulative photographic record of the oscilloscope display was made for each series. The first (Fig. 1a) was the conventional afterloaded isotonic contraction sequence, with afterload increased in 1-gram steps from 0 (pure isotonic) to the level required to prevent shortening (pure isometric). The second series (Fig. 1b) was an approximation to physiologic conditions, in which isometric relaxation occurred at peak shortening. The same increments of afterload were employed.

As is shown in Figure 1, the initial phases of contraction are the same for both loading sequences. On the other hand, the relaxation phases differ markedly. This is significant in that the performance of the intact ventricle may be considerably influenced by the dynamics of relaxation. In particular, the phase of ventricular filling, initiated by opening of the mitral valve, does not begin until isometric relaxation is complete. The results depicted in Fig. 1b show that this phase extends longer into the cycle as afterload increases, thus allowing less time for filling at a constant heart rate. In Fig. 1a, on the other hand, it can be seen that for the conventionally sequenced contraction the endpoint of isometric relaxation is essentially independent of afterload.

Previous investigators have found an 'uncoupling effect' (2,3), whereby fiber shortening during a contraction influences the duration and intensity of the active state. This is presumably the mechanism by which an isometric contraction

lasts longer than an isotonic contraction. Furthermore, the effect of a 'quick stretch' or 'quick release', in which a muscle is subjected to rapid length changes during a contraction, is to significantly reduce the intensity and duration of active state. Such a mechanism might be expected to operate during the isotonic relaxation phase of the conventional afterloaded isotonic contraction, when the muscle is actively stretched by the afterload.

Despite its importance to in vivo performance, the phenomenon of relaxation in the isolated heart muscle has received little attention. Previous studies (4) have employed either isometric or afterloaded isotonic loading conditions. Our results suggest, however, that the simulation of physiologic loading conditions significantly alters the parameters of relaxation. Hence, in relating data obtained from studies of isolated heart muscle to measures of in vivo performance, it would seem of considerable importance to apply the appropriate loading conditions.

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References and Notes

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