Tension Developed by Papillary Muscles from Hypertrophied Rat Hearts

By ANDREW KERR, JR., M.D., ALAN R. WINTERBERGER, M.D., and MARY GIAMBATTISTA, M.D.

TO DETERMINE whether, in certain aspects, hypertrophied heart muscle behaves differently from normal heart muscle simple observations were performed. Papillary muscle strips from the left ventricle of rats, the hearts of which had been caused to hypertrophy, were compared with papillary strips from normal rats by measuring tension developed at various weights in a perfused isolated muscle strip preparation. Having parallel muscle fibers and sharing in hypertrophy of the left ventricle, papillary muscle is well suited to studies of isometric contraction.

Methods

Hypertrophy of the left ventricle was achieved by the method of Hajdu and Beznak. Silver rings of an internal diameter of 1.50 mm. were snugly placed about the ascending aorta of male rats between the ages of 30 and 90 days weighing 150 to 250 Gm. Blue Spruce Farm Sprague-Dawley rats were used for operation and for control animals. Between 21 and 90 days after placement of the ring, the rat hearts were tested. Animals failing to gain weight normally were discarded. The animal was weighed, given ether anesthesia, and the heart quickly removed. Following the method of Hoffman and Kelly, the actively beating fresh heart was transferred to oxygenated Tyrode's solution, the left ventricle opened, and a papillary muscle, gently handled, was tied at its apex with 0000 silk and excised at its base. The muscle was inserted into a plastic muscle holder and its base firmly pressed against two pin-point platinum stimulating electrodes. The strip was then placed in a muscle warmer and perfused at a rate of 3 ml./min. with Tyrode's solution (NaCl, 142 mM/L; KCl, 2.7; dextrose, 5.5; NaHCO3, 12.5; MgCl2, 0.5; NaH2PO4, 3.7). A mixture of 95 per cent O2 and 5 per cent CO2 was delivered through a sintered disk at the bottom of the muscle warmer at a rate of 6 ml./min. The muscle warmer was surrounded by a constant temperature bath kept at 27 C. The suture from the apex was attached vertically to a horizontally placed Grass force displacement transducer (Model FT 0.03). Gram weights were used to calibrate the displacement of the transducer which was connected through a preamplifier to a channel of a Grass recorder. A micrometer screw adjustment was used to tighten the suture and the muscle was placed under 1 Gm. of tension. The preparation was then left in the muscle bath for one hour before stimulation. A Grass stimulator (Model S4C) and isolation unit were used. The muscle was stimulated at 5-second intervals with a rectilinear pulse of 10-msec. duration. Voltage was increased until a maximum response was evoked. Resting tension was then increased stepwise to various levels from 1 to 10 Gm. and the tension developed by the muscle strip to stimulation at each of these levels recorded at paper speeds of 1 and 10 mm/sec. Following this, in 19 instances, the temperature of the bath was raised to 37 C, the resting tension was set at 2.0 Gm., and the muscle was stimulated as usual. After a baseline had been established, the gas perfusion mixture was switched to 95 per cent N and 5 per cent CO2. Stimulation was continued until the strip was no longer responsive. The papillary muscle strip was cut at the apical suture and from the compressed part of its base that had been in the muscle holder. It was dried in an oven at 150 C. for two hours to produce constant dried weight and weighed on a microelectric balance to the nearest milligram. The average height in millimeters of tension developed at each of the levels of resting tension was measured from the records and converted to grams of tension developed. This figure was corrected for milligrams of dried muscle weight, so that results are expressed as grams of tension developed per milligram of dried muscle weight at various grams of resting tension. The heart was prepared for weighing according to the method of Addis & Gray and hypertrophy of the heart determined from their tables.

From the Medical Service, Veterans Administration Hospital, and the Department of Medicine, State University of New York, Upstate Medical Center, Syracuse, New York.

Supported in part by grants from New York Heart Assembly and Heart Association of Onondaga County.

Drs. Giambattista and Winterberger were recipients of student research fellowships during the summers of 1958 and 1959.

Received for publication August 5, 1960.
The mean maximum tension developed per milligram of dried papillary muscle weight by muscles from 17 animals with hypertrophied hearts was 1.95. The similar tension developed by 17 muscles from normal-weight hearts was 1.29. The difference between these two means is significant ($P<.01$) by the $t$-test ($t=2.98$). The difference between the two groups is apparent, (fig. 1) as well as a progressive trend in keeping with results. The amount of tension developed increased from the nonoperated group, to the operated group without increased heart weight, to the group with borderline hypertrophy, to those with frank hypertrophy.

The response to stimulation under anaerobic conditions was better by the strips from hypertrophied hearts. When a steady state was achieved with nitrogen perfusate, the seven strips from hypertrophied hearts maintained an average tension of 18 per cent of their value in oxygen, while the other ten strips declined to an average of 5 per cent of their former values.

Discussion

These results, in keeping with more extensive studies of hypertrophied skeletal muscle, indicate that the hypertrophied heart muscle is capable of better performance than nonhypertrophied heart muscle. This is contrary to the usual clinical belief.

Experimental studies of the behavior of hypertrophied hearts are few. Dieckhoff used the heart-lung preparation in testing cat hearts made hypertrophic by avulsion of aortic cusps. These hearts responded better than normal. Beznak achieved hypertrophy in rat hearts by hypertension and found cardiac output increased at rest and in response to infusions. Whitehorn and Grimmena have indicated that greater tension developed, when compared with littermate controls, for given diastolic lengths of columnae carneae strips from the left ventricle of rat hearts caused to hypertrophy from repeated swimming to exhaustion.

Biochemical studies of hypertrophied heart muscle similar to the extensive ones by...
Palladin\(^6\) for skeletal muscle are lacking. Pilot studies of ours\(^10\) indicated increases in succinic dehydrogenase in hypertrophied hearts. Producing hypertrophy of hearts by repeated exposure of rats to low atmospheric pressure, Sobel and Cohen\(^11\) studied chemical changes of proteins. They demonstrated an increase in the more active metabolic parts of protein, greater than with normal growth of rat heart muscle. Thus, while Beznak\(^12\) has clearly demonstrated that without growth hormone cardiac hypertrophy will not develop, the biochemical changes may not parallel those of growth. Palladin demonstrated more effective anaerobic as well as aerobic metabolism for hypertrophied skeletal muscle, and our studies with nitrogen perfusion tend to indicate this for hypertrophied heart muscle as well.

The amount of hypertrophy produced experimentally is not as great as occurs in human disease. Linzbach\(^5\)\(^13\) studies of human hearts indicated a critical point (500 Gm. for the adult) beyond which deleterious microscopic changes appear. Lowe and Bate\(^14\) demonstrated abnormal microscopic changes as well as probable hyperplasia in grossly hypertrophied hearts. Thus, the better performance of hypertrophied hearts noted experimentally may not apply in all clinical instances. The clinical aspects of this problem have been ably discussed by Grant.\(^15\)

**Summary**

Papillary muscle strips from hypertrophied left ventricles of 17 rats were tested for tension developed in response to electrical stimulation in a perfused, oxygenated, isometric muscle chamber. The maximum tension developed was significantly greater per unit weight than that developed by papillary muscles from normal ventricles. Greater tension was also developed by the papillary muscles from hypertrophied hearts when tested with an anaerobic perfusate.

**References**

Tension Developed by Papillary Muscles from Hypertrophied Rat Hearts
ANDREW KERR, JR., ALAN R. WINTERBERGER and MARY GIAMBATTISTA

Circ Res. 1961;9:103-105
doi: 10.1161/01.RES.9.1.103

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1961 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/9/1/103

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/