Effect of Exercise Conditioning on the Intrinsic Contractile State of Cat Myocardium

JOHN F. WILLIAMS, JR., M.D., AND RALPH D. POTTER

SUMMARY Fourteen adult cats were exercised on a motor-driven treadmill 5 days each week for 6 weeks to determine the effect of exercise conditioning on the intrinsic contractile state of the myocardium. The exercise program was sufficient to produce a cardiovascular training effect manifested by slower exercising heart rates and resting heart rates after atropine by the end of the 6th week. The mechanical function of the isolated right ventricular papillary muscle from exercised cats was compared with that of 17 sedentary adult cats. There were no significant differences between exercised and control cats in heart weight-body weight ratios, resting and active length-tension relations, maximal rate of isometric force development at the peak of the length-tension curve ($L_{\text{max}}$), time to peak force at $L_{\text{max}}$, maximal force development with paired stimulation and norepinephrine, or force-velocity relations. These results indicate that the intrinsic contractile state of feline myocardium is unaffected by exercise conditioning.

ALTHOUGH the exact role of exercise in preventing or modifying certain forms of heart disease has not been determined, enhanced cardiac performance has been observed after exercise conditioning. Several studies have analyzed the mechanisms responsible for this improved cardiac function and a variety of potentially important physiological and biochemical changes have been described, including an increase in the basic contractile state of the myocardium. However, these observations of contractile state have been made under conditions in which it is difficult to exclude alterations in other factors which may have affected measurements of this variable. For example, changes in loading conditions, autonomic stimulation, or humoral cardioactive substances may have occurred with training in studies performed in vivo, whereas in those studies in vitro employing whole hearts, differences in muscle mass, fiber length, or ventricular geometry may have occurred. Therefore, in our present study the effect of exercising cat myocardium was determined by examining the mechanics of isolated right ventricular papillary muscles from cats subjected to prolonged repetitive exercise.

Methods

Fourteen adult cats performed treadmill exercise 5 days weekly for 6 weeks. The workload was adjusted to produce marked fatigue after 45–60 minutes of exertion. This necessitated gradually increasing the speed and incline of the treadmill during the 6-week training period. At the end of the study, treadmill speed and incline ranged from 1.5 to 2 miles per hour and from 15% to 20%, respectively. In nine of those studies in vitro employing whole hearts, differences in muscle mass, fiber length, or ventricular geometry may have occurred. Therefore, in our present study the effect of exercising cat myocardium was determined by examining the mechanics of isolated right ventricular papillary muscles from cats subjected to prolonged repetitive exercise.

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eter stops, isometric length-tension curves were determined by stretching the muscle by known increments from a point at which active force development was just apparent to the first point at which active force declined from its maximum. In addition to developed force the maximal rate of force development (dF/dt) and the time from onset of contraction to peak force also were determined at the peak of the isometric length-tension curve. The muscle then was again lightly preloaded and allowed to contract isotonically. After muscle shortening had returned to a value similar to that observed before the isometric study, resting muscle length was fixed at this light load and the force-velocity relationship was determined by measuring maximal velocity of shortening after 0.5-g increments in afterload. The muscle then was returned to the peak of the length-tension curve and allowed to contract isometrically. Active force at this time was essentially identical to that observed at the peak of the previously measured isometric length-tension curve. Paired electrical stimulation was begun at a frequency of 12 pairs/min, with the interval between pairs adjusted to produce a maximal force response. Graded concentrations of norepinephrine (10^-8-10^-2 M) were added to the bath; this generally resulted in only a slight additional increase in active force. In preliminary studies the addition of calcium to the bath (in final concentrations of 2.5-12.5 mM) at this time did not result in further augmentation of active force. We therefore termed the developed force with paired stimulation and norepinephrine the "maximal force index."

Muscle length at peak active force development (L\(_{\text{max}}\)) and the length at which the force-velocity curve was obtained were measured by means of a calibrated reticle. Cross-sectional area was determined from the wet weight of the papillary muscle and its length at L\(_{\text{max}}\), assuming the muscle to be a cylinder with a specific gravity of 1.055.

The great vessels were removed from the remainder of the heart, which was washed free of blood, blotted dry, and weighed. The atria then were removed. The right ventricle was dissected from the left ventricle and the septum and weight of each ventricular specimen were determined.

The data from the exercising cats were compared with data from 17 nonexercised cats maintained under otherwise comparable conditions.

Student's t-test was utilized to determine the statistical significance of differences between groups.³

Results

Heart rates measured during exercise and after atropine are presented in Table 1. Unfortunately, "resting" heart rates could not be determined because frequent and marked changes in heart rate occurred even when the cages were covered and placed in isolated rooms. A decrease in heart rate at comparable workloads was observed in each of the five cats after 6 weeks of training. The maximal exercising heart rate also was less after 6 weeks in each of the nine cats, although the workload was even greater during this period. Maximal heart rate after atropine was less in each cat after 6 weeks of exercise training. Since heart rate just prior to atropine administration was not significantly different at 1 week and 6 weeks, the increment in heart rate also was less at the latter period. The workload (i.e., treadmill speed and incline, and duration of exercise) after 6 weeks in cats in which heart rates were not measured was not significantly different from that of cats in which heart rates were measured.

Anatomical data are presented in Table 2. None of the exercising cats lost weight during the training period, and the body weight of these cats at the completion of the study was not significantly different from that of the nonexercising controls. Similarly, heart weight-body weight, right ventricular-body weight, and left ventricular-body weight ratios were not significantly different between the two groups. Cross-sectional area of the papillary muscle also was comparable, with values ranging from 0.6 to 1.7 mm² and 0.6 to 1.4 mm² in the exercising and nonexercising groups, respectively.

Length-tension relationships are illustrated in Figure 1. There were no significant differences in resting or active length-tension relationships between the two groups. Active force at L\(_{\text{max}}\) averaged 5.3 ± 0.4 (SEM) g/mm² and 4.9 ± 0.3 g/mm² in the exercising and nonexercising groups, respectively.

Force-velocity relations are presented in Figure 2. Preload was not significantly different, averaging 0.48 ± 0.04 g/mm² in the nonexercised cats and 0.46 ± 0.05 g/mm² in the exercised ones. There were no significant differences in the velocity of shortening at any load; the maximal measured velocity averaged 1.10 ± 0.10 and 1.12 ± 0.05 muscle lengths per second in the exercising and nonexercising groups, respectively.

The maximal rate of force development and the time to peak force development at L\(_{\text{max}}\) were essentially identical (Fig. 3). Maximal force index (Fig. 4) was slightly greater in

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>1st Week</th>
<th></th>
<th>6th Week</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>At comparable workloads (n = 5)</td>
<td>277 ± 5.2</td>
<td>&lt;0.001</td>
<td>225 ± 3.2</td>
<td></td>
</tr>
<tr>
<td>At peak workloads (n = 9)</td>
<td>289 ± 5.7</td>
<td>&lt;0.001</td>
<td>267 ± 3.9</td>
<td></td>
</tr>
<tr>
<td>After atropine (n = 4)</td>
<td>256 ± 12.1</td>
<td>&lt;0.01</td>
<td>231 ± 11.1</td>
<td></td>
</tr>
</tbody>
</table>

Results (beats/min) are expressed as mean ± SEM.

### Table 2

<table>
<thead>
<tr>
<th>n Body wt (kg)</th>
<th>Body wt (kg)</th>
<th>Heart wt/ Body wt (g/kg)</th>
<th>RV wt/ Body wt (g/kg)</th>
<th>LV wt/ Body wt (g/kg)</th>
<th>Papillary muscle cross-sectional area (mm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>17 2.82</td>
<td>±0.11</td>
<td>3.51</td>
<td>0.71</td>
<td>2.35</td>
</tr>
<tr>
<td></td>
<td>2.60±0.15</td>
<td>±0.02</td>
<td>1.40</td>
<td>0.74</td>
<td>2.30</td>
</tr>
<tr>
<td>Exercised</td>
<td>14 2.60</td>
<td>±0.14</td>
<td>3.40</td>
<td>0.74</td>
<td>2.30</td>
</tr>
<tr>
<td></td>
<td>2.60±0.15</td>
<td>±0.03</td>
<td>1.40</td>
<td>0.74</td>
<td>2.30</td>
</tr>
</tbody>
</table>

Results are given as mean ± SEM. RV wt = right ventricular weight; LV wt = left ventricular weight.
the exercising cats but the difference was not statistically significant.

Discussion

These results demonstrate that an increase in contractile function does not occur in the exercise-conditioned feline myocardium. However, several factors must be considered in the interpretation of these results. To assess contractile state, contractile element function and active state must be measured. Problems associated with expressing muscle function in terms of contractile element function recently have been reviewed. Nevertheless, none of the measured functions of the muscle from exercising cats was significantly different statistically from the controls. Furthermore, the comparable time to peak isometric force between groups suggest that duration of active state also was similar. It also must be considered that the average cross-sectional area of the muscles from control and exercised cats, although comparable, was larger than optimum and some degree of hypoxia may have been present. However, comparison of the data from four of the exercising cats and seven of the nonexercising cats with muscles equal to or less than 1.0 mm² (a size which does not present a significant barrier to oxygen diffusion) revealed similar results.

If the mechanical performance of the muscles were limited by our techniques and both groups were performing maximally, i.e., at a common upper limit, an increase in developed force and velocity of shortening of exercising muscles might not be apparent. The ability of both groups of muscles to respond to paired stimulation and norepinephrine
with a significant increment in force development precludes this possibility. Therefore, we believe the data support our conclusion that exercise training did not significantly alter the intrinsic contractile state of these muscles.

A number of factors may account for the difference between our conclusions in this study and those of previous investigations, most notably, differences in the intensity and duration of exercise. In two studies reporting enhanced cardiac performance after prolonged exercise, an exercise program was utilized which resulted in the development of myocardial hypertrophy.1, 2 Our exercise program was not of sufficient magnitude to produce cardiac hypertrophy but did result in a lesser heart rate during both submaximal and maximal workloads and a lesser increment in heart rate after atropine by the end of 6 weeks of training. A slower heart rate at rest and during comparable workloads following repetitive exercise is a generally accepted indicator of the development of a cardiovascular training effect. In addition, others have demonstrated that the development of a training effect is manifest by lesser increment in heart rate after atropine.3, 4 We could not obtain an accurate resting heart rate in our cats but our program was sufficient to produce a cardiovascular training effect, as indicated by the other criteria. However, others have concluded that even relatively mild degrees of exercise may produce an increase in contractile state.5 They based this conclusion on an observed increase in cardiac myosin ATPase activity with mild exercise and on a previous report equating an increase in activity of this enzyme with an increase in contractile state.6 Unfortunately, contractile function was not measured directly in the former study and it has not been demonstrated that changes in myosin ATPase activity are universally associated with changes in contractile state.

Each of the above studies reporting enhanced cardiac function after exercise training1, 2, 11 have used rats as the experimental animal, and species differences may account for the varying results. Exercise-induced enhancements of contractile state, however, has not been a universal finding in the rat.12

In those studies performed in vivo, differences in loading conditions, autonomic stimulation, or circulating cardioactive substances may affect the contractile state directly or the variables used to reflect changes in contractile state. Changes in one or more of these factors with exercise training cannot be excluded in the study of Winters et al.,3 employing systolic time intervals in humans, or that of Crews and Aldinger,1 who measured isometric tension developed in the intact hearts of rats. However, either species differences or other factors may be operative to account for the observation of Penpargkul and Scheuer,4 who reported enhanced cardiac performance in isolated working rat hearts from exercise-conditioned rats. In the latter study, cardiac output and cardiac work were greater and left ventricular function increased in rats conditioned by a swimming program. Interestingly, these investigators also observed that an increase in myocardial oxygen requirements in conditioned rats was met principally by an increase in coronary flow, whereas in nonconditioned rats coronary arteriovenous oxygen difference increased without a significant increase in flow. The authors concluded that the enhanced cardiac function associated with exercise probably was due to improved mechanisms of oxygen delivery. In this regard, several investigators have reported that exercise results in increased myocardial vascularity.17-19 Thus, the apparent opposing conclusions of our present study and the above investigations could be reconciled if the mechanisms responsible for enhanced contractile performance after prolonged exercise were operative only in vivo or were dependent on substrate supply by an intact coronary vascular bed. Even if correct, this would not detract from our conclusion that the intrinsic contractile state of the myocardium is unaffected by exercise sufficient to produce a cardiovascular training effect.

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