Kawasaki Med. J. Vol. 3: No. 2, 83-90, 1977

EFFECTS OF EPINEPHRINE ON THE MECHANICAL WORK DONE BY RABBIT CARDIAC MUSCLE UNDER INERTIA LOADING

Moto MATSUMURA and Kazunori OCHI

Department of Physiology, Kawasaki Medical School, Kurashiki, 701-01, Japan

Accepted for Publication on Dec. 9, 1976

Abstract

The mechanical work done by isolated rabbit papillary muscle was investigated under constant load but different degrees of inertia. When the muscle was stimulated at a beat rate of 6/min in the standard medium solution, the work done by muscle to impart the velocity to the lever (work for the velocity factor) was much smaller than the work done by muscle to lift the load by a certain distance (work for the length factor). For the muscle treated with 2×10^{-6} g/ml epinephrine, the total mechanical work increased with an increase in the moment of the inertia lever showing the maximum at the equivalent mass of about 150-300 g. The increase in the mechanical work was mainly due to the increase in the work for the velocity factor rather than in the work for the length factor, and the former attained to 22-68% of the total work under the optimum equivalent mass. The result suggests that the muscle liberates extra mechanical energy when the shortening is restricted by the inertia.

INTRODUCTION

The contractile properties of the isolated cardiac muscle have been compared with those of the skeletal muscle[1,2,3,4]. In these studies, however, the contraction was isometric or after-loaded isotonic and it was, as Brady[2] pointed out, different in some respects from the contraction of the heart as an organ. First, the tension during the after-loaded contraction of the isolated cardiac muscle remained constant but the pressure during the ejection phase of the heart *in situ* changed with time. Secondly, the intraventricular pressure fell below the arterial pressure during the latter half of the ejection phase[5], although the tension of the isolated heart muscle was equal to the load upon muscle during shortening[1,6]. And thirdly, the ventricular volume was minimum when the intraventricular pressure returned to the diastolic level, al-

though the muscle shortening in the after-loaded contraction reached a peak during the tension was maintained at the load level. These differences might come in part from the elastic property of the aortic wall and the inertia of the blood.

Recently, Paulus *et al.*[7] suggested that the inertia force should be considered to explain the mechanics of the heart as a pump. Therefore, it seems to be interesting to investigate the contraction of the isolated cardiac muscle under various degrees of inertia. The inertia lever is a convenient tool for this purpose because it provides the way by which the inertia force can be changed easily without a change in load upon muscle. The inertia lever method also makes it possible to divide the mechanical energy liberated by muscle into the potential energy that is expended in lifting a load and the kinetic energy that is expended in shortening with a certain velocity. The present study was conducted to find the effects of epinephrine on the work to impart the velocity to the inertia lever (work for the velocity factor) and the work to lift a load by a certain distance (work for the length factor) done by the rabbit papillary muscle during a twitch.

METHODS

The materials were right ventricular papillary muscles of the albino rabbit. Although the detailed description of the experimental procedures will appear elsewhere, the experimental arrangement is diagrammatically illustrated in Fig. 1. The parameters measured are pre-load (m_1), after-load (m_2), equivalent mass (M) of the inertia lever, the shortening (L), the shortening velocity (V) of the muscle, and its square (V^2). The mechanical work (W) done by muscle is described by the following equation,

$$W = m \cdot g \cdot h + \tfrac{1}{2} \cdot M \cdot V_0^2, \qquad (1)$$

where $m = m_1 + m_2$, g is the acceleration of gravity, h is the amount of muscle shortening and V_0 is the peak of the shortening velocity. The first term, $m \cdot g \cdot h$, indicates the work done by muscle to lift a load (the length factor) and the second term, $\frac{1}{2} \cdot M \cdot V_0^2$, indicates the work done to impart the velocity to the inertia lever (the velocity factor). The standard medium solution contains (mM): NaCl 130, KCl 4, $CaCl_2$ 5, $NaHCO_3$ 10, and glucose 5.6. Epinephrine is added to the standard medium solution at the concentration of 2×10^{-6} g/ml.

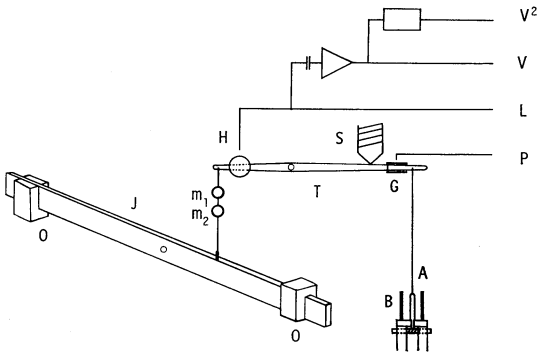

Fig. 1. Schematic diagram of the experimental arrangement. A, rabbit papillary muscle. B, Ag-AgCl electrodes for massive stimulation. S, stopper. T, isotonic lever. m_1, pre-load. m_2, after-load. O, balance weights to change the moment of the inertia lever, J. Tension (P) was recorded with strain gauge, G, length (L) with photo cell, H, and velocity (V) was obtained by differentiating the trace L.

RESULTS

1. Tension and length changes in the contraction under inertia loading.

When the muscle contracted with an after-load but no inertia, it developed the tension before starting to shorten. This tension was equal to the load and was maintained constantly during the shortening period (Fig. 2, A). On the contrary, if the muscle contracted under inertia loading, the larger tension than a load developed at the start of shortening period, as shown in Fig. 2, B. The tension above the resting load level corresponded to the inertia force that imparted the angular acceleration to the equivalent mass of the inertia lever. When the shortening velocity reached the peak, the movement of the inertia lever became faster than that of the isotonic lever and the connecting chain between the two levers was slackened. No inertia force was detected, but only the tension equal to the pre-load was maintained.

2. Work to impart the velocity to the inertia lever and work to lift the load.

Fig. 3, A, B, and C show the simultaneous records of tension, shortening, shortening velocity and its square during a twitch under different degrees of inertia when the muscle was stimulated at a rate of 6/min in the standard solution. The calculated mechanical work done by muscle from eqn. (1) is illustrated in Fig. 4. As shown in Fig. 4, the total work done by muscle in the standard solution was kept

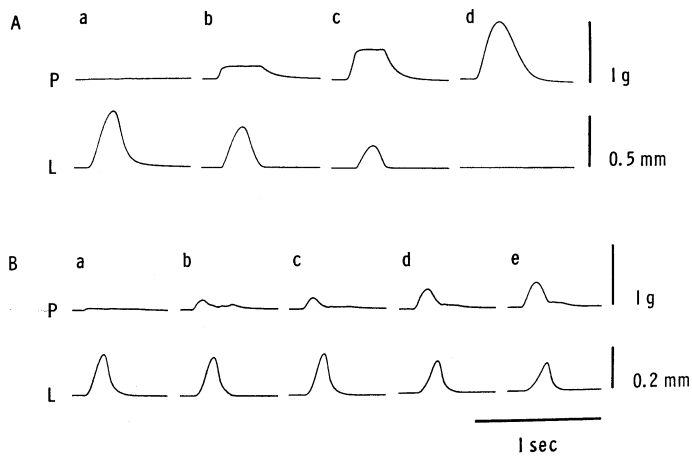

Fig. 2. Tension (trace P) and shortening (trace L) in after-loaded isotonic contraction (A), and contraction under inertia loading (B). In A, pre-load is 0.67 g and after load is 0 g in a, 0.20 g in b, 0.49 g in c and 1.0 g in d (isometric). Muscle length 7.0 mm and weight 10.0 mg. In B, pre-load is always 0.67 g and the equivalent mass of the inertia lever is 0 g in a, 11.5 g in b, 20.1 g in c, 73 g in d, and 143 g in e. Muscle length 6.2 mm and weight 9.0 mg. In both A and B, the beat rate is 6/min and the muscle temperature is 32°C.

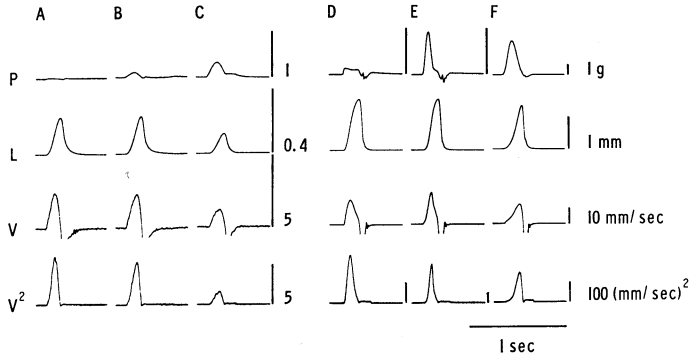

Fig. 3. Tension (trace P), muscle length (trace L), velocity (trace V), and the square of the velocity (trace V^2) in the contraction under inertia loading. Pannels A, B and C are from the papillary muscle immersed in the standard medium solution, and the equivalent mass is 0 g in A, 20.1 g in B, and 143 g in C. Calibrations are common to A, B and C. Pannels D, E and F are from the muscle treated with 2×10^{-6} g/ml epinephrine and the equivalent mass is 0 g in D, 20.1 g in E and 143 g in F. Note the different calibrations in traces P and V^2. Muscle length 6 mm and weight 6.4 mg. 32°C.

nearly constant up to the equivalent mass of 31 g and decreased slightly with a further increase in the equivalent mass. The work for the velocity factor ($\frac{1}{2}\cdot M\cdot V_0^2$) was only 0.4 erg, while the total work ($m\cdot g\cdot h+\frac{1}{2}\cdot M\cdot V_0^2$) amounted 16.1 erg under the equivalent mass of 11.5 g. Results on the mechanical work done by muscle immersed in the standard medium solution are illustrated in Table 1. The work for the velocity factor during the contraction of the control muscle at the beat rate of 6/min was less than 4% of the total work and was regarded to be negligible.

3. Mechanical work done by muscle treated with epinephrine.

Fig. 3, D, E, and F are the records obtained from a muscle treated with 2×10^{-6} g/ml epinephrine. At the rate of 6/min, addition of epinephrine augumented the shortening of muscle by about ten times under a load of 0.67 g and equivalent mass of up to 150 g. Because the time to the peak of shortening was more or less abbreviated by epinephrine, the shortening velocity increased by more than 10 times and the square

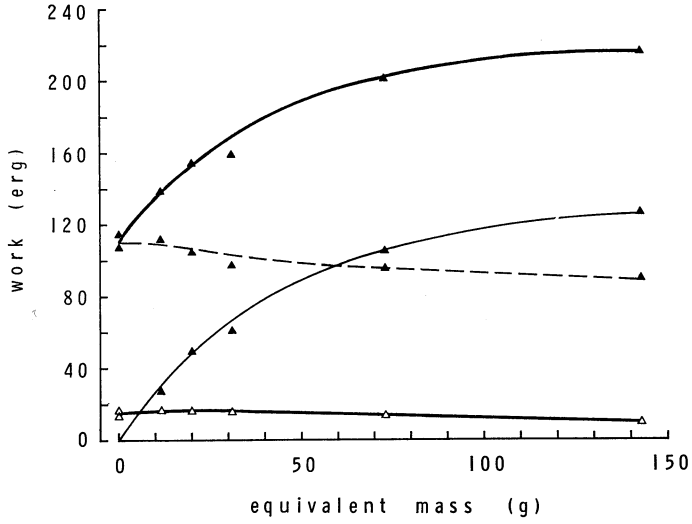

Fig. 4. The relationship between the equivalent mass and the mechanical work. Filled symbols show the work done by epinephrine-treated muscle. Thin continuous line indicates $\frac{1}{2}\cdot M\cdot V_0^2$, thin broken line $m\cdot g\cdot h$ in eqn. (1), and the thick continuous line indicates the sum of both. Open symbols show the work done by control muscle, and only the total mechanical work is indicated because the work for $\frac{1}{2}\cdot M\cdot V_0^2$ is small and the work for $m\cdot g\cdot h$ is close to the total work. Plots are obtained from the same muscle as that shown in Fig. 3.

TABLE 1

Work for the length factor ($m \cdot g \cdot h$) and the work for the velocity factor ($\frac{1}{2} \cdot M \cdot V^2_0$) done by muscle in either standard or 2×10^{-6} g/ml epinephrine solution under the optimum equivalent mass, where the total work shows the maximum. For each muscle preparation, the upper rows indicate the values from the epinephrine-treated muscles and the lower rows with parentheses from the controls. The pre-load upon muscle was 0.67 g. 32°C.

i	ii		iii	iv	v	vi	vii	viii
date	muscle length (mm)	muscle weight (mg)	equivalent mass (g)	work for $m \cdot g \cdot h$ (erg)	work for $\frac{1}{2} \cdot M \cdot V_0^2$ (erg)	ratio of (v) to (iv+v) (%)	$[Ca]_0$ (mM)	beat rate (/min)
Jul. 6	7	10	143 (6.1)	55.2 (13.5)	41.3 (0.1)	43 (0.7)	5	6
Sept. 17	4.5	2	292 (80.5)	8.7 (2.8)	2.5 (0.1)	22 (3)	5	6
Oct. 21	6	6.4	143 (20.1)	88.6 (15.8)	126.5 (0.6)	59 (3.7)	5	6
Oct. 19	6	3.9	97 (97)	51.0 (35 7)	16.9 (8.8)	25 (20)	5	60
Oct. 21	6	6.4	575 (143)	72.2 (34.8)	161.7 (15.1)	68 (30)	10	6

of the velocity amounted about 100 times as much as the control. Therefore, the second term in eqn. (1) was no longer negligible. It should be noted that the peak shortening velocity under the equivalent mass of 20.1 g was larger than that under that of 2.0 g (Fig. 3, D, E). The force-velocity relation has been known to be time-dependent[6,7]. The equivalent mass-velocity relation was also time-dependent and rather complicated, and the relationship between them was not studied further in the present work. Fig. 4 illustrates the work for the velocity factor and the work for the length factor as well as the total mechanical work done by muscle treated with 2×10^{-6} g/ml epinephrine. The work for the length factor slightly decreased with the increase in the equivalent mass because the inertia lever acted as a resistance against the muscle shortening. On the other hand, the work for the velocity factor increased and, as a result, the total mechanical work increased with the increase in the equivalent mass up to 150-300 g. Table 1 illustrates the mechanical work done by muscle treated with epinephrine. In the Table, the work for the length factor and the work for the velocity

factor are calculated under the optimum equivalent mass where the muscle performs the maximum work. It is concluded that the work for the velocity factor is no longer negligible but take 22-68% of the total work.

DISCUSSION

It was known[7] that catecholamine increased the shortening velocity in isotonic contraction under zero load, V_{max}, which indicated the maximum turnover rate of the attachment and detachment of cross-bridges between actin- and myosin-filaments[9,10]. Catecholamine was known also to intensify and abbreviate the active state of muscle[11]. In the contraction under inertia loading, too, epinephrine abbreviated the time to the peak and increased the shortening velocity as well as the amount of shortening.

Sonnenblick[1] reported that the work done by papillary muscle in after-loaded twitch had the maximum under the load of about a half of isometric tension and that the optimum load where the maximum work was performed shifted to the heavier one by the treatment with epinephrine. Similarly, in the contraction under inertia loading, the optimum equivalent mass was shifted towards the heavier one by epinephrine.

The mechanical work done by cardiac muscle was described with the term of work done to lift a load and to accelerate the lever system. When the muscle was immersed in the standard solution and was stimulated at the rate of 6/min, the work for the velocity factor was much smaller than that for the length factor over the range of the equivalent mass. On the other hand, if the muscle was treated with epinephrine, the velocity factor held around 40% of the total work under the optimum value of the equivalent mass. In regards to the contraction of the heart as an organ[12], the mechanical work in one cardiac cycle was calculated from the sum of the energy to eject the output volume against the blood pressure and the energy to impart the certain velocity to blood at the root of the aorta, but the latter was much smaller than the former. During the muscle exercise, however, the total mechanical work increased and the latter accounted for nearly one quarter of the total work. It may be said that the kinetic energy plays an important role when the contraction is quickened by the treatment with epinephrine or during the muscle exercise.

Acknowledgment

We thank Dr. Kazuro Takada for helpful discussion. Thanks are also due to Miss Y. Soda for preparation of the manuscript. Supported by the project research grant-in-aid from Kawasaki Medical School.

REFERENCES

1) Sonnenblick, E. H. Implication of muscle mechanics in the heart. Fed. Proc. 21: 975-990, 1962
2) Brady, A. Active state in cardiac muscle. Physiol. Review 48: 570-600, 1968
3) Jewell, B. R. and Blinks, J. R. Drugs and the mechanical properties of heart muscle. Ann. Rev. Pharmacol. 8: 113-130, 1968
4) Edman, K. A. P. and Nilson, E. The mechanical parameters of myocardial contraction at a constant length of the contractile element. Acta. Physiol. Scand. 72: 205-219, 1968
5) Rushmer, R. F. Structure and function of the cardiovascular system. W. B. Saunders Company, Philadelphia, pp 56-58, 1972
6) Edman, K. A. P. and Nilson, E. Relationship between force and velocity of shortening in rabbit papillary muscle. Acta Physiol. Scand. 85: 488-500, 1972
7) Paulus, W. J., Claes. V. A. and Brutsaert, D. L. Physiological loading of isolated mammalian muscle. Circul. Res. 39: 42-53, 1976
8) Sonnenblick, E. H. Force-velocity relations in mammalian heart muscle. Amer. J. Physiol. 202: 931-939, 1962
9) Pollack, G. H. Maximum velocity as an index of contractility in cardiac muscle. Circul. Res. 26: 111-127, 1970
10) Katz, A. M. The force velocity curve. A biochemist's view point. Cardiology 57: 2-10, 1972
11) Sonnenblick, E. H. Active state in heart muscle. Its delayed onset and modification by inotropic agents. J. gen. Physiol. 50: 661-676, 1967
12) Davson, H. and Eggleton, M. G. Principles of human physiology. 14th ed. J. & A. Churchill, London, pp 161-162, 1968