Experimental Studies of Coronary Insufficiency

II. Changes in Surface Electrogram, Myocardial Contractility, and Contractile State of the Left Ventricle Following Partial Coronary Occlusion*

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Surface electrogram, myocardial tension, left ventricular pressure, and dp/dt of the pressure were simultaneously recorded in anesthetized open-chest dogs. A large branch of the left anterior descending coronary artery was partially occluded. ST-T changes in surface electrogram recorded in an ischemic area were divided into two groups in the consideration of the progressing process. Those changes were classified into four stages by pattern. Changes in myocardial tension measured with a strain gauge arch was compared with those in surface electrogram recorded at a site close to the arch. As a result, there was a close relationship between changes in surface electrogram and the decreases in myocardial tension. The contractile state of the left ventricle estimated by $\text{Max } dp/dt$, $\Delta t \text{ } dp/dt$ and the index $dp/dt/\text{IIT}$ was enhanced transiently during mild ischemia, although it was depressed during more severe ischemia. These results suggest a compensatory increase in contractility of nonischemic muscle.

IN THE former report it has been shown that the developed tension obtained with a strain gauge arch sutured, along the superficial muscle bundle, to the ventricular wall supplied by the anterior descending coronary artery decreased progressively after its occlusion and that the changes in the developed tension might reflect the course of the decrease in myocardial contractility in the ischemic area.

Alterations of the electrocardiogram characterized by displacement of the ST segment and modification in the shape of the T wave were first described to myocardial infarction by PARDEE.¹ Subsequently, experimental works²⁻⁴ have shown that similar electrocardiographic changes can be reproduced in the dog by complete occlusion of a coronary artery. Relations between electrocardiographic changes and muscle contrac-

tion⁵ or hemodynamic events⁶⁻⁸ have been already investigated. However relationships between changes of surface electrograms and those of myocardial contractility on the local ventricular surface has not been investigated in situ. Meanwhile SARNOFF and coworkers^{9,10} have estimated the ventricular function by the shift of ventricular function curve which is obtained by plotting the stroke work against the left ventricular end diastolic pressure or the mean left atrial pressure. Recently SONNENBLICK and coworkers^{11,12} attempt to assess the contractile state of the ventricle in intact dog and men by the indices independent of changing end diastolic pressure and afterload. The first purpose of the present paper is to investigate the changes in surface electrogram on an ischemic area of the ventricle following partial coronary occlusion,

(Received for Publication; May 2, 1969)

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* The outline of this study was reported at the 24th Tokai Regional Meeting of the Japanese Circulation Society in 1967.

and to compare them with changes in myocardial contractility simultaneously observed in the same area. The second purpose is to investigate how the decrease of contractility in the ischemic myocardium is reflected in the contractile state of the left ventricle.

METHODS

Experimental Preparations

Six adult mongrel dogs weighing between 10 and 15 kg were anesthetized and thoracotomies were performed as described in the former report. A small segment of the left anterior descending coronary artery (LAD) was dissected at or just below the tip of the left atrial appendage and it was partially occluded. Coagulation was prevented by an initial dose of 200 units/kg of heparin followed 100 units/kg doses hourly. The experimental preparation was shown schematically in Fig.1. One or two strain gauge arches (Model L-6)¹³ were sutured at certain areas on the ventricular surface supplied by LAD, so as to include the area of severest ischemia in case with one arch sutured or to include the area of severest ischemia as well as the area of lesser ischemia in case with two arches sutured. Care was taken to align the axes of the arches with superficial muscle bundle. The arches were placed without stretching the resting length of muscle bundle. Unipolar surface electrogram was taken with tiny recording electrode from the site on the left ventricle close to the strain gauge arch. An electrode, however, was obliged to be placed 3 to 5 mm away from the arch because surface electrogram showed abnormal ST segment elevation in the control period when it was placed just below the arch. Left ven-

tricular pressure was determined with the intracardiac micromanometer¹⁴ inserted into the left ventricular cavity through the carotid artery. The first derivative of the pressure with regard to time (dp/dt) was measured by means of a R-C differentiating circuit with a time constant of 0.5 msec. Recordings were taken by photographic or direct writing recorders. A paper speed was 50 mm or 100 mm per second.

Calculations:

Developed tension (DT), which was used as an index of contractility of local myocardium was calculated by subtracting the resting tension from the peak systolic tension. R-R interval, and amplitudes of ST deviation and T wave were measured in surface electrogram. For the estimation of the contractile state of the left ventricle, maximal rate of left ventricular pressure rise (Max dp/dt), time from the top of R wave in surface electrogram to Max dp/dt (Δt dp/dt), and Isometric Time-Tension Index ($dp/dt/IIT$)^{11,15} were calculated. DT, Max dp/dt and $dp/dt/IIT$ were expressed as a percentage change from control which was taken as 100 per cent. Each value was averaged from 10 consecutive cardiac cycles. Statistical evaluation was carried out using Student's t-test.

RESULTS

1. Changes in surface electrogram and their classification.

Twelve series of surface electrograms were obtained during ischemia in 6 experiments. Changes in surface electrogram following partial coronary occlusion varied with individual animals and with the sites on the ventricular surface where they

Fig.1. Diagram of experimental preparation and typical tracings. The left anterior descending coronary artery was partially occluded. Myocardial tension was measured with a strain gauge arch sutured along the superficial muscle bundle. Left ventricular pressure and its first derivative were determined with an intracardiac micromanometer.

Fig. 2. Surface electrograms (B, C, D) during ischemia and (E) during recovery of two dogs. A: controls. B: inversion of T wave was seen, which was classified as stage 2. C: ST depression or slight ST elevation was seen, which was classified as stage 3. D: ST elevation and upward peaking of T wave was observed, which was classified as stage 4.

were recorded even in the same animal, but could be divided into two large groups, I and II. Surface electrograms classified to group I were recorded from the center of the ischemic area in all the 6 experiments, and in those recorded from the relatively peripheral part in 3 experiments. In this group, the terminal portion of T wave was inverted immediately after occlusion. Thereafter the inverted T deflection diminished in amplitude as ST segment became elevated and rounded with the convexity upwards. Subsequently marked elevation of the ST junction and upward peaking of T wave developed (Fig. 2, lower row). In two experiments, surface electrograms simultaneously recorded over the central and the peripheral parts of the ischemic areas showed such changes as belonging to this group. In them, changes of tracings from the central part preceded those from the peripheral part chronologically (Fig. 4). Surface electrograms belonging to the group II were recorded from the peripheral part of the ischemic area in 3 experiments. In this group also, the terminal portion of T wave was inverted at first. Then ST segment was depressed as the inverted portion of the T wave became deeper. When the occlusion was continued further, elevation of the ST junction appeared (Fig. 2, upper row). In an experiment, surface electrograms were recorded simultaneously at two points close to a strain gauge arch in the ischemic area. Changes in surface electrograms at these two points were found to belong to the different groups each other. The slight ST segment elevation from the one point coincided with the ST depression from the other point chronologically (Fig. 6). Accordingly, the ST-T changes of the two groups may be classified

Fig. 3. Schematic representation of ST-T changes. These are classified into four stages, i. e., stage 1 (thin solid line), stage 2 (dotted line), stage 3 (interrupted line) and stage 4 (thick solid line).

into several stages as follows (Fig. 3):

Stage 1. No significant ST-T changes are noted, as compared with the control surface electrogram.

Stage 2. No remarkable changes except inversion of T wave are observed.

Stage 3. ST depression, or slight ST elevation without being accompanied by upward peaking of T wave is seen.

Stage 4. Marked ST elevation accompanied by upward peaking of T wave appears.

2. Relation of changes between surface electrogram and myocardial tension.

Fig. 4 shows surface electrograms and myocardial tension curves simultaneously recorded from the periphery (upper) and the center (lower) of the ischemic area in an experiment. In the center, as T wave was inverted (stage 2) and then ST segment exhibited a slight elevation (stage 3) in the surface electrograms, the myocardial tension curve decreased gradually in amplitude. In stage

Fig.4. Surface electrograms and myocardial tension tracings, during ischemia and recovery, from the periphery (upper) and the center (lower) of the ischemic area in one dog. A: controls. B: 20 seconds after partial coronary occlusion: Inversion of T wave and decrease in the amplitude of tension curve in the center of the ischemic area. C and D: 25 seconds and 38 seconds after occlusion respectively. E: 48 seconds after occlusion; Inversion of tension tracing in systole in the center of the ischemic area. F: 45 seconds after releasing the tie.

Fig.5. Simultaneous changes in ST deviation, amplitude of T wave and developed tension (DT) (A) from the periphery of the ischemic area and (B) from the center of it during ischemia and recovery. Data on this graph are from the same experiment as Fig.4. Note that the stages of ST-T changes from the center of the ischemic area precede those from the periphery.

Fig.6. Surface electrograms taken from two points close to a strain gauge arch and myocardial tension tracings during ischemia and recovery. A: controls. B: 7 seconds after partial coronary occlusion. C and D: 35 seconds and 112 seconds after occlusion respectively: Slight ST elevations in upper records and ST depressions in lower records. E: about 50 seconds after releasing the tie.

Fig.7. Simultaneous changes in ST deviation, amplitude of T wave and developed tension (DT) from the same experiment as Fig.6. Upper and lower graphs show ST-T changes of surface electrograms recorded from the two points close to the strain gauge arch in the ischemic area.

4, when ST elevation as well as upward peaking of T wave were observed, a negative portion appeared in the myocardial tension curve (Fig. 4D). When the occlusion was continued further, the curve turned to be completely inverted in systole (Fig. 4E). In the periphery of the ischemic

area, all the changes in records of epicardial lead and myocardial tension were a little later to appear than in the center. Changes in ST-T and developed tension in this experiment are graphically depicted in Fig.5. When the surface electrograms were compared between the two sites,

Fig. 8. Relationship between changes in developed tension and stages of ST-T changes in 6 dogs during ischemia. 5(A) and 5(B) are that from the center of the ischemic area and that from the peripheral part of it in the same dog respectively.

stages 2, 3, and 4 appeared 6, 8, and 10 seconds earlier, respectively, in the center than in the periphery. In the center, developed tension ranged from 95 to 66, 66 to 42, and 42 to 0% in stages 2, 3, and 4 of surface electrograms, respectively. In the periphery, it ranged 98 to 69, 69 to 42, and less than 42% in stages 2, 3, and 4, respectively. In short, the changes in ST-T of surface electrogram and those in developed tension were essentially same, area by area.

Fig. 6 shows the records during another experiment. In this case, surface electrograms were taken at two points close to a strain gauge arch. At the upper row of the figure, slight elevation of ST segment appeared in succession to changes in T wave. At the lower row, depression of ST

segment appeared in the same time (Fig. 6C and D). The tension curve was reduced in height when the T wave turned to be inverted. Then it showed, further, a tendency to decrease a little in height. These changes are illustrated graphically in Fig. 7. Developed tension ranged 96 to 69 and 90 to 60% in stages 2 and 3, respectively. Changes in developed tension corresponding to each stage of surface electrograms in 6 animals are shown graphically in Fig. 8. Developed tension was reduced an average of 3.7% before the appearance of ST-T changes. The mean value of developed tension ranged 96.3 to 66.4, 66.4 to 38.6, and less than 38.6% in stages 2, 3 and 4, respectively. A considerably close relationship was recognized between the changes in surface electrogram and the decreases in developed tension during ischemia following partial coronary occlusion.

3. Changes in contractile state of the left ventricle.

Data on contractile state of the left ventricle are presented in table 1 and graphically illustrated in Fig. 10. These data were obtained at each stage of surface electrograms recorded in the center of the ischemic area. Fig. 9 shows the simultaneous records of surface lead, left ventricular pressure and dp/dt of the pressure. Heart rate increased a little in 3 of 6 experiments as ischemia increased in severity. Its fluctuation, however, did not surpass 3% of the control value. In the other 3 cases, heart rate remained constant or decreased a little. Peak left ventricular pressure increased significantly in 3 cases during ischemia following partial coronary occlusion. It remained unchanged in the other 3 cases, and decreased in no cases. In the experiment shown in the figure, it increased a little in stage 2 and 3 (Fig. 9B and C). Max dp/dt averaged 105.6% of the control value in

Fig. 9. Surface electrogram, left ventricular pressure curve and dp/dt recorded simultaneously during ischemia and recovery. A: controls. B and C: 15 seconds and 25 seconds after partial coronary occlusion respectively. D: 45 seconds after occlusion; Marked decrease in upward deflection of dp/dt. E: about 50 seconds after releasing the tie.

Fig.10. Max dp/dt, Δt dp/dt and $\frac{dp/dt}{IIT}$ during each stage of ST-T changes recorded in the central part of the ischemic area. The average of the group is shown with each horizontal line. Prolongations of Δt dp/dt, and marked decreases in Max dp/dt and $\frac{dp/dt}{IIT}$ were seen in stage 4.

stage 2, increasing significantly in two cases compared with control. In stage 3, it averaged 96.3%, increasing in two cases and decreasing in three. In stage 4, it averaged 70.4%, exhibiting significant decreases in all cases.

The time to maximum dp/dt (Δt dp/dt) was reduced an average of 5.7 msec from a mean control value of 49.3 msec in stage 2. In 3 cases, its reduction was significant, as compared with control. Two cases of these 3 accompanied significant increases in Max dp/dt at the same time. In the remaining case, however, Max dp/dt did not increase, though Δt dp/dt declined clearly. In stage 3, Δt dp/dt averaged 46.2 msec, being reduced in 3 cases and increasing in one case compared with control. Also in this stage, however, there was a case in which a reduction of Δt dp/dt was not accompanied by an increase in Max dp/dt. In stage 4, Δt dp/dt averaged 50.6 msec, showing a significant increase in all cases. In the experiment shown in the figure, a reduction of Δt dp/dt accompanied by an increase in Max dp/dt was observed in stage 2 (Fig.9B). In stage

3, however, Max dp/dt hardly changed although Δt dp/dt decreased (Fig.9C).

Isometric Time-Tension Index dp/dt/IIT averaged 105.3% of the control value in stage 2, increasing significantly in 3 cases compared with control. In stage 3, it averaged 101.3%, increasing in 3 cases and decreasing in 3. In stage 4, it averaged 64.8%, exhibiting significant decreases in all cases. In stage 3, Max dp/dt and dp/dt/IIT failed to show a definite tendency; they were in a transitional period from stage 2, when they often increased temporarily, to stage 4, when they decreased clearly.

DISCUSSION

In the present study, changes in surface electrograms following partial coronary occlusion could be divided into two large groups, I and II. In group I, the following sequence of electrocardiographic events was observed. Initially T wave became inverted. Then the inverted T deflections diminished in amplitude as ST segment elevated and rounded with the convexity upwards. Subsequently marked displacement of the ST junction with upward peaking of T wave appeared. These observations are consonant with those made by BAILEY et al.³ who produced myocardial ischemia by complete coronary occlusion. In the group II, which was noticed in surface electrograms recorded over the relatively peripheral part of the ischemic area, T wave initially became inverted and then ST segment was depressed. Some reports¹⁶⁻¹⁸ have already been made on the experimental depression of ST segment in surface electrograms. EKMEKCI et al.¹⁸ observed a slight depression of ST segment in most tracings from the periphery of the ischemic area about 15 to 20 minutes after the ligation of the left anterior descending coronary artery. Then they concluded that ST segment elevation was associated with more severe ischemia than ST segment depression. In the present study, ST segment depression was recognized also in the periphery of the ischemic area. It appeared, however, in a relatively early period. Consequently, it cannot be determined whether the ST segment depression recognized in the present study was of the same character as that observed by EKMEKCI et al. or not. In an experiment, in which surface electrograms were recorded from the two points close to a strain gauge arch in the ischemic area, the tracing from the one point presented slight ST segment elevation, and that from the other point showed ST segment depression at the same

TABLE I CHANGES IN PARAMETERS USED FOR THE ESTIMATION OF CONTRACTILE STATE OF THE LEFT VENTRICLE DURING ISCHEMIA

Dog No.		Heart Rate (beat/min)	Peak LVP (mmHg)	Max dp/dt (%)	t dp/dt (msec)	$\frac{dp/dt}{HT}$ (%)
1	Control	158	111 $\pm$ 1.3	100 $\pm$ 2.1	44 $\pm$ 1.0	100 $\pm$ 5.3
	Stage 2	159	112 $\pm$ 1.9	100 $\pm$ 1.9	40 $\pm$ 0.9**	107 $\pm$ 5.6*
	Stage 3	159	113 $\pm$ 1.2	103 $\pm$ 1.7*	38 $\pm$ 1.3**	112 $\pm$ 4.9**
	Stage 4	159	108 $\pm$ 1.4	57 $\pm$ 1.9**	53 $\pm$ 0.8**	50 $\pm$ 2.2**
2	Control	185	111 $\pm$ 2.2	100 $\pm$ 3.6	50 $\pm$ 1.2	100 $\pm$ 4.9
	Stage 2	188	111 $\pm$ 1.4	103 $\pm$ 2.2	50 $\pm$ 1.0	102 $\pm$ 5.5
	Stage 3	188	113 $\pm$ 1.8	85 $\pm$ 3.0**	49 $\pm$ 1.0	86 $\pm$ 5.6**
	Stage 4	189	109 $\pm$ 1.6	65 $\pm$ 2.9**	56 $\pm$ 1.2**	61 $\pm$ 3.8**
3	Control	173	136 $\pm$ 1.1	100 $\pm$ 4.5	65 $\pm$ 3.1	100 $\pm$ 10.6
	Stage 3	170	143 $\pm$ 2.2**	94 $\pm$ 3.5**	69 $\pm$ 2.6*	89 $\pm$ 7.1
4	Control	205	101 $\pm$ 1.2	100 $\pm$ 4.1	47 $\pm$ 1.2	100 $\pm$ 6.0
	Stage 2	206	112 $\pm$ 1.7**	122 $\pm$ 3.3**	41 $\pm$ 0.9**	111 $\pm$ 5.8**
	Stage 3	208	113 $\pm$ 1.3**	117 $\pm$ 2.8**	39 $\pm$ 0.8**	110 $\pm$ 4.4**
	Stage 4	208	108 $\pm$ 1.7**	91 $\pm$ 3.6**	49 $\pm$ 0.4**	63 $\pm$ 3.7**
5	Control	221	123 $\pm$ 1.7	100 $\pm$ 3.6	50 $\pm$ 0.9	100 $\pm$ 4.4
	Stage 2	222	129 $\pm$ 1.8**	104 $\pm$ 1.9**	48 $\pm$ 1.6**	106 $\pm$ 6.2*
	Stage 3	224	129 $\pm$ 1.3**	100 $\pm$ 2.5	43 $\pm$ 0.9**	115 $\pm$ 4.5**
	Stage 4	226	125 $\pm$ 1.4	78 $\pm$ 2.7**	52 $\pm$ 1.2**	70 $\pm$ 3.1**
6	Control	180	93 $\pm$ 2.0	100 $\pm$ 3.5	40 $\pm$ 0.4	100 $\pm$ 2.1
	Stage 2	178	93 $\pm$ 1.7	99 $\pm$ 3.9	39 $\pm$ 1.0	102 $\pm$ 5.7
	Stage 3	178	92 $\pm$ 1.6	79 $\pm$ 1.9**	39 $\pm$ 1.2	96 $\pm$ 5.3*
	Stage 4	178	91 $\pm$ 2.1	61 $\pm$ 2.5**	43 $\pm$ 1.2**	80 $\pm$ 7.0**

Note: Values are mean $\pm$ S.D.

** Highly significant difference compared with control value ($p < 0.01$)

* Significant difference compared with control value ($p < 0.05$)

time. From these results, the degrees of myocardial ischemia demonstrated in surface electrograms were classified into four stages. Then, changes in surface electrogram were compared with those in developed tension, which was used as an index of contractility of local myocardium.

By using a small-sized semiconductor strain gauge arch,¹³ it was possible to compare changes between surface electrogram and developed tension simultaneously at two sites, i.e., in the center and the periphery of the ischemic area. As a result, it was of interest to note that changes in surface electrogram and the decreases in developed tension proceeded at almost the same rate in each area, although the severity of ischemia caused by occlusion was not the same in every experiment and even in every area tested. WEGRIA et al.¹⁹ studied correlation between the reduction of the left anterior descending coronary blood flow and the appearance of changes in surface

electrogram in anesthetized dogs. They observed generally "slight" changes in both the ST segment and T wave with a reduction of blood flow of 35 to 70%, and always "marked" changes with a reduction of 70 to 100%. NAKANO²⁰ noted that the stepwise decreases in the left anterior descending coronary blood flow reduced stepwise myocardial contractile force of the ischemic area of the ventricle, as determined by a strain gauge arch in anesthetized dogs. In short, these investigators^{19,20} demonstrated that a decrease in quantity of coronary blood flow enhanced both the degree of changes in surface electrogram and the degree of reduction in myocardial contractility. The results of the present study may be essentially the same as those made by these investigators. The present study, however, was unique in that surface electrogram and myocardial tension curve were taken simultaneously in a localized ischemic area of the ventricle to com-

pare with each other.

Displacement of the ST segment is generally attributed to incomplete polarization or depolarization of injured myocardial cells,²¹⁻²³ occurring in regions of ischemia. Formerly elevation and depression of the ST segment were regarded as reciprocal effects of the same injury current. PRINZMETAL, TOYOSHIMA and coworkers,²⁴ however, observed such a type of the ST segment depression as inexplicable by the reciprocal effects, shown at mildly injured myocardium such as the margin of an area of infarction. They called it a primary type of ST segment depression. MIZUNO²⁵ noticed in coronary insufficiency that a qualitatively severe myocardial ischemia caused ST segment elevation, and that mild ischemia induced sometimes a primary type of ST segment depression without ST segment elevation elsewhere. He also suggested that both changes might be brought about by the difference in mainly potassium ion concentration passing through the myocardial cell membrane associated with coronary insufficiency. According to him, during severe ischemia ST segment elevation may be caused by increase in intracellular potassium efflux, whereas during mild ischemia ST segment depression may be induced by increase in extracellular potassium influx as a result of anaerobic glycolysis. It has been shown that maintenance of normal ion fluxes, upon which the transmembrane potential depends, requires an adequate supply of high-energy phosphate compounds.^{26,27} It has also been noted that myocardial hypoxia is associated with rapid reductions of high-energy phosphate compounds.²⁸⁻³⁰ In ischemia, the rapid reduction of adenosine triphosphate (ATP) and creatine phosphate (CP) would be reflected in diminished transmembrane potential and in the base line shift of surface electrogram. It has been known that such high-energy phosphate compounds as ATP and CP are the immediate energy sources for muscle contraction.^{31,32} Therefore, the rapid reduction in ATP and CP in the myocardium caused by ischemia would be reflected in a decline in myocardial contractility. In this manner, the reduction in high-energy phosphate compounds induced by ischemia would be reflected in the base line shift of epicardial lead electrically on one hand, and would be reflected in a decrease in myocardial contractility mechanically on the other. Accordingly, a close relationship may have been demonstrated between the electrical and the mechanical events.

In the present studies, the contractile state of

the left ventricle was evaluated by using the indices such as Max dp/dt, Δt dp/dt and Isometric Time-Tension Index dp/dt/IIT. WALLACE et al.³³ have shown that changes in Max dp/dt reflect those in the contractile state of the ventricle but that this index is a complex function, subject not only to changes in contractility, but also to ventricular end diastolic pressure, aortic diastolic pressure and the manner of ventricular activation. HISADA et al.³⁴ also noted that Max dp/dt increased as ventricular end-diastolic pressure or ventricular systolic pressure increased. On the other hand, it has recently been shown that changes in Max dp/dt are associated with changes in myocardial oxygen consumption.³⁵ MASTON et al.¹² have demonstrated that the time to maximum dp/dt (Δt dp/dt) is inversely related to the contractile state of the ventricle regardless of its preload and afterload and that an elevation of Max dp/dt in the face of a decline in Δt dp/dt always reflects an augmentation of the contractile state of the ventricle. The index dp/dt/IIT has been shown to be a reliable index of contractile state of the ventricle which is independent of changing end diastolic pressure, afterload, and stroke work.^{11,15} This index has also been considered to enable distinction between the Frank-Starling mechanism and true inotropic shifts in ventricular function.

It is anticipated that a decrease in myocardial contractility of the ischemic area of the ventricle following partial coronary occlusion may naturally be reflected as a decline of the contractile state of the ventricle. CASE et al.³⁶ studied the quantitative relationship between coronary blood flow and the ventricular function, and demonstrated that left ventricular function was quantitatively related to left main coronary artery blood flow. In a period when changes in surface electrogram recorded in the center of the ischemic area following partial coronary occlusion progressed to stage 4, developed tension decreased to about 40% or less and myocardial tension curve began to be inverted. In this period, Max dp/dt and dp/dt/IIT decreased to about 70% and 65% of the control value respectively, and Δt dp/dt increased significantly in all cases.

These results indicate that the reduction in myocardial contractility of the ischemic area of the ventricle induced a decline in the contractile state of the left ventricle, and agree with those reported by CASE et al. However, in a period when changes in surface electrogram were so mild as to be shown in stage 2, some cases showed in-

creases in Max dp/dt and $dp/dt/IIT$ accompanied by decreases in Δt dp/dt , although developed tension in the ischemic area was reduced in all cases. In that period, there were no cases in which Max dp/dt or $dp/dt/IIT$ decreased. These parameters showed no definite tendency in stage 3, which presented a transitional aspect between stages 2 and 4. Such a transient increase in the contractile state of the left ventricle as shown in stage 2 has been already noted in some investigators. RUSHMER et al.³⁷ studied the effects of acute coronary occlusion on ventricular performance in unanesthetized dogs, and they noticed that such parameters as ventricular pressure, Max dp/dt , stroke volume, stroke work and effective power except duration of systole displayed a very large transient increase immediately after coronary occlusion. Similarly, STONE et al.³⁸ observed that small amounts of injected microspheres into the coronary artery stimulated cardiac pumping ability, which was demonstrated as an increased cardiac output and left ventricular minute work. As a reason for such a transient increase in the contractile state of the ventricle, it can be presumed that the myocardial contractility in the non-ischemic area may have increased by some neurohumoral reflex. RICHARDSON et al.³⁹ measured a sixfold increase over control levels in circulating norepinephrine concentration after coronary occlusion. It is assumed that such norepinephrine may have enhanced the myocardial contractility of the non-ischemic area and even the contractile state of the ventricle as the result. In fact, a compensatory increase in the contractility of non-ischemic muscle has been suggested from enzymatic changes³⁰ and from an increase in oxygen consumption of the non-ischemic muscle.⁴⁰

In conclusion, acute partial coronary occlusion caused individual muscle fibers, which constitute the left ventricle, to be in different contractile states. As a result, severely ischemic area of the ventricle bulged during systole. On the other hand, the contractile state of the left ventricle during ischemia seems to be determined by the contractility of the individual muscle fibers, and by the abnormality in the dimensional changes of the left ventricle.

SUMMARY

Changes in surface electrogram and myocardial contractility in an ischemic area, and those in contractile state of the left ventricle were studied during experimental coronary insufficiency in-

duced by partial occlusion of the left anterior descending coronary artery.

1. Changes in surface electrogram were divided into two groups. Those of the two groups could be classified into four stages, from 1 to 4. In stage 1, no significant changes were noted as compared with control; in stage 2, T wave became inverted; in stage 3, ST segment was depressed or slightly elevated; and in stage 4, ST segment was elevated and T wave peaked upwards.

2. Changes in myocardial tension measured with a strain gauge arch was compared with those in surface electrogram recorded at a site close to the arch. In stages 1, 2, 3 and 4, developed tension was 100 to 96, 96 to 66, 66 to 39, and less than 39%, respectively. There was a close relationship between changes in surface electrogram and decreases in developed tension. It was presumed that a decrease in high-energy phosphate compounds caused by ischemia might play an important role in bringing about such close relationship between the electrical and the mechanical events.

3. The contractile state of the left ventricle estimated by Max dp/dt , Δt dp/dt and the index $dp/dt/IIT$ was clearly depressed when surface electrogram, recorded in the center of the ischemic area, showed stage 4. In stage 2, it was enhanced in some cases, although developed tension in the ischemic area was distinctly reduced. No definite tendency was shown in stage 3. These results suggest a compensatory increase in contractility of non-ischemic muscle.

Acknowledgement

The author is most grateful to Emeritus Prof. Susumu Hibino and Prof. Kazuo Yamada, for their valuable guidance. The author also expresses his sincere gratitude to Dr. Yasushi Mizuno and Dr. Sumio Hisada, for their precious advices and suggestions. Thanks are also extended to Dr. H. Takada and Dr. A. Kaito, for their kind advices and helps.

REFERENCES

1. PARDEE, H. E. B.: An electrocardiographic sign of coronary artery obstruction. *Arch. Intern. Med.* **26**: 244, 1920.
2. WOOD, F. C., WOLFERTH, C. C., & LIVEZEY, M. M.: Experimental coronary occlusion: Inadequacy of the three conventional leads for recording characteristic action current changes in certain sections of the myocardium; an electrocardiographic study. *Arch. Int. Med.* **51**: 771, 1933.
3. BAYLEY, R. H., LADUE, J. S., & YORK, D. J.: Electrocardiographic changes (local ventricular ischemia and injury) produced in the dog by temporary

- occlusion of a coronary artery, showing a new stage in the evolution of myocardial infarction. *Am. Heart J.* **27**: 164, 1944.
4. BAYLEY, R.H., LADUE, J.S., & YORK, D.J.: Further observations on the ischemia-injury pattern produced in the dog by temporary occlusion of a coronary artery. Incomplete T diversion patterns, theophylline T reversion and theophylline conversion of the negative T pattern. *Am. Heart J.* **27**: 657, 1944.
 5. SAYEN, J.J., SHELDON, W.F., PEIRCE, G., & KUO, P. T.: Polarographic oxygen, the epicardial electrocardiogram and muscle contraction in experimental acute regional ischemia of the left ventricle. *Circulation Res.* **6**: 779, 1958.
 6. CASE, R. B., ROSELLE, H. A., & CRAMPTON, R. S.: Relation of S-T depression to metabolic and hemodynamic events. *Cardiologia* **48**: 32, 1966.
 7. SCHEUER, J., & BRACHFELD, N.: Coronary insufficiency: Relations between hemodynamic, electrical, and biochemical parameters. *Circulation Res.* **18**: 178, 1966.
 8. SCHEUER, J., & STEZOSKI, S. W.: Effects of high-energy phosphate depletion and repletion on the dynamics and electrocardiogram of isolated rat hearts. *Circulation Res.* **23**: 519, 1968.
 9. SARNOFF, S. J., & BERGLUND, E.: Ventricular function. I. Starling's law of the heart studied by means of simultaneous right and left ventricular function curves in the dog. *Circulation* **9**: 706, 1954.
 10. SARNOFF, S. J.: Myocardial contractility as described by ventricular function curves; Observations on Starling's law of the heart. *Physiological Rev.* **35**: 107, 1955.
 11. SIEGEL, J. H., SONNENBLICK, E. H., JUDGE, R. D., & WILSON, W. S.: The quantification of myocardial contractility in dog and man. *Cardiologia* **45**: 189, 1964.
 12. MASTON, D. T., SONNENBLICK, E. H., ROSS, J., JR., COVELL, J. W., & BRAUNWALD, E.: Time to peak dp/dt: A useful measurement for evaluating the contractile state of the human heart. (Abstr.) *Circulation* **32** (suppl. II): II-145, 1965.
 13. HISADA, S.: Experimental studies on myocardial contractility: Direct measurements of the contractility of left ventricular myocardium with the strain gauge arch. *Jap. Circulation J.* **32**: 789, 1968. (in Japanese)
 14. HISADA, S., TAKADA, H., YOSHIDA, S., HOTTA, S., MIZUNO, Y., HIBINO, S., IGARASHI, I., & CHIKU, T.: A microminiature pressure transducer utilizing semiconductor strain gauges. *Jap. J. of Med. Electronics and Biol. Engineering* **4**: 288, 1966. (in Japanese)
 15. SIEGEL, J. H., & SONNENBLICK, E. H.: Isometric time-tension relationships as an index of myocardial contractility. *Circulation Res.* **12**: 597, 1963.
 16. KIMURA, E., KANAZAWA, T., SUZUKI, N., OHARA, F., YAMAMOTO, F., SUZUKI, U., TAKAHASHI, A., & TAKAHASHI, N.: *Naika* **1**: 45, 1958. (in Japanese)
 17. PRINZMETAL, M., GOLDMAN, A., SHUBIN, H., BOR, N., & WADA, T.: Angina pectoris. II. Observations on the classic form of angina pectoris. *Am. Heart J.* **57**: 530, 1959.
 18. EKMEKCI, A., TOYOSHIMA, H., KWOCZYNSKI, J. K., NAGAYA, T., & PRINZMETAL, M.: Angina pectoris. IV. Clinical and experimental difference between ischemia with S-T elevation and ischemia with S-T depression. *Am. J. Cardiol.* **7**: 412, 1961.
 19. WEGRIA, R., FRANK, C. W., MISRAHY, G. A., WANG, H., MILLER, R., & CASE, R. B.: Immediate hemodynamic effects of acute coronary artery occlusion. *Am. J. Physiol.* **177**: 123, 1954.
 20. NAKANO, J.: Effect of changes in coronary arterial blood flow on the myocardial contractile force. *Jap. Heart J.* **7**: 78, 1966.
 21. WILSON, F. N., MACLEOD, A. G., & BARKER, P. S.: The distribution of the action currents produced by heart muscle and other excitable tissues immersed in extensive conducting media. *J. Gen. Physiol.* **16**: 423, 1933.
 22. WILSON, F. N., JOHNSTON, F. D., HILL, I. G. W., & GRANT, G. C.: The form of the electrocardiogram in experimental myocardial infarction. *Proc. Soc. Exper. Biol. & Med.* **30**: 799, 1933.
 23. WILSON, F. N., MACLEOD, A., JOHNSTON, F. D., & HILL, I. G. W.: Monophasic electrical response produced by the contraction of injured heart muscle. *Proc. Soc. Exper. Biol. & Med.* **30**: 797, 1933.
 24. TOYOSHIMA, H., EKMEKCI, A., FLAMM, E., MIZUNO, Y., NAGAYA, T., NAKAYAMA, R., YAMADA, K., & PRINZMETAL, M.: Angina pectoris. VII. The nature of S-T depression in acute myocardial ischemia. *Am. J. Cardiol.* **13**: 498, 1964.
 25. MIZUNO, Y.: Pathological physiology of coronary insufficiency: Nature of ST-T changes and influences on myocardial contractility. Proceedings of the 17th general assembly of the Japan medical congress IV: 380, 1967. (in Japanese)
 26. CALDWELL, P. C., HODGKIN, A. L., KEYNES, R. D., & SHAW, T. Y.: The effects of injecting energy-rich phosphate compounds on the active transport of ions in giant axons of *Laligo*. *J. Physiol.* **152**: 561, 1960.
 27. DYDYNKA, M., & HARRIS, E. J.: Consumption of high-energy phosphates during active sodium and potassium interchange in frog muscle. *J. Physiol.* **182**: 92, 1966.
 28. FEINSTEIN, M. B.: Effects of experimental congestive heart failure, ouabain, and asphyxia on the high-energy phosphate and creatine content of the guinea pig heart. *Circulation Res.* **10**: 333, 1962.
 29. BESTON, E. S., EVANS, G. T., HALLAWAY, B. E., PHIBBS, C., & FREIER, E. F.: Myocardial creatine phosphate and nucleotides in anoxic cardiac arrest and recovery. *Am. J. Physiol.* **201**: 687, 1961.
 30. BRAASCH, W., GUDBJARNASON, S., PURI, P. S., RAVENS, K. G., & BING, R. J.: Early changes in energy metabolism in the myocardium following acute coronary artery occlusion in anesthetized dogs. *Circulation Res.* **23**: 429, 1968.
 31. CAIN, D., & DAVIES, R.E.: Breakdown of adenosine triphosphate during a single contraction of working muscle. *Biochem. Biophys. Res. Commun.* **8**: 361, 1962.
 32. POOL, P. E., & SONNENBLICK, E. H.: The mecha-

- nochemistry of cardiac muscle. I. The isometric contraction. *J. Gen. Physiol.* **50**: 951, 1967.
33. WALLACE, A. G., SKINNER, N. S., JR., & MICHELL, J. H.: Hemodynamic determinants of the maximal rate of rise of left ventricular pressure. *Am. J. Physiol.* **205**: 30, 1963.
 34. HISADA, S., KAITO, A., TAKADA, H., YOSHIDA, S., & MIZUNO, Y.: Myocardial Contractility. *Saishin-igaku* **23**: 38, 1968. (in Japanese)
 35. GRAHAM, T. P., ROSS, J., JR., COVELL, J. W., SONNENBLICK, E. E., & CLANCY, R. L.: Myocardial oxygen consumption in acute experimental cardiac depression. *Circulation Res.* **21**: 123, 1967.
 36. CASE, R. B., BERGLUND, E., & SARNOFF, S. J.: Ventricular function. II. Quantitative relationship between coronary flow and ventricular function with observations on unilateral failure. *Circulation Res.* **2**: 319, 1954.
 37. RUSHMER, R. F., WATSON, N., HARDING, D., & BAKER, D.: Effects of acute coronary occlusion on performance of right and left ventricles in intact unanesthetized dogs. *Am. Heart J.* **66**: 522, 1963.
 38. STONE, H. L., BISHOP, V. S., & GUYTON, A. C.: Cardiac function after embolization of coronaries with microspheres. *Am. J. Physiol.* **204**: 16, 1962.
 39. RICHARDSON, J. A., WOODS, E. F., BAGWELL, E. E.: Circulating epinephrine and norepinephrine in coronary occlusion. *Am. J. Cardiol.* **5**: 613, 1960.
 40. DRISCOL, T. E., & ECKSTEIN, R. W.: Coronary inflow and outflow responses to coronary artery occlusion. *Circulation Res.* **20**: 485, 1967.