Experimental Studies of Coronary Insufficiency

I. Changes in Myocardial Contractility in the Ischemic Area of the Ventricle Following Acute Coronary Occlusion*

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Changes in the myocardial contractility following acute and complete coronary occlusion were investigated in anesthetized open-chest dogs. Developed tension (DT) obtained with a strain gauge arch, without stretching the resting length of muscle, at the area supplied by the left anterior descending coronary artery decreased progressively and disappeared within one minute after its occlusion. When the myocardial segment was stretched with a modified strain gauge arch, DT could be recognized even in the ischemic myocardium in which DT disappeared without stretching. The resting length-developed tension curve, however, was shifted remarkably to the lower right during ischemia. The mechanism of occurrence of "bulge" in the ischemic area of the ventricle was discussed.

IT IS well known that an ischemic area of ventricular myocardium may bulge or balloon out during systole. This remarkable phenomenon was first observed in animal experiments by TENNANT and WIGGERS.¹ Subsequently it was confirmed experimentally by the motion-picture method.^{2,3} This phenomenon was recognized also clinically by many investigators using roentgenkymogram,^{4,5} electrokymogram,^{6,7} and kinecardiogram.⁸ HARRISON⁹ called attention to the "disorganized pattern of contraction" frequently recorded in kinecardiograms of subjects with coronary heart disease, and applied the term "asynergy" to this condition. HERMAN et al.¹⁰ showed that there were four distinct local types of asynergy, and employed the term "dyskinesis" to express the paradoxical systolic expansion of part of the wall. It has been already shown that the phenomenon of bulge is not due to the impairment of electrical conductivity to and from the ischemic area.^{1,2} The mechanism of the phenomenon, however, has not been well known yet.

Recently the strain gauge arches have been

used generally for measurement of the contractility of the local ventricular myocardium.¹¹⁻¹⁴ The availability and the limitation of this method has been also investigated.¹⁵ The first purpose of the present paper is to evaluate the changes in myocardial contractility in the ischemic area following acute coronary occlusion by using newly developed semiconductor strain gauge arches. The second purpose is to examine the mechanical properties of the ischemic myocardium which is suffering from "bulge" or "dyskinesis", and to discuss the mechanism of occurrence of the phenomenon.

METHODS

Twelve adult mongrel dogs weighing 10 to 24 kg were anesthetized with intraperitoneal injection of 30 mg/kg of sodium pentobarbital. Under artificial respiration with a mixture of air and oxygen, the chest was opened in the fifth bilateral intercostal space. The pericardial sac was incised longitudinally to expose the anterior wall of the left ventricle. A small segment (3 to 5 mm) of the

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left anterior descending coronary artery (LAD) was gently dissected at or just below the tip of the left atrial appendage, at a distance that averaged 2.3 cm (range, 1.9 to 3.2 cm) from the mouth of the left main coronary artery, as measured in post-mortem examination. A silk suture 20 cm long was passed under the artery without compressing the vessel, and its ends were loosely retained for subsequent closure of the artery. Coagulation was prevented by an initial dose of 200 units/kg of heparin followed 100 units/kg doses hourly. The present studies were composed of two series of experiments.

1. Experiments on changes in myocardial tension following coronary occlusion.

In this series of experiments, myocardial tension was measured with a small-sized semiconductor strain gauge arch, Model L-6.¹⁵ The arch of this model consists of a small structure weighing less than 1 g with two legs 10 mm apart. The strain gauge arch was sutured to the ventricular wall supplied by LAD. Attention was paid to align the axis of the arch with the superficial muscle bundle. The arch was fixed at two points by silk sutures which were placed to avoid occlusion of any visible coronary vessels. Care was taken not to stretch the resting length of muscle. Unipolar surface electrogram was taken with tiny recording electrode from a point on the ventricle adjacent to the strain gauge arch. Aortic or left ventricular pressure was recorded with a pressure transducer connected to an 8F catheter inserted through the carotid artery (Fig. 1). After a control record influences of LAD occlusion on myocardial tension tracings, surface electrograms and aortic or left ventricular pressure curves were

Fig. 1. Diagram of experimental setup I. Myocardial tension in the area supplied by the left anterior descending coronary artery was measured with a strain gauge arch sutured along the superficial muscle bundle.

observed. These pressure curves were used chiefly for analysis of the cardiac cycle.

2. Experiments on changes in resting length-developed tension relation following coronary occlusion.

In this series of experiments, myocardial tension was measured with a semiconductor strain gauge arch, Model VL-5.¹⁵ This arch had such a structure that the distance between the two legs could be adjusted from 15 to 22 mm by means of a micro-screw. This arch was fixed at four points by suturing, along the superficial muscle bundle, to the ventricular wall supplied by LAD. Before inducing coronary occlusion, the myocardial segment was stretched by distances of 0.8 mm in order to record myocardial tension tracings in the control period. Then the screw was revolved reversely. The same procedure as this was repeated 1 to 3 minutes after LAD occlusion. In this manner, influences of coronary occlusion on relationship between resting length and myocardial tension were observed.

Recordings were taken by photographic or direct writing recorders. A paper speed was 100 mm or 1.25 mm per second. Developed tension was calculated by subtracting the resting tension from the peak systolic tension. Developed tension was expressed by weight in grams or as a percent change from control which was taken as 100 per cent.

RESULTS

1. Changes in myocardial tension following coronary occlusion.

All the experimental cases, numbering eight, showed the same tendency. Fig. 2 shows the records of a representative experiment. After coronary occlusion myocardial tension curves decreased immediately in amplitude. Then they decreased progressively and began to be inverted 30 seconds after occlusion. The curves were completely inverted later than 45 seconds. When the occlusion was removed, there was an immediate decrease in negative portion. Then there was a gradual increase in height of the curve. At last, the value exceeded the control value once in 40 seconds after releasing the tie. In other cases, detailed observation was made on changes in the contours of myocardial tension curves with the lapse of time. Fig. 3 shows superimposed myocardial tension tracings obtained at various intervals after coronary occlusion in an experiment. Ten seconds after occlusion a negative portion

Fig.2. An experiment illustrating changes in surface electrograms, left ventricular pressure curves and myocardial tension tracings following coronary occlusion. About 30 seconds after occlusion myocardial tension tracings began to be inverted.

Fig.3. Superimposed myocardial tension tracings obtained at control period and at various intervals after coronary occlusion. Tension curves were completely inverted in systole later than 30 seconds.

Fig.4. Changes in developed tension following coronary occlusion. Zero time shows control period. Each point represents mean $\pm$ SD in 8 dogs. Developed tension decreased progressively and disappeared later than 50 seconds after coronary occlusion.

appeared over the period of cardiac cycle from the isometric contraction to the early ejection. It became deeper and deeper. The myocardial tension curves were completely inverted during systole later than 30 seconds after occlusion. The pattern of the tension curve revealed a sharp decline in the isovolumic contraction period. In the ejection period the decline diminished. Immediately before the end of the ejection period, the curve changed into a sharp rise in direction. In other words, the myocardial tension curve presented a mirror pattern of the intraventricular pressure curve. Fig.4 shows the changes in developed tension in eight cases following coronary occlusion. After coronary occlusion developed

tension decreased progressively and disappeared eventually in all the cases 50 seconds later.

In the surface electrogram, ST segment began to be elevated 25 to 40 seconds after coronary occlusion. The peak left ventricular pressure showed a transient increase within 20 seconds in some cases, but a slight decrease later than 40 seconds after occlusion.

2. Changes in resting length-developed tension relation following coronary occlusion.

Experiments were performed in four dogs. As all the cases showed the same tendency, a typical experiment was illustrated in Fig.5. The myocardial tension curve, even in the control period,

Fig.5. Superimposed myocardial tension tracings obtained sequentially from various resting length (upper figures) and resting length-developed tension relations (lower figures) in one dog. Initial length 19.2 mm. A, controls. B, about 3 minutes after coronary occlusion. Discussion in text.

increased in height at almost the same proportion as myocardial segment was stretched. The same procedure was repeated 3 minutes after coronary occlusion, when the myocardial tension tracing was inverted. As the myocardial segment was stretched, the inverted portion decreased gradually in the curve. When the myocardial segment became 19.2 mm in length, or increased in length by 32 per cent, the curve took a perfectly upward direction (upper row in Fig.5). The relationships between myocardial segment length and the developed tension were plotted in lower row in Fig.5. Both during control period and during ischemia, there was an increase in developed tension caused by an increase in myocardial segment length. The resting length-developed tension curve, however, was shifted remarkably to the lower right during ischemia, as compared with that obtained during the control period.

DISCUSSION

The myocardial tension curve along the superficial muscle bundle in an ischemic area decreased in amplitude immediately after coronary occlusion, and was inverted during systole within one minute. These results agree with those obtained by TENNANT and WIGGERS¹ and indicate that the ischemic myocardium "bulges" or "balloons" out during systole. HERMAN et al.¹⁰ studied "asynergy", the term proposed by HARRISON⁹ and classified asynergy into four distinct localized types: akinesis, or total lack of motion of a portion of left ventricular wall; dyskinesis, or paradoxical systolic expansion of part of the wall; asyneresis, or diminished motion of part of the wall; and asynchrony, or disturbed temporal sequence of contraction. When the changes induced by acute coronary occlusion are analyzed on the basis of the conception of asynergy, it can be interpreted that asyneresis occurs immediately to the ventricular wall supplied by the coronary artery, akinesis 30 to 40 seconds, and dyskinesis later than 50 seconds after occlusion.

In this study, developed tension obtained with a strain gauge arch without stretching the resting length of muscle along the superficial muscle bundle decreased progressively and disappeared later than 50 seconds after coronary occlusion. HISADA¹⁵ noted that the myocardial tension curves obtained with the strain gauge arch in this direction would reflect the contractile state of the muscle bundle itself beneath the arch without interference from the extracardiac factors. The changes in developed tension in the present study seem to have reflected the course of decrease in the myocardial contractility in the ischemic area.

It is doubtful, however, that the disappearance of developed tension obtained by this method will be interpreted as a fundamental loss of myocardial contractility. AYGEN and BRAUNWALD¹⁶ showed that Starling's law could be applied to a segment of human heart muscle because the lengthening of a segment of myocardium increased its force of contraction. These investigators used a modified Walton-Brodie strain gauge arch to stretch a myocardial segment. A similar method using the strain gauge arch, Model VL-5 was employed to evaluate the mechanical properties of an ischemic myocardium which was suffering from bulge or dyskinesis. As a result, when the myocardial segment was stretched gradually, an upward-directing curve was obtained during sys-

tole. In other words, developed tension appeared. The resting length-developed tension curve, however, was shifted distinctly to the lower right, as compared with that obtained during the control period. These results indicate that the myocardial contractility is reduced remarkably during ischemia, but that Starling's law can be also applied to the ischemic myocardium. PRINZMETAL et al² removed a bulged portion of myocardium from a heart and placed in a dish filled with saline, and observed that vigorous contractions occurred following electrical stimulation. They also demonstrated that the function of conductivity in an ischemic region in situ was retained apparently unaltered for at least 19 minutes after coronary occlusion. These results, as well as those of the present investigation, suggest that "bulge" may not be due to the fundamental loss of myocardial contractility, but that it may be induced because the contractility of the ischemic myocardium has become too weak to sustain the intraventricular pressure rise.

It has been reported that during myocardial anoxia high-energy phosphates decreased rapidly.¹⁷⁻¹⁹ It has also been known that these high-energy phosphates are energy source for muscle contraction.^{20,21} SCHEUR and STEZOSKI¹⁹ demonstrated in the isolated rat hearts that adenosine triphosphate and creatine phosphate declined by anoxia to 50 per cent of the control during the first minute and remained at this level for the following 5 minutes. The changes in the contractility in the ischemic myocardium, as evaluated with the strain gauge arches, are consistent with the course of reduction of high energy phosphates observed by SCHEUR and STEZOSKI.

In the surface electrogram, ST segment began to be elevated 25 to 40 seconds after coronary occlusion. By this time, developed tension had been reduced to less than 50 per cent of control, and an inverted portion had begun to appear in the myocardial tension curve. SAYEN and co-workers showed that the ST segment deviation in surface electrogram was a slow and an insensitive indicator of early localized ischemia as compared with polarographic oxygen. More detailed investigation will be needed to discuss the relationship between changes in myocardial contractility and changes in surface electrogram.

SUMMARY

Changes in the myocardial contractility in the ischemic area were studied during experimentally induced acute coronary insufficiency.

1. A strain gauge arch, Model L-6 was sutured along the superficial muscle bundle to the ventricular wall supplied by the anterior descending coronary artery without stretching the resting length of muscle. The myocardial tension curve began to decrease in amplitude immediately and then decreased progressively after the coronary occlusion, and was completely inverted during systole within one minute. It was presumed that the developed tension determined from the curve might reflect the course of the reduction of myocardial contractility in the ischemic area.

2. The mechanical properties of the ischemic myocardium were evaluated by using a strain gauge arch, Model VL-5, which permitted controlled alteration of the length of the myocardial segment to which it was attached. This arch was placed along the superficial muscle bundle. When the myocardial tension curve was completely inverted during systole following coronary occlusion, the myocardial segment was stretched gradually. As a result, an upward-directing curve was obtained. The resting length-developed tension curve, however, was shifted remarkably to the lower right during ischemia, as compared with the control period. These results indicate that Starling's law can be applied even to the ischemic myocardium from which developed tension disappeared and which was affected with "bulge", and that contractility remained still in this myocardium. Accordingly, it was presumed that the phenomenon of "bulge" might not be due to fundamental loss of myocardial contractility, but that it might be induced because the contractility of the ischemic myocardium became too weak to withstand the intraventricular pressure rise.

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