# Experimental Myocardial Infarction

## II. ACUTE DEPRESSION AND SUBSEQUENT RECOVERY OF LEFT VENTRICULAR FUNCTION: SERIAL MEASUREMENTS IN INTACT CONSCIOUS DOGS

RAJ KUMAR, WILLIAM B. HOOD, JR., JULIO JOISON, JOHN C. NORMAN, and WALTER H. ABELMANN

*From the Thorndike Memorial Laboratory, Harvard (Second and Fourth) Medical Services, and Sears Surgical Laboratory, Harvard Surgical Service, Boston City Hospital, and the Departments of Medicine and Surgery, Harvard Medical School, Boston, Massachusetts 02118*

ABSTRACT Acute myocardial infarction causes depression of left ventricular function, but the capacity of the ventricle to recover from such an injury remains unknown. This problem was explored by measuring left ventricular function in eight intact conscious dogs before, 1 hr after, and again 6–8 days after myocardial infarction. Acute myocardial infarction was produced using a technique which entails gradual inflation over an average period of 1 hr of a balloon cuff previously implanted around the left anterior descending coronary artery. Occurrence of anterior wall infarction was detected electrocardiographically and later confirmed by postmortem examination. Left ventricular function was evaluated from the relationship between left ventricular developed pressure (left ventricular peak systolic pressure minus left ventricular end-diastolic pressure) and left ventricular end-diastolic pressure during transient aortic occlusion with a balloon catheter. Left ventricular function curves were obtained by plotting left ventricular–developed pressure at increasing left ventricular end-diastolic pressures up to 50 mm Hg. Acute myocardial infarction caused marked depression of left ventricular function measured 1 hr after onset of infarction, but 1 wk later all eight animals showed improvement with return of function toward the control levels. A small but significant descending limb was noted at left ventricular end-diastolic pressures above 35 mm Hg. Quantitatively, the descending limb was similar before, 1 hr after, and 1 wk after myocardial infarction. Hemodynamic data revealed evidence of left ventricular failure in all animals, but variability in individual hemodynamic parameters was noted. The data indicate that the marked depression of left ventricular function observed immediately after experimental acute myocardial infarction undergoes considerable resolution within 1 wk, but that functional recovery remains incomplete.

*Received for publication 26 May 1969.*

## INTRODUCTION

Previous investigators have demonstrated depression of left ventricular function during experimental coronary occlusion (1, 2). This depression is reversible with restoration of blood flow to the ischemic area. When one or more coronary vessels are permanently occluded, thus allowing the ischemia to persist, acute myocardial infarction occurs. Under these experimental conditions a reduction in arterial blood pressure and/or cardiac output has been observed (3–9). Depression of cardiac output in patients with acute myocardial infarction and hypotension has also been reported in clinical studies (10–18).

Most of these observations in both clinical and experimental myocardial infarction have been made acutely, and little quantitative information about the healing stage after coronary occlusion is available. It has been the impression that improvement of left ventricular function occurs during recovery, but this has not been consistently documented (14, 15, 17).

The present investigation in dogs was designed to assess the recovery of left ventricular function after experimental acute myocardial infarction. Pressure loading of the left ventricle was employed to test ventricular performance. Left ventricular function was evaluated by the relationship of left ventricular end-diastolic pressure

to left ventricular–developed pressure during transient aortic obstruction (19–22). In addition, routine hemodynamic measurements were carried out. Serial studies were executed in all animals. Animals were studied before, 1 hr after, and again 1 wk after experimental myocardial infarction, and each animal served as its own control.

## METHODS

Eight adult mongrel dogs of both sexes, weighing 18–26 kg, were selected for study. The technique of producing myocardial infarction by slow occlusion of a small balloon cuff around the left anterior descending coronary artery in intact conscious dogs has been described previously in studies from this laboratory (23, 24). Coronary occlusion balloon devices were implanted under 30 mg/kg pentobarbital anesthesia. Animals were intubated and ventilated with a Bennett intermittent positive pressure respirator (Bennett Respirator Products, Inc., Santa Monica,, Calif.). Through a left thoracotomy, the pericardial sac was opened, and the left anterior descending coronary artery was isolated 4–10 mm below its origin. An inflatable balloon cuff device, of the type developed by Chimoskey, Szentivanyi, Zakheim, and Barger (25), was implanted around the vessel. In three dogs, bipolar pacing wires were sutured to the left atrial appendage. The ascending aorta was isolated and banded 3–7 mm proximal to the origin of the innominate artery by an umbilical tape. To protect the aorta from damage, this tape was passed through a 0.6 cm diameter tunnel of Teflon graft material which was cut to fit snugly around the aorta. Banding was carried out in such a way that there was a 10–25 mm systolic and less than 3 mm mean pressure gradient across the band. The purpose of this procedure was to permit later studies involving inflation of a catheter-tip balloon in the ascending aorta, thus imposing a pressure load upon the left ventricle, without having the balloon expelled from the aortic root by the force of ventricular contraction. Atrial pacing wires and the Silastic tube leading to the balloon cuff were exteriorized on the dog's back. All animals received 1.2 million U of procaine penicillin and 600 mg lincomycin intramuscularly daily for 7 days after operation.

Animals were allowed to recover for 10–15 days after surgery. On the day of study animals were sedated with 15 mg morphine sulphate given intramuscularly. Under local anesthesia, a femoral cutdown was done to permit introducing an 8F Cournand catheter into the pulmonary artery and a specially made balloon catheter into the left ventricle. The latter was a 6–8F double lumen catheter with one end hole and one side hole 12 cm from the end. A balloon large enough to obstruct the aorta when inflated was constructed around the proximal hole. Under fluoroscopic control, the catheter was placed on the left side of the heart in such a way that the tip lay in the left ventricle and the balloon lay in the aortic root proximal to the aortic band.

After recording a 9 lead electrocardiogram, cardiac output was measured in duplicate by the indicator dilution technique, using indocyanine green. Pressures were recorded in the right atrium, right ventricle, pulmonary artery, aorta, and left ventricle. The latter three pressure measurements were always recorded simultaneously. Then the aorta was transiently occluded by inflating the balloon catheter with 100% carbon dioxide until left ventricular end-diastolic pressure rose to 50 mm Hg. The carbon dioxide was injected manually, but under fluoroscopic control, so that the balloon could be seen to impact and become immobilized against the aortic band. The volume of carbon dioxide required to inflate the balloon varied from 10 to 25 ml. This procedure caused obstruction of the aorta proximal to the band, but well above the coronary ostia. This permitted evaluation of left ventricular function by the relation of left ventricular–developed pressure (left ventricular peak systolic pressure − left ventricular end-diastolic pressure) to left ventricular end-diastolic pressure.

The obstruction produced by inflating the intra-aortic balloon was sudden, but development of a rise in end-diastolic pressure to greater than 50 mm Hg required at least 5 sec and sometimes up to 12 sec. In each case, a beat by beat plot of left ventricular–developed pressure vs. left ventricular end-diastolic pressure was carried out. For purposes of tabulating the data and statistical analysis, the left ventricular–developed pressure was read from the ventricular function curve thus constructed at left ventricular end-diastolic pressure intervals of 5 mm Hg. This technique of left ventricular function assessment has been evaluated and validated by Goodyer, Goodkind, and Landry (19), Goodyer, Goodkind, and Stanley (20), Monroe, Gamble, LaFarge, and Edalji (22), and has been used subsequently by Hood, McCarthy, and Lown (21).

Then the myocardial infarction was produced by slow infusion of saline by means of a Sage model 172 microflow pump (Sage Instruments, Inc., White Plains, N. Y.) into the balloon cuff around the left anterior descending coronary artery, as previously reported (23, 24). After this, the balloon was left inflated. Onset of myocardial infarction was confirmed by either sinus tachycardia or electrocardiographic changes or both. 1 hr after the infarction, left ventricular function was reassessed in all dogs. Pressures and cardiac output were again measured. All the dogs tolerated the procedure well. Only one dog appeared uncomfortable during myocardial infarction. In three dogs, a few ventricular premature beats were observed within 15 min after the onset of myocardial infarction, and these were treated with 20–40 mg of lidocaine given intravenously. The last dose of lidocaine was always given more than 40 min before the study of ventricular function, and no other drug was used.

After the study, the dogs were returned to the kennel and ambulated daily. 6–8 hr after infarction all dogs developed ventricular tachycardia except one, which displayed only sinus tachycardia. Ventricular tachycardia subsided spontaneously in less than 3 days. Serum glutamic oxaloacetic transaminase (SGOT), lactic dehydrogenase (LDH), and creatine phosphokinase (CPK) were measured as previously reported (23, 24) before and 24 hr after the infarct.

Dogs were restudied 6–8 days after the infarction, again under sedation with 15 mg morphine sulfate. Pressures, cardiac output, and left ventricular function were reassessed in all dogs. In three of these eight animals, left ventricular function curves were constructed at all three stages, i.e. control, and at 1 hr, and again 1 wk after infarction, while the heart rate was controlled by pacing the atrium at 180 beats/min.

In carrying out ventricular function testing, an average of five curves were made for every animal during each state. Only the ventricular function curves in which no ventricular arrhythmia occurred (19) were analyzed. Pressure tracings were made using a multichannel photographic recorder (Hewlett-Packard Co., Palo Alto, Calif.). Left ventricular pressure was measured simultaneously at both low and high gains, and during aortic obstruction, tracings were made continuously at 50 or 100 mm/sec. This facili-

TABLE I

*Animal Weights and Time Intervals Between Surgery, Myocardial Infarction, and Restudy*

| Dog. No. | Weight | Time of infarction after surgery | Time of restudy after infarction |
|---|---|---|---|
| | *kg* | *days* | *days* |
| 4347 | 25.0 | 12 | 7 |
| 4379 | 23.5 | 14 | 7 |
| 4518 | 26.5 | 10 | 7 |
| 4698 | 20.0 | 11 | 6 |
| 4694 | 18.2 | 10 | 7 |
| 4770 | 24.1 | 15 | 8 |
| 4771 | 24.1 | 14 | 8 |
| 4785 | 22.2 | 15 | 8 |

tated accurate determination of left ventricular end-diastolic pressure at fast heart rates produced by aortic obstruction. It should be noted that no correction of left ventricular end-diastolic pressure was made for intrapleural pressure changes in these intact conscious dogs. However, it is probable that only a small error is involved by omitting the pleural pressure since large elevations of left ventricular end-diastolic pressure were produced during inscription of left ventricular function curves.

Animals were sacrificed on an average of 2 days after restudy, i.e. 8–10 days after myocardial infarction, and the size of infarct measured as per cent of left ventricular mass, using techniques previously described (23, 24).

Each dog served as its own control. Hemodynamic and left ventricular function parameters were compared between control vs. acute myocardial infarction, acute myocardial infarction vs. recovery, and control vs. recovery. Results were analyzed by paired *t* test (26).

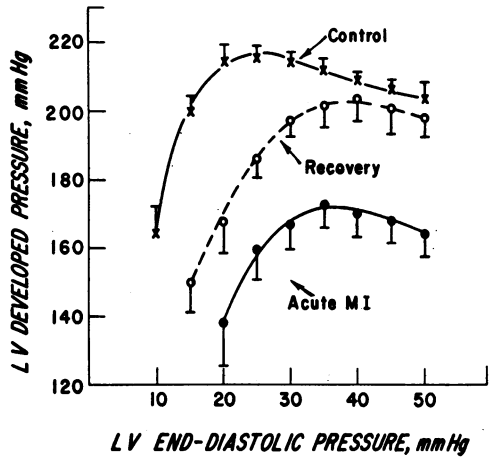


FIGURE 1 Left ventricular (LV) function curves (mean ±SEM) during control state, acute myocardial infarction (MI), and recovery. Curves differ from one another significantly at all levels except control and recovery curve above left ventricular end-diastolic pressures of 35 mm Hg (see Table II).

## RESULTS

Identifying data and time intervals before and after myocardial infarction are given in Table I. Table II summarizes the left ventricular function data, and Table III presents the hemodynamic studies.

The average weight of the animals studied was 23 kg. Myocardial infarction was produced on an average of 13 days after surgery, and restudy was done 6–8 days after the myocardial infarction. Presence of infarction was confirmed in every animal by elevations of SGOT, CPK, and LDH 24 hr after infarction, and by post-

TABLE II

*Summary and Statistical Analysis of Left Ventricular Developed Pressure (mm Hg) at Different Left Ventricular End-Diastolic Pressures during Control State, Acute Myocardial Infarction, and Recovery**

| Left ventricular end-diastolic pressure, *mm Hg*..... | | 10 | 15 | 20 | 25 | 30 | 35 | 40 | 45 | 50 |
|---|---|---|---|---|---|---|---|---|---|---|
| I Control | Mean | 164 | 200 | 215 | 216 | 215 | 212 | 209 | 206 | 204 |
| | SEM | 10.3 | 4.6 | 4.5 | 3.5 | 3.0 | 3.2 | 3.9 | 4.5 | 4.9 |
| II Acute myocardial infarction | Mean | | | 138‡ | 160§ | 167§ | 173 | 170 | 168 | 164 |
| | SEM | | | 13.1 | 9.1 | 7.5 | 6.5 | 6.2 | 6.5 | 6.4 |
| III 6–8 days after myocardial infarction | Mean | | 150‡ | 168§ | 186 | 198 | 202 | 204 | 201 | 199 |
| | SEM | | 9.0 | 9.3 | 5.8 | 5.1 | 4.9 | 4.9 | 5.7 | 5.9 |
| Test of significance paired *t* | | | | | | | | | | |
| I vs. II | *P* | | | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| I vs. III | *P* | | <0.001 | <0.001 | <0.005 | <0.05 | NS | NS | NS | NS |
| II vs. III | *P* | | | <0.01 | <0.01 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

* Data derived from eight animals except where noted.
‡ Four animals.
§ Seven animals.

mortem examinations. The size of the infarct at postmortem was 30 ±8 (SD)% of left ventricular weight.

## Ventricular function study

*Left ventricular function curves.* Ventricular function curves were constructed by plotting left ventricular–developed pressure against increasing left ventricular end-diastolic pressure during transient aortic obstruction. An end-diastolic pressure of 50 mm Hg or more could be produced in all animals. The left ventricular function curves constructed in this manner in different animals were quite similar to each other during the control state as evident from the small standard error. The mean left ventricular function curves in the control state, acute myocardial infarction and recovery are shown in Fig. 1. The developed pressures at end-diastolic pressures from 10 to 50 mm Hg are given in Table II.

The control ventricular function curve before infarction showed a rapidly rising developed pressure at the onset of aortic obstruction (ascending limb), followed by a steady increase in left ventricular end-diastolic pressure with no further increase in developed pressure (plateau) (Fig. 1). 1 hr after induced myocardial infarction, there was marked depression of left ventricular function, with significant reduction of developed pressure at all levels of left ventricular end-diastolic presure on both ascending limb and plateau. This shift to the right of the ventricular function curve was observed in every animal. On restudy 1 wk after acute myocardial infarction, considerable recovery of ventricular function was noted. Now there was a significant increase of developed pressure at all levels of left ventricular end-diastolic pressure, compared with the curve 1 hr after infarction. Again, this shift to the left of the ventricular function curve was a consistent finding. However, when these curves obtained 1 wk after infarction were compared with the control curves before infarction, it was noted that recovery of ventricular function was not complete. This was most evident along the ascending limb of the curve, which remained significantly depressed. However, at high end-diastolic pressure (above 35 mm Hg), the same plateau of developed pressure was achieved in both states (Fig. 1).

*Maximal developed pressure ("maximum strength").* These data were also examined in terms of the maximal developed pressure which the ventricle could generate in the three different study states. Maximal pressure at the plateau of the ventricular function curve is a reflection of "maximum strength" since ventricular contraction is essentially isometric (19). Maximal developed pressure in the control state was 216 ±3.4 (SEM), mm Hg, while in acute myocardial infarction it was reduced to 174 ±6.3 mm Hg, or a 20% reduction. 7 days after

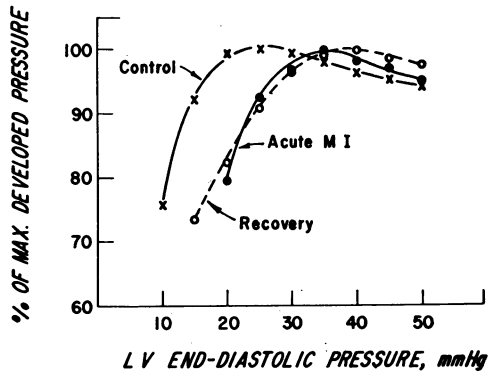


FIGURE 2 Left ventricular developed pressure plotted as percentage of maximal developed pressure vs. left ventricular end-diastolic pressure. Note that during acute myocardial infarction and recovery, maximal developed pressures are attained at higher levels of left ventricular end-diastolic pressure than in the control state.

myocardial infarction, the left ventricle had recovered its capacity to generate 95% of the normal maximal developed pressure (205 ±4.2 mm Hg). However, these maximal developed pressures were generated at progressively more elevated left ventricular end-diastolic pressures of 25.5 ±1.0, 36.5 ±1.0, and 40.0 ±0 (SEM) mm Hg, respectively in the three states.

*Per cent of maximal developed pressure at different end-diastolic pressures.* The above findings imply certain similarities in the behavior of the infarcted and recovered ventricle in the manner pressure is generated at different filling pressures. Left ventricular–developed pressure represented as the percentage of maximal developed pressure at different end-diastolic pressures is shown in Fig. 2. It is noted that the normal ventricle can generate its maximal developed pressure at a left ventricular end-diastolic pressure of 25 mm Hg. In contrast, both the acutely infarcted and recovered ventricle develop only 92% of their maximal developed pressure at this left ventricular end-diastolic pressure. In these two states, maximal developed pressure was not attained until higher levels of left ventricular end-diastolic pressure were reached (35 and 40 mm Hg, respectively). In fact, the curves of the acutely infarcted and recovered ventricle, plotted in this way, are virtually identical.

*Descending limb.* The plateaus of the ventricular function curves showed a descending limb in all three states. From the peak of the individual left ventricular function curves (left ventricular maximal developed pressure), the descent of the plateau at left ventricular end-diastolic pressure of 50 mm Hg was 6.0 ±1.5 (SEM)% in the control state, 5.5 ±1.4 (SEM)% after acute myocardial infarction, and 3.2 ±1.3 (SEM)% after recovery (Fig. 1). The changes, although small are significant

($P < 0.05$) in each case; however, comparison of the magnitude of the descent between control, acute myocardial infarction, and recovery revealed no significant difference.

*Ventricular function at controlled heart rates.* During aortic obstruction, it was noted that the heart rate increased from 81 ±5.6 to 164 ±8.3 beats/min (SEM) in the control state, from 114 ±0.7 to 167 ±10 beats/min (SEM) in acute myocardial infarction, and from 92 ±6.4 to 148 ±7.9 beats/min (SEM) during recovery. The heart rates during aortic obstruction did not differ significantly from each other in control states, acute myocardial infarction, and recovery. Since the rates were not all identical before aortic obstruction, further tests were done to determine whether alterations in rate might affect the conclusions drawn from tests of ventricular function. Atrial pacing at a constant rate of 180 beats/min was maintained in three animals during aortic occlusion. In all three animals, acute depression followed by recovery of ventricular function was noted after acute myocardial infarction in both the presence and absence of control of heart rate.

*Repeated testing.* Animals tolerated repeated obstruction of the aorta for 12 sec or less without whining or other evidence of pain. Ventricular function curves were reproducible in all animals. The coefficient of variation calculated from multiple left ventricular function curves in individual animals ranged from 1 to 4% at levels of end-diastolic pressure of 10–50 mm Hg.

*Hemodynamic measurements.* Hemodynamic data are summarized in Table III. With acute infarction, there was a significant increase in heart rate and left ventricular end-diastolic pressure and 39% decrease in stroke volume. Other hemodynamic measurements were more variable: average values for cardiac output and left ventricular systolic pressure were reduced, but not significantly. During recovery, left ventricular end-diastolic pressure declined in six of the eight animals, but did not return to normal. Cardiac output and stroke volume increased significantly during recovery, compared with acute infarction (Table III). These findings indicate onset of left ventricular failure with infarction, and suggest a degree of recovery during the week after infarction. However, these changes in hemodynamic measurements were less consistent than the results of tests of ventricular function (see above).

## DISCUSSION

Impairment of left ventricular performance has been described in both clinical and experimental myocardial ischemia (1–6, 8–18). In many of these studies, depression of ventricular function was defined in terms of diminished cardiac output, stroke volume, and increased cardiac filling pressures. However, it is well recognized that hemodynamic measurements may fall within the normal range in the presence of myocardial infarction (15, 17, 27).

More subtle changes in ventricular performance can be brought out by stressing the left ventricle with pressure or volume loads, that is, by construction of ventricular function curves, and in experimental acute coronary ischemia, depression is uniformly demonstrated (1, 2). Indeed, ventricular function in experimental myocardial infarction may be abnormal in the presence of hemodynamic values which are normal or nearly so (21). These findings suggest the need for carrying out sensitive tests of ventricular function in assessing serial changes after myocardial infarction. Due to disparate contractile behavior of normal and ischemic muscle in the presence of focal myocardial infarction, force velocity analysis of ventricular function is not applicable in this preparation (28).

The method of Goodyer et al. (19, 20) for pressure loading of the left ventricle was chosen because of its reproducibility, suitability for serial studies, and speed with which ventricular function could be tested in the intact, conscious animal. With this method, alterations in heart rate and marked arterial hypotension distal to the obstruction (21) are produced. These changes might independently alter ventricular contractility. However, changes in heart rate in this range in the present study and in that of Goodyer et al. (20), and transient carotid hypotension have been shown to have little effect on myocardial contractility (29–31).

The present study indicates that marked depression of left ventricular function follows acute myocardial infarction. Both the ascending limb and the plateau of the function curves were equally depressed. 7 days after myocardial infarction, considerable recovery in left ventricular function was seen. Recovery on the ascending limb was incomplete; however, at left ventricular end-diastolic pressures above 35 mm Hg the plateau of the recovery curve approximated the control curve before infarction (Fig. 1). Despite this capacity of the ventricle during recovery to generate maximal developed pressures similar to the control state, the pattern of pressure generation, in relation to end-diastolic pressure, was similar to that of the acutely infarcted ventricle (Fig. 2).

Presence of a descending limb in the function curve of the normal left ventricle is disputed (22, 32), but has been described in the damaged ventricle (1, 32). In the present study, a small but significant descending limb of comparable magnitude was noted before and after infarction and during recovery, but only with left ventricular end-diastolic pressures above 35 mm Hg, well above the physiologic range.

It should be noted that demonstration of a descending limb in this preparation is contingent upon the analysis

TABLE III

*Hemodynamic Data in Control State, Acute Myocardial Infarction, and during Recovery, with Statistical Analysis*

| Dog. No. | | Heart rate | Cardiac output | Stroke volume | Pressures: Pulmonary Artery Systolic | Pulmonary Artery Diastolic | Pulmonary Artery Mean | Aortic Systolic | Aortic Diastolic | Aortic Mean | Left ventricular Systolic | Left ventricular End-Diastolic | Right atrial |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | *beats/min* | *liters/min* | *ml/beat* | *mm Hg* | | | *mm Hg* | | | *mm Hg* | | *mm Hg* |
| 4347 | I Control | 96 | 2.75 | 26.8 | | | | 118 | 64 | | 157 | 5 | 3 |
| | II Acute MI | 130 | 1.96 | 15.1 | | | | | | | 145 | 20 | 3 |
| | III Recovery | 110 | 2.27 | 20.6 | | | | 110 | 64 | | 148 | 15 | 2 |
| 4379 | I Control | 90 | 3.00 | 33.3 | | | | 133 | 76 | 90 | 155 | 6 | 2.5 |
| | II Acute MI | 130 | 2.38 | 18.3 | | | | | | | 121 | 15 | 1.5 |
| | III Recovery | 72 | 3.32 | 46.1 | 20 | 5 | 9 | 140 | 68 | 83 | 160 | 10 | |
| 4518 | I Control | 62 | 3.52 | 56.7 | 22 | 5 | 9 | 122 | 82 | 98 | 135 | 10 | |
| | II Acute MI | 140 | 3.46 | 24.7 | 31 | 22 | 26 | | | | 125 | 27 | |
| | III Recovery | 85 | 5.02 | 59.1 | 23 | 7 | 11 | 117 | 83 | 97 | 145 | 21 | |
| 4698 | I Control | 100 | 4.06 | 40.6 | 26 | 6 | 14 | 145 | 68 | 85 | 137 | 7 | 0 |
| | II Acute MI | 150 | 4.34 | 28.9 | 36 | 10 | 21 | 155 | 105 | 130 | 155 | 23 | 6 |
| | III Recovery | 110 | 7.17 | 65.1 | 26 | 7 | 14 | 160 | 85 | 120 | 175 | 13 | 1 |
| 4694 | I Control | 62 | 2.87 | 46.2 | 23 | 5 | 12 | 120 | 58 | 81 | 160 | 5 | 1 |
| | II Acute MI | 70 | 2.29 | 32.7 | 19 | 5 | 10 | | | | 130 | 21 | |
| | III Recovery | 85 | 4.56 | 53.6 | 30 | 6 | 14 | 125 | 65 | 90 | 130 | 10 | 1 |
| 4770 | I Control | 96 | 3.88 | 40.4 | 15 | 4 | 8 | 137 | 87 | 107 | 140 | 3 | −1 |
| | II Acute MI | 96 | 2.41 | 25.1 | 24 | 10 | 13 | | | | 145 | 15 | |
| | III Recovery | 110 | 5.55 | 50.4 | 28 | 7 | 15 | 112 | 80 | 91 | 150 | 16 | 1 |
| 4771 | I Control | 66 | 3.01 | 45.5 | 22 | 6 | 11 | 113 | 61 | 79 | 145 | 7 | 0 |
| | II Acute MI | 104 | 3.82 | 36.7 | 27 | 10 | 15 | | | | 130 | 17 | |
| | III Recovery | 60 | 3.10 | 51.6 | 30 | 11 | 15 | 160 | 90 | 120 | 160 | 22 | 2 |
| 4785 | I Control | 80 | 4.13 | 51.6 | 20 | 6 | 12 | 135 | 56 | 90 | 135 | 4 | 1 |
| | II Acute MI | 90 | 2.49 | 27.6 | 30 | 8 | 15 | 160 | 110 | 125 | 150 | 28 | |
| | III Recovery | 72 | 2.64 | 36.7 | 30 | 8 | 13 | 155 | 108 | 126 | 155 | 7 | 1 |
| Means | I Control | 81.5 | 3.40 | 42.6 | 21 | 5 | 11 | 128 | 69 | 90 | 145 | 5.8 | 1 |
| ±SEM | | 5.7 | 0.19 | 3.4 | 1.5 | 0.3 | 0.8 | 4.0 | 4.0 | 3.6 | 3.5 | 0.7 | 0.4 |
| | II Acute MI | 113.7* | 2.89 | 26.1* | 28 | 11 | 16 | | | | 137 | 20.7* | |
| | | 9.8 | 0.30 | 2.5 | 2.4 | 2.4 | 2.0 | | | | 4.4 | 1.7 | |
| | III Recovery | 88.0‡ | 4.20‡ | 47.0‡ | 27 | 7 | 13 | 135 | 80 | 104 | 152‡ | 14.2*‡ | 1 |
| | | 7.0 | 0.59 | 4.9 | 1.6 | 0.8 | 0.8 | 7.6 | 5.3 | 6.5 | 4.6 | 1.9 | 0.2 |

* Mean values significantly different from control state ($P < 0.05$).

‡ Mean values significantly different from acute myocardial infarction (MI) ($P < 0.05$).

of the relation of left ventricular–developed pressure, i.e., peak systolic minus end-diastolic pressure at various end-diastolic pressure levels. If only peak pressures are considered, these continue to rise along with left ventricular end-diastolic pressure throughout the obstruction.

Although some inconsistencies were present, depression followed by recovery of left ventricular function was reflected in alterations in hemodynamics. Acute myocardial infarction was always accompanied by tachycardia, marked elevation in left ventricular end-diastolic pressure, and a moderate fall in stroke volume. In most instances, left ventricular systolic pressure and cardiac output decreased and pulmonary arterial pressure rose. 7 days after myocardial infarction, left ventricular end-diastolic pressure was decreased but still abnormally high, while cardiac output and stroke volume had returned to normal. However, in contrast to ventricular function curves, which showed depression followed by recovery in all animals, hemodynamic changes were variable, as in most of the clinical studies which have been reported (12, 15, 18, 27).

Precise mechanisms of the recovery of left ventricular function after infarction are not known at present. Presumably, the depression of function in acute infarction results from loss of a fraction of functioning myocardium, sequestration of blood during systole by ballooning of the injured segment and various metabolic alterations interfering with energy utilization. Several mechanisms for recovery are possible: (*a*) Stiffening of infarcted myocardium during recovery from acute myocardial infarction (33) may increase the effective stroke volume. (*b*) Improvement in function of noninfarcted myocardium may occur (34) as a result of hypertrophy (35). (*c*) There may be recovery of ischemic tissue around the margin of infarct. (*d*) Rise in catecholamine levels (36) may increase the contractility of the heart. (*e*) Metabolic readjustments in nonischemic and ischemic myocardium (37) may play a role.

No attempt has yet been made to interrelate these diverse observations, or to determine the relative importance of each, although all of these effects are obviously pertinent to understanding the natural history of experimental canine coronary occlusion.

The demonstration of the remarkable propensity of normal ventricle to recover from acute myocardial infarction may help to explain cases of patients showing return to seemingly normal cardiac function (15–17, 27). These findings of the present study may have implications regarding temporary support for the circulation in the phase immediately after myocardial infarction in anticipation of some degree of spontaneous repair.

## ACKNOWLEDGMENTS

We are thankful to Dr. Christopher A. S. Pegg for helping with surgery in the animals, to Richard Wagner, B. E. E., Miss Mary T. Collins, R.N., Miss Dolores M. Dec, R.N., Jonathan S. Rothman, Robert P. Sather, James E. Martin, Philip Bornstein, Mrs. Faye M. Alpert, and Mrs. Vivianne L. Baskins for assistance in the experiments, and to Hynson, Westcott & Dunning, Inc., Baltimore, Md., for the supply of Indocyanine Green.

This work was supported by Grants PH43-68-684, HE 10539, HE 5244, and AM 10517 from the National Institutes of Health, and by the Ernest W. Lawson Grant, Northeast Chapter, Massachusetts Heart Association.

## REFERENCES

1. Case, R. B., E. Berglund, and S. J. Sarnoff. 1954. Ventricular function. II. Quantitative relationship between coronary flows and ventricular function with observations on unilateral failure. *Circ. Res.* **2**: 319.
2. Stone, H. L., J. S. Bishop, and A. C. Guyton. 1963. Cardiac function after embolization of coronaries with microspheres. *Amer. J. Physiol.* **204**: 16.
3. Orias, O. 1932. The dynamic changes in the ventricles following ligation of the ramus descendens anterior. *Amer. J. Physiol.* **100**: 629.
4. Tennant, R., and C. J. Wiggers. 1935. The effect of coronary occlusion on myocardial contraction. *Amer. J. Physiol.* **112**: 351.
5. Wegria, R., G. W. Frank, G. A. Misrahy, H. H. Wang, R. Miller, and R. B. Case. 1954. Immediate hemodynamic effects of acute coronary occlusion. *Amer. J. Physiol.* **177**: 123.
6. Agress, C. M., H. F. Glassner, M. J. Binder, and J. Fields. 1961. Hemodynamic measurements in experimental coronary shock. *J. Appl. Physiol.* **10**: 469.
7. Renais, J., L. Scébat, and J. Lenègre. 1964. Ischémie myocardique expérimentale du chien. IV. Conséquences hémodynamiques. *Arch. Mal. Coeur Vaisseaux.* **57**: 602.
8. Khomazyuk, A. I., A. P. Nescheret, and N. P. Kuzminsky. 1965. Some new ways of experimental research of myocardial infarction. *Kardiologiya.* **5**: 19.
9. Goldfarb, D., and V. L. Gott. 1968. Cardiovascular alterations during declining and steady-state low cardiac output secondary to coronary insufficiency in the dog. *J. Thorac. Cardiovasc. Surg.* **56**: 578.
10. Grishman, A., and A. M. Master. 1941. Cardiac output in coronary occlusion studied by the Wezler-Boeger physical method. *Proc. Soc. Exp. Biol. Med.* **48**: 207.
11. Pritchard, W. H. and H. K. Hellerstein. 1950. Cardiac catheterization following acute myocardial infarction. *J. Clin. Invest.* **29**: 839.
12. Freis, E. D., H. W. Schnaper, R. L. Johnson, and G. E. Schreiner. 1952. Hemodynamic alterations in acute myocardial infarction. I. Cardiac output, mean arterial pressure, total peripheral resistance, "central" and total blood volumes, venous pressure, and average circulation time. *J. Clin. Invest.* **31**: 131.
13. Gilbert, R. P., M. Goldberg, and J. Griffin. 1954. Circulatory changes in acute myocardial infarction. *Circulation.* **9**: 847.
14. Smith, W. W., N. S. Wikler, and A. C. Fox. 1954. Hemodynamic studies of patients with myocardial infarction. *Circulation.* **9**: 352.
15. Gammill, J. F., J. J. Applegarth, C. E. Reed, J. D. Fernald, and A. J. Antenucci. 1955. Hemodynamic changes

following acute myocardial infarction using the dye injection method for cardiac output determination. *Ann. Intern. Med.* **43**: 100.
16. Lee, G. de J. 1957. Total and peripheral blood flow in acute myocardial infarction. *Brit. Heart J.* **19**: 117.
17. Broch, O. J., S. Humerfelt, J. Haarstad, and J. R. Myhre. 1959. Hemodynamic studies in acute myocardial infarction. *Amer. Heart J.* **57**: 522.
18. Gunnar, R. M., A. Cruz, J. Boswell, B. S. Co, R. J. Pietras, and J. R. Tobin, Jr. 1966. Myocardial infarction with shock: hemodynamic studies and results of therapy. *Circulation.* **33**: 753.
19. Goodyer, A. V. N., M. J. Goodkind, and A. B. Landry. 1962. Ventricular response to pressure load. *Circ. Res.* **10**: 885.
20. Goodyer, A. V. N., M. J. Goodkind, and E. J. Stanley. 1964. The effects of abnormal concentrations of the serum electrolytes on left ventricular function in the intact animal. *Amer. Heart. J.* **67**: 779.
21. Hood, W. B., Jr., B. McCarthy, and B. Lown. 1969. Aortic pressure loading in dogs with myocardial infarction. *Amer. Heart. J.* **77**: 55.
22. Monroe, R. G., W. J. Gamble, C. G. LaFarge, and A. Edalji. 1969. Mean wall stress developed by the left ventricle at high end-diastolic pressures. *Fed. Proc.* **28**: 517.
23. Hood, W. B., Jr., J. Joison, R. Kumar, I. Katayama, R. S. Neiman, and J. C. Norman. Experimental myocardial infarction. I. Production of left ventricular failure by gradual coronary occlusion in intact conscious dogs. *Cardiovasc. Res.* In press.
24. Joison, J., R. Kumar, W. B. Hood, Jr., and J. C. Norman. 1969. An implantable system for producing left ventricular failure for circulatory-assist device evaluation. *Trans. Amer. Soc. Artifi. Intern. Organs.* **15**: 417.
25. Chimoskey, J. E., M. Szentivanyi, R. Zakheim, and A. C. Barger. 1967. Temporary coronary occlusion in conscious dogs. Collateral flow and electrocardiogram. *Amer. J. Physiol.* **212**: 1025.
26. Snedecer, G. W. 1956. Statistical Methods Applied to Experiments in Agriculture and Biology. The Iowa State University Press, Ames. 5th edition. 49.
27. Murphy, G. W., G. Glick, B. F. Schreiner, and P. N. Yu. 1963. Cardiac output in acute myocardial infarction. Serial determination by precordial radioisotope dilution curves. *Amer. J. Cardiol.* **11**: 587.
28. Hood, W. B., Jr., V. H. Covelli, W. H. Abelmann, and J. C. Norman. 1969. Persistence of contractile behavior in acutely ischemic myocardium. *Cardiovasc. Res.* **3**: 249.
29. Cotton, M. DeV., and N. C. Moran. 1957. Effects of increased reflex sympathetic activity on contractile force of the heart. *Amer. J. Physiol.* **191**: 461.
30. Sarnoff, S. J., J. P. Gilmore, S. K. Brockman, J. H. Mitchell, and R. J. Linden. 1960. Regulation of ventricular contraction by the carotid sinus. *Circ. Res.* **8**: 1123.
31. Tearney, R. J., and E. W. Hawthorne. 1969. Mechanoreceptor reflex influences on cardiac activity in awake instrumented dogs. *Fed. Proc.* **28**: 584.
32. Sarnoff, S. J., and E. Berglund. 1954. 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.
33. Bianco, J. A., W. B. Hood, Jr., V. H. Covelli, and J. C. Norman. 1968. Diminished ventricular compliance in experimental acute myocardial infarction. *Circulation.* **38** (Suppl. 6): 42.
34. Hood, W. B., Jr., and R. B. Whiting. 1968. Experimental myocardial infarction—increased fiber shortening in noninfarcted muscle. *Clin. Res.* **16**: 514.
35. Bergmann, V. W. 1968. Der Bindegewebsgehalt im Herzmuskel des Menschen bei acutem und chronischem Myokardinfarkt. *Arch. Kreislaufforsch.* **56**: 106.
36. Richardson, J. A., E. F. Woods, and E. E. Bagwell. 1960. Circulating epinephrine and norepinephrine in coronary occlusion. *Amer. J. Cardiol.* **5**: 613.
37. Gudbjarnason, S., and P. S. Puri. 1969. Adenine-nucleotide levels of non-ischemic cardiac muscle following coronary occlusion. *Fed. Proc.* **28**: 452.