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N71-34051

CIRCULATORY RESPONSES TO HYPOXIA IN EXPERIMENTAL MYOCARDIAL INFARCTION

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This work was supported in part by NIH grants Nos. HE-09058, HE-5709, and HE-5866, and a grant from the National Aeronautics and Space Administration, No. NGL-020-305.

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SYNOPSIS

Three levels of decreased arterial oxygen saturation elicited a graded circulatory response in dogs, manifested by stepwise increases in cardiac output, left ventricular dp/dt, and stroke volume and decreases in systemic vascular resistance. Responses to similar hypoxia challenges following experimental myocardial infarction were qualitatively similar but quantitatively less. Although the circulatory compensation for hypoxia was less effective following myocardial infarction, no further deterioration of the hemodynamics was noted.

INTRODUCTION

Arterial hypoxia is common in patients with cardiac and/or pulmonary disease. Recently several investigations have demonstrated that patients with severe myocardial infarction frequently develop decreased arterial oxygen tensions due to abnormalities of ventilation and perfusion (MacKenzie, Flenley, Taylor, McDonald, Staunton, and Donald, 1964; McNicol, Kirby, Bhoola, Everest, Price, and Freedman, 1965; Valentine, Fluck, Mounsey, Reid, Shillingford, and Steiner, 1966). Although the circulatory responses to systemic hypoxia in normal man have been described by several authors (Korner, 1959; Fishman, Fritts, and Cournand, 1960; Chidsey, Frye, Kahler, and Braunwald, 1961), little is known about the circulatory responses to mild systemic hypoxia in patients who have developed acute myocardial infarction. The general response to hypoxia in both conscious and anesthetized subjects is characterized by tachycardia, increased cardiac output and decreased systemic vascular resistance when the subject is allowed to alter his ventilation (Korner, 1959). When ventilation has been controlled during hypoxia experiments, the resultant data have varied considerably, perhaps due to the curariform compounds used as neuromuscular blocking agents (Murray and Young, 1963; Kontos, Mauck, Richardson, and Patterson, 1965). In animal studies most investigators interested in the mechanisms of hypoxia response have used oxygen levels which are incompatible with life over long periods rather than the more moderate levels of hypoxia

commonly found in patients (Korner, 1959; Woods and Richardson, 1959; Korner and White, 1966). To our knowledge no hypoxia studies have been conducted in animals with experimental myocardial infarctions.

This investigation was designed to permit comparison of the hemodynamic responses to hypoxia of normal animals with responses of the same animals after acute coronary artery ligation; and, by studying three levels of hypoxia, to clarify the circulatory mechanisms involved in the hypoxia response, particularly in the response to the mild hypoxia seen in clinical situations. The particular advantage of this model is that it allows estimation of the size of myocardial infarction, identification of the hemodynamic changes occurring with hypoxia, and control of the arterial blood gases, which may also alter circulatory dynamics.

METHODS

Studies were performed on twenty-one mongrel dogs weighing 8-24 kg. The animals were anesthetized with a mixture of alpha-chloralose (80 mg/kg) and urethane (500 mg/kg), with supplemental doses being administered to maintain light anesthesia, as judged by the corneal reflexes.

A midsternal thoracotomy was performed, and the animals were instrumented for physiological measurements. Central aortic pressure was monitored through a PE 260 catheter introduced into the right femoral artery. A similar catheter was advanced from the left carotid artery to the left ventricle. Left atrial pressure was measured through a PE 260 flange-tipped catheter placed directly in the left atrium through a stab wound in the appendage. All catheters were stiff polyethylene and were less than 50 cm in length. Pressures were measured

with Statham P23Db or P23De pressure transducers. The maximal rate of left ventricular pressure development (LV dp/dt) was recorded directly from the left ventricular pressure curve by means of an RC differentiator sensitive to 35 cps and was used as an index of myocardial contractility (Gleason and Braunwald, 1962). The right femoral vein was cannulated for drug and dextran administration.

Cardiac output was measured by means of a gated sine-wave electromagnetic flowmeter (Biotronex), placed on the ascending aorta just distal to the coronary arteries. Each flowprobe was calibrated by means of comparisons with multiple cardiac outputs, determined by standard indicator dilution techniques. The electrocardiogram was monitored continuously. All recordings were made on an 8-channel Beckman Model R direct-writing oscillograph. To assure temperature stability at 38.5°C throughout each study, all experiments were conducted on a Gorman-Rupp aquamatic pad, Model K-1-3.

A cuffed endotracheal tube connected to a Bennett Model PR-1A respirator was used to ventilate each animal. At various times throughout the study the lungs were expanded maximally to prevent the development of atelectasis. Compressed air, 12% oxygen-88% nitrogen and 8% oxygen-92% nitrogen were the gas mixtures used for ventilation. To assure respiratory stability, arterial pH, pO_2, and pCO_2 were monitored with a Model AME-1 Astrup microapparatus; calibrations were made several times daily. Ventilation was adjusted on the basis of oxygen tension in the arterial blood, measured by means of a modified Clark pO_2 electrode (Astrup, Jorgensen, Anderson, and Engel, 1960; Jensen, 1963), as well as the pH and pCO_2 readings. The percent oxygen saturation has been

calculated for each measurement using the pO_2 and pH to facilitate comparison of this study to previous works. Initial pH values varied from 7.34 to 7.40 and control pO_2 readings were maintained above 85 mmHg. Control pCO_2 values were all greater than 30 mmHg. Blood samples were withdrawn for determinations before each hypoxia challenge and at 2 minute intervals throughout the period of altered inspired gas mixtures. Blood samples ranged in size from 1 to 1.5 cc to avoid significant blood loss during the experiment. Packed cell volume and hemoglobin content were determined at the beginning and end of each study. Hemoglobin was measured by the cyanmethemoglobin method, using a Beckman Model B Spectrophotometer with a wavelength of 540 millimicrons.

The surgical procedure required approximately one hour. Dextran 70 was given to replace blood loss. After a 20-30 minute stabilization period, control recordings and blood gases were obtained. Each dog was then ventilated with 12% oxygen in nitrogen for 10 minutes, followed by 8% oxygen in nitrogen for 8 minutes. These time limits were selected because they allowed arterial oxygen saturations to stabilize above 70% while ventilating with the 12% oxygen mixture and between 50% and 70% while ventilating with 8% oxygen. Subsequently the oxygen saturation fell below 50% in some of the animals. Data were recorded continuously throughout the period of hypoxia. All twenty-one animals were then ventilated with 100% oxygen for 10 minutes, to assure rapid recovery, before being returned to compressed air ventilation. At the end of the hypoxic period, 6% Dextran 70 was administered to replace blood withdrawn for blood gas analysis.

Myocardial infarction was produced by ligation. All coronary artery branches on the posterior surface, not visibly supplying the septum or right ventricle, were ligated. After 15 minutes, the anterior descending branch of the left coronary artery was dissected free and ligated one-third the distance from the apex. To suppress ventricular arrhythmias during the ligation period, 0.5 mg/min lidocaine was infused using a Harvard infusion pump, and 1 cc quantities of 1 mg/cc lidocaine were applied directly to the myocardial surface. Following ligation of the coronary arteries and discontinuation of the lidocaine infusion, 30 minutes recovery time was allowed for hemodynamic stability to develop and for elimination of lidocaine from the system. The lidocaine half-life in plasma is approximately 13 minutes (Klein, Sutherland, and Morch, 1968) and clinical effects have generally disappeared after 10 to 20 minutes. The hypoxia challenges were then repeated following the same experimental protocol.

The extent of nonperfused area of the myocardium was determined at the end of each study by injecting Evans blue dye into the right and left coronary ostia. After fixing the hearts in formalin the left ventricle, including the septum, was separated and weighed. The nonperfused area of the free left ventricular wall, unstained by the Evans blue dye, was dissected and its weight compared to the weight of the entire left ventricle. The infarcted area is expressed as percent weight of the total left ventricle, including the septum.

Stroke volume was determined by dividing mean cardiac output by heart rate, and is expressed in milliliters per beat. An index of systemic vascular resistance was calculated in arbitrary units by

dividing mean aortic pressure by cardiac output (SVR/units). An IBM 360/50 digital computer, programmed to calculate means and standard errors and to perform paired and unpaired t-test analyses was used to analyze and evaluate the data.

The two main hypoxia data groups, pre-myocardial infarction and post-myocardial infarction have been divided into three levels of arterial oxygen saturation. The "moderate" hypoxia category (A) includes arterial oxygen saturations from normal to 70%, or hypoxia compatible with life. "Severe" hypoxia (B) represents oxygen saturations from 70% to 50%, a range known to result in excess lactate production (Huckabee, 1958). "Extreme" hypoxia (C) indicates less than 50% saturation, which is the threshold for stimulation of the sympathetic nervous system (Ng, Levy, DeGeest, and Zieske, 1966; Downing and Siegel, 1963) and catecholamine release from the adrenal glands (Baugh, Cornett, and Hatcher, 1959). Furthermore, when isolated hearts are perfused with hypoxic blood, 50% saturation represents the boundary between stimulation and inhibition of myocardial contractility (Ng et al., 1966). Some animals did not provide data at each of the hypoxia levels; therefore the "n" figures in Tables 1, 2 and 3, which indicate the number of values available for the computation of the mean of each parameter, vary. Control values for each parameter were obtained prior to the two hypoxia challenges. Where data were not available at a particular level of hypoxia, the control value for that animal has been omitted at that level, thus accounting for the slight variances in control mean values listed in each table.

RESULTS

Response to hypoxia before and after myocardial infarction

Prior to ligation of coronary arteries, hypoxia produced statistically significant increases in cardiac output, left ventricular dp/dt and stroke volume at all decreased arterial oxygen saturation levels and a significant decrease in systemic vascular resistance (Table 1). Aortic systolic pressure, left ventricular systolic and end diastolic pressures, and mean left atrial pressure increased significantly at the lower arterial oxygen saturations. The decrease in heart rate, while progressive, was not statistically significant.

Following coronary artery ligation, hypoxia produced increases in cardiac output, left ventricular dp/dt, left ventricular end diastolic pressure, stroke volume and mean left atrial pressure and a decrease in systemic vascular resistance. These changes were generally smaller and less consistently significant (Table 2) than those occurring before coronary artery ligation. Heart rate decreased slightly during hypoxia, but the changes were not statistically significant.

Comparison of responses to hypoxia before and after myocardial infarction reveals that the absolute changes occurring before coronary artery ligation were significantly greater for cardiac output ($p<0.05$ at all three levels), left ventricular dp/dt (Figure 1), left ventricular systolic pressure ($p<0.05$ at severe hypoxia) and stroke volume ($p<0.05$ at extreme hypoxia). In Figure 2 the percentage changes occurring in cardiac output before and after myocardial infarction are shown. Left ventricular end diastolic pressure rose, following infarction, to a significantly greater

extent in the moderate hypoxia range only. All other parameters showed no statistically significant differences.

Responses to myocardial infarction

Extent of myocardial infarction

The extent of the myocardial infarction varied in the 21 dogs from 20% to 41% of the total left ventricular weight; the average infarcted area was 29% ± 1.2%. The pattern of acute myocardial infarction with ST elevations, Q waves and T wave inversion was noted on the electrocardiogram.

Hemodynamic response to infarction

Comparison of pre-infarction and post-infarction control values for the 21 dogs subjected to hypoxia shows statistically significant decreases in cardiac output ($p<0.05$), left ventricular dp/dt ($p<0.01$), aortic pressure ($p<0.05$), left ventricular systolic pressure ($p<0.01$) and heart rate ($p<0.05$) following myocardial infarction. Systemic vascular resistance ($p<0.05$) and left ventricular end diastolic pressure ($p<0.01$) increased significantly.

Blood gases, hemoglobin, hematocrit

Blood gases obtained throughout the study are listed in Table 3. The values in each category are averaged, with "n" indicating the number of animals included in the computation. All pO_2 and percent oxygen saturation changes during hypoxia differed significantly ($p<0.01$), whether compared to their controls or to preceding or subsequent changes; comparisons before and after myocardial infarction, however, showed no significant differences. Following myocardial infarction, the arterial oxygen saturations of fewer animals fell below 50%, perhaps because of the slightly higher ventilation

pressures and/or rates required to maintain normal pH and pCO_2 values. Prior to myocardial infarction, the average respiratory rate was 6.7 per minute and the pressure on the respirator averaged 16.2 cm of water. Following ligation of the coronary arteries, average respiratory rate and pressure were 6.9 per minute and 17.8 cm of water.

Packed cell volume and hemoglobin content were determined at the beginning and end of each investigation. The initial and final hematocrit averages were 43.1 ± 1.3% and 39.1 ±1.5%. Average hemoglobin content, expressed in grams %, was 14.5 ± 0.5 at the onset and 13.7 ± 0.5 at the conclusion of the studies.

DISCUSSION

The circulatory responses to hypoxia which have been reported are complex and have raised much controversy (Korner, 1959). The general response in our study was characterized by an increase in cardiac output and arterial pressure and a decrease in systemic vascular resistance. These results are similar to those achieved with controlled ventilation by previous investigators (Murray et al., 1963). In this study specific hemodynamic changes were measured at several distinct levels of arterial oxygen. With mild to moderate hypoxia (O_2 saturation of greater than 70%) the cardiac output, left ventricular dp/dt, and stroke volume rose while systemic vascular resistance decreased. Heart rate did not change, but the rapid rates recorded initially suggest that the animals were under high adrenergic stimulation. However, the circulatory changes noted probably resulted from further increased sympathetic nervous stimulation to the heart and blood vessels. At lower arterial oxygen levels (severe and extreme hypoxia) there were also increases in aortic pressure, left ventricular systolic and end-diastolic

pressures, and mean left atrial pressure. Although these changes were small, they suggest even greater sympathetic stimulation to the circulatory system. The mechanisms by which stimulation of the circulatory system occurs in response to hypoxia are multiple and complex (Korner, 1959; Kontos et al., 1965; Daly and Scott, 1964). Stimulation of the peripheral aortic and carotid chemoreceptors (Daly and Scott, 1963; Daly and Ungar, 1966; Downing, Remensnyder, and Mitchell, 1962), medullary chemoreceptors (Downing, Mitchell and Wallace, 1963), and stretch receptors in the lung due to increased ventilation (Daly et al., 1963; Kontos et al., 1965) may all contribute. At lower oxygen saturations the release of catecholamines from the adrenal glands occurs (Baugh et al., 1959). Direct depression of the heart (Harrison, Blalock, Pilcher, and Wilson, 1927; Kahler, Goldblatt, and Braunwald, 1962; Ng et al., 1966) and blood vessels (Kahler et al., 1962; Ross, Fairchild, Weldy and Guyton, 1962) by hypoxia, usually noted below 50% saturation, was probably masked by the intense adrenergic stimulation. The slight slowing of the heart rate and elevation of the left ventricular end diastolic pressure may have been manifestations of this direct effect.

Coronary artery ligation produced electrocardiographic and hemodynamic consequences consistent with acute myocardial infarction. The large size of the infarction, as determined by the non-perfused tissue after termination of the experiment, suggests that long term survival in these animals would have been unlikely (Kumar, Hood, Joison, Norman, and Abelmann, 1970). With myocardial damage of this severity, there was significant depression of the cardiac output, left ventricular dp/dt, arterial pressure and heart rate. Systemic vascular resistance and left ventricular end diastolic pressure increased. These changes were profound immediately

after coronary artery ligation but, after 30 minutes, stabilized at a moderately depressed level. Control studies conducted in our laboratory have shown that animals prepared in this manner remain stable for more than 3 hours (Nola, Pope, and Harrison, personal communication). The circulatory changes noted in our anesthetized dogs are greater than those reported in intact awake dogs when coronary arterial ligation is carried out (Kumar et al., 1970) and may reflect the effects of anesthesia in modifying the animals' normal compensatory mechanisms to stress. However, the severity of the hemodynamic changes observed can be compared with those found in human subjects with severe myocardial depression (Thomas, Malmcrona, and Shillingford, 1965).

Once the circulatory depression was stable, further challenge with hypoxia at various levels was accomplished. The qualitative response to the various levels of hypoxia was similar to that observed in the animals before infarction; specifically, an increase in cardiac output, left ventricular dp/dt and stroke volume with mild to moderate hypoxia and increases in arterial pressure, left ventricular systolic and end diastolic pressures, and left atrial pressure with more severe hypoxia. Systemic vascular resistance fell at all hypoxia levels. The changes after myocardial infarction in cardiac output, left ventricular dp/dt, stroke volume and arterial pressure were quantitatively less than those observed before myocardial infarction when the same hypoxic challenge was given. It appears likely that the same compensatory mechanisms were activated to meet the stress of hypoxia, but in the presence of severe myocardial damage they were less effective. No further depression of the already damaged heart was observed, even at the level of extreme hypoxia . If these levels had been maintained for longer periods, perhaps further hemodynamic deterioration would have occurred.

Ventricular premature beats were observed in these animals immediately after coronary artery ligation and during hypoxia. There was, however, no detectable increase in premature beats during the post-infarction hypoxia challenges.

The implications raised by this study merit further comment. First, the circulatory response to the stress of hypoxia after acute myocardial infarction is qualitatively similar to that observed in the same animals before infarction. Although considerable effort was made to maintain blood volume, hematocrit, ventilation, and blood gases at comparable levels for each hypoxic challenge, the quantitative response to comparable levels of hypoxia was less after myocardial infarction. This inability of the animals to compensate for the hypoxic stress appears to be due to the circulatory damage produced by the coronary artery ligation. Secondly, there appears to be a graded circulatory response to various levels of arterial hypoxia. With mild to moderate hypoxia the hemodynamic changes were less than those occurring at the severe or extreme levels of hypoxia. There was an almost stepwise response of cardiac output, left ventricular dp/dt, stroke volume and systemic vascular resistance to the progressively more severe levels of hypoxia. When the most severe levels were reached, arterial pressure and left ventricular end diastolic pressure increased. Thirdly, although the levels of hypoxia were extreme, no further deterioration of the hemodynamics was noted in the heart damaged by myocardial infarction.

It is not possible to extrapolate from these studies to human myocardial infarction, but several points merit further comment. In order to respond to hypoxia a number of compensatory mechanisms in the circulatory

system are activated. In the presence of acute myocardial infarction these compensatory mechanisms are less effective in responding to the stress of hypoxia. It is suggested, therefore, that hypoxia should be avoided after myocardial infarction when ever possible. The administration of oxygen after myocardial infarction may also produce circulatory changes in patients (Foster, Casten, and Reeves, 1969), but these changes appear preferable to those noted with hypoxia.

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TABLE 1 - RESPONSE TO HYPOXIA PRIOR TO MYOCARDIAL INFARCTION

	Control n = 21	ΔA	Signif of ΔA	Control n = 21	ΔB	Signif of ΔB	Control n = 16	ΔC	Signif of ΔC	Significanc of Comparison ΔA-ΔB	ΔB-Δ
ean Ao Flow cc/min	1736±157	140±30	p<0.01	1736±157	337±57	p<0.01	1720±200	519±77	p<0.01	p<0.01	NS
V dp/dt mmHg/sec	4066±292	250±55	p<0.01	4066±292	1043±218	p<0.01	3972±350	1248±288	p<0.01	p<0.01	NS
o Systolic Pres. mmHg	140±4.2	-1.0±2.0	NS	140±4.2	5.4±2.7	NS	139±5.2	15.3±4.2	p<0.01	NS	p<0.0
o Mean Pres. mmHg	117±3.6	-0.4±1.9	NS	117±3.6	4.2±2.5	NS	116±4.6	7.1±4.0	NS	NS	NS
V Systolic Pres. mmHg	141±3.5	2.4±1.5	NS	141±3.5	13.0±2.4	p<0.01	140±4.2	22.5±4.0	p<0.01	p<0.01	p<0.0
V end Diastolic Pres. mmHg	6.0±0.4	-0.2±0.3	NS	6.0±0.4	0.6±0.5	NS	5.9±0.4	1.5±0.6	p<0.05	NS	NS
an LA Pres. mHg	6.0±0.3	0.2±0.2	NS	6.0±0.3	0.6±0.3	p<0.05	5.9±0.4	1.6±0.7	p<0.05	NS	NS
roke Volume l/beat	10.4±1.0	0.8±0.2	p<0.01	10.4±1.0	2.1±0.3	p<0.01	10.0±1.2	3.9±0.4	p<0.01	p<0.01	p<0.0
R mHg/lit/min	78±6.8	-5.5±1.7	p<0.01	78±6.8	-9.0±2.8	p<0.01	80±8.5	-16±3.2	p<0.01	NS	NS
art Rate eats/min	171±4.9	-0.6±1.8	NS	171±4.9	-3.6±4.7	NS	174±5.9	-12.5±7.0	NS	NS	NS

All figures represent means ± standard errors

ΔA = absolute change at > 70% arterial oxygen saturation before myocardial infarction

ΔB = absolute change at 50 - 70% arterial oxygen saturation before myocardial infarction

ΔC = absolute change at < 50% arterial oxygen saturation before myocardial infarction

The following abbreviations apply to Tables 1 and 2:

n = number of studies
Ao = aorta
dp/dt = rate of change of pressure

LV = left ventricle
LA = left atrium
SVR = systemic vascular resistance
NS = not significant

TABLE 2 - RESPONSE TO HYPOXIA AFTER MYOCARDIAL INFARCTION

	Control n = 21	ΔA_1	Signif of ΔA_1	Control n = 20	ΔB_1	Signif of ΔB_1	Control n = 9	ΔC_1	Signif of ΔC_1	Significance Comparisons ΔA_1-ΔB_1	Significance Comparisons ΔB_1-ΔC
Mean Ao Flow cc/min	1222±127	46±26	NS	1250±130	197±36	$p<0.01$	1339±213	227±106	NS	$p<0.01$	NS
LV dp/dt mmHg/sec	2546±164	75±40	NS	2554±174	486±118	$p<0.01$	2340±277	942±263	$p<0.01$	$p<0.01$	NS
Ao Systolic Pres. mmHg	126±3.2	-1.5±1.9	NS	126±3.4	4.0±3.1	NS	123±5.1	11.1±8.3	NS	NS	NS
Ao Mean Pres. mmHg	105±3.4	-1.2±1.7	NS	106±3.6	2.1±2.4	NS	101±5.8	4.1±6.4	NS	NS	NS
LV Systolic Pres. mmHg	127±3.7	-1.3±1.8	NS	128±3.8	4.3±2.8	NS	123±6.3	8.6±6.8	NS	NS	NS
LV end Diastolic Pres. mmHg	7.6±0.5	0.9±0.3	$p<0.05$	7.8±0.5	1.3±0.4	$p<0.01$	8.6±0.8	1.2±0.7	NS	NS	NS
Mean LA Pres mmHg	6.8±0.5	-0.1±0.2	NS	7.1±0.5	0.9±0.3	$p<0.05$	7.3±0.7	0.9±0.6	NS	$p<0.05$	NS
Stroke Volume ml/beat	8.0±0.8	0.4±0.2	$p<0.05$	8.1±0.9	1.6±0.3	$p<0.01$	9.1±1.5	1.9±0.7	$p<0.05$	$p<0.01$	NS
SVR mmHg/lit/min	100±8.3	-5.5±2.2	$p<0.05$	98±8.4	-12.0±3.6	$p<0.01$	88±12.5	-10.0±7.8	NS	NS	NS
Heart Rate beats/min	156±5.4	-3.4±1.8	NS	157±5.6	-5.4±3.0	NS	151±7.3	-7.2±5.3	NS	NS	NS

All figures represent means ± standard errors.

ΔA_1 = absolute change at > 70% arterial oxygen saturation after myocardial infarction

ΔB_1 = absolute change at 50 - 70% arterial oxygen saturation after myocardial infarction

ΔC_1 = absolute change at < 50% arterial oxygen saturation after myocardial infarction

Other abbreviations - See Table 1

TABLE 3 - ARTERIAL BLOOD GASES

	Pre-Myocardial Infarction				Post-Myocardial Infarction			
	Control	A	B	C	Control	A1	B1	C1
		n = 21	n = 21	n = 16		n = 21	n = 20	n = 9
pH	7.38±0.01	7.40±0.01	7.40±0.01	7.37±0.01	7.36±0.00	7.40±0.01	7.38±0.01	7.34±0.02
pO_2	89.6±2.3	48.0±1.0	33.0±0.5	25.8±0.8	86.7±1.6	49.0±1.2	33.8±0.5	27.2±1.1
$\%O_2$Sat.	96.2±0.2	79.8±0.9	59.3±0.7	41.8±1.9	95.5±0.3	79.8±1.0	59.8±0.8	42.6±1.3
pCO_2	30.5±0.7	28.8±1.0	28.8±1.1	31.2±1.1	30.1±0.4	28.6±1.2	28.9±1.8	35.4±3.7

All figures represent means ± standard errors

n = number of studies
A = values obtained at > 70% arterial oxygen saturation, before myocardial infarction
B = values obtained at 50-70% arterial oxygen saturation, before myocardial infarction
C = values obtained at < 50% arterial oxygen saturation before myocardial infarction
A1 = values obtained at > 70% arterial oxygen saturation, after myocardial infarction
B1 = values obtained at 50-70% arterial oxygen saturation, after myocardial infarction
C1 = values obtained at < 50% arterial oxygen saturation, after myocardial infarction

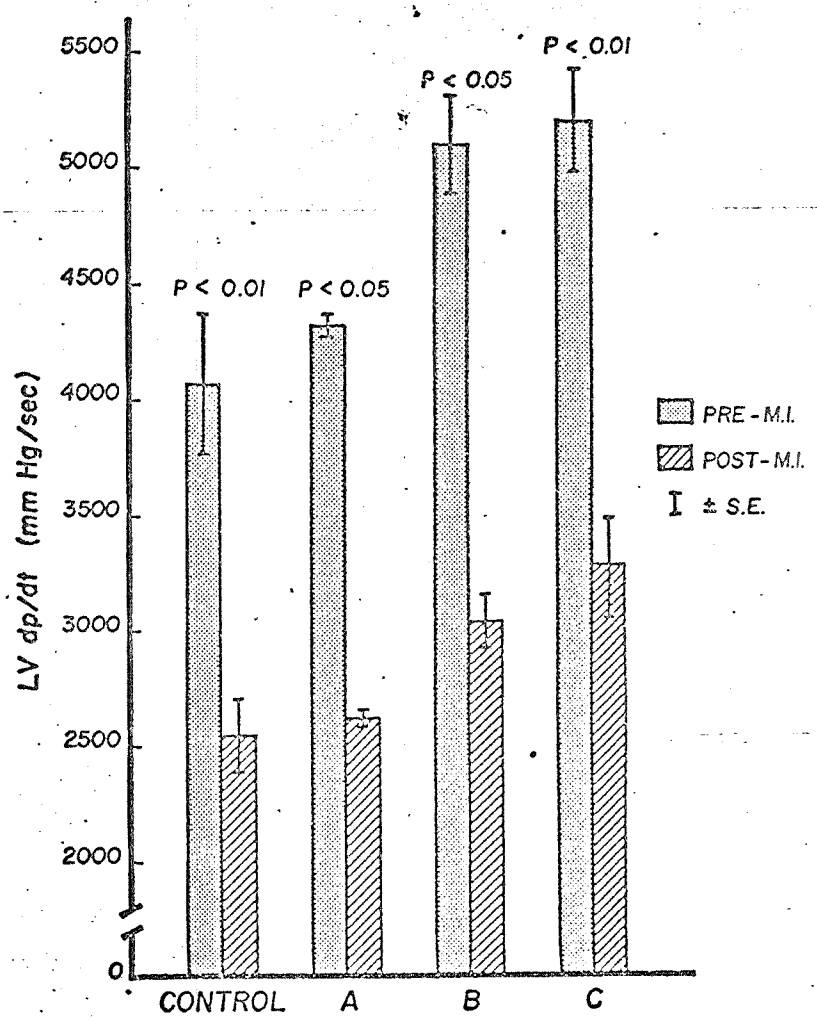
5500
5000
4500
4000
3500
3000
2500
2000
0
LV dp/dt (mm Hg/sec)
P < 0.01
P < 0.05
P < 0.05
P < 0.01
PRE-M.I.
POST-M.I.
± S.E.
CONTROL
A
B
C

Fig. 1

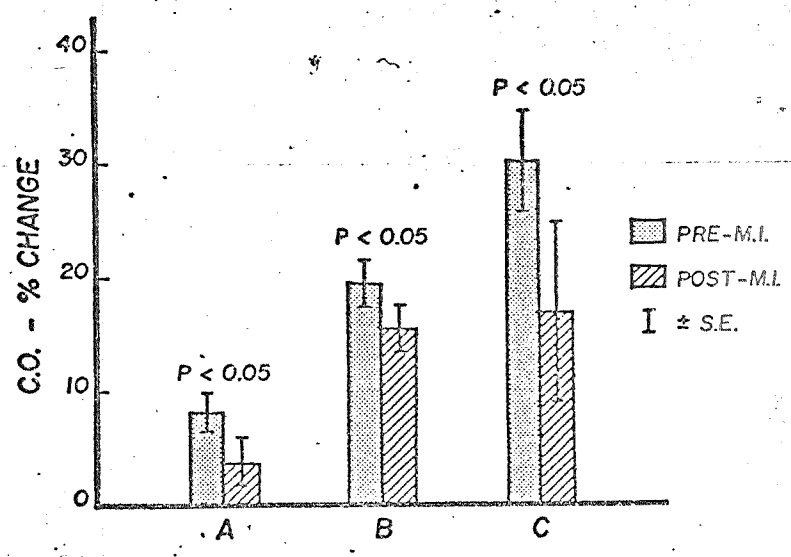

Fig. 2

FIGURE 1 - The rate of change of left ventricular pressure (mean and standard error) during the control period and at three levels of decreased arterial oxygen saturation before and after myocardial infarction is shown. The significance of the comparison of the pre- and post-myocardial infarction data at each level is shown by the P values in the figure.

A = > 70% arterial oxygen saturation
B = 50 - 70% arterial oxygen saturation
C = < 50% arterial oxygen saturation

FIGURE 2 - The changes in cardiac output, expressed in mean percent change of aortic flow ± standard error, at three levels of decreased arterial oxygen saturation before and after myocardial infarction are shown. The significance of the comparison of the pre- and post-myocardial infarction data at each hypoxia level is shown by the P values in the figure.

A = > 70% arterial oxygen saturation
B = 50 - 70% arterial oxygen saturation
C = < 50% arterial oxygen saturation

ACKNOWLEDGMENTS

The technical assistance of Mr. Fred Davis and Mr. George Snidow helped to make this study possible.