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Original Contributions

The oxygen consumption paradox of "stunned myocardium" in dogs*)

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Summary: The contractile state of the heart is a major determinant of myocardial oxygen consumption. Since regional myocardial contractility can be severely impaired following a transient coronary occlusion, post-ischemic myocardium is frequently assumed to consume less oxygen. To test this assumption, regional myocardial function and oxygen consumption were studied in anesthetized dogs during 2 h of myocardial reperfusion following either a 15-min (Group I) or 4-h (Group II) left anterior descending coronary artery occlusion. Both groups developed similar post-ischemic regional dysfunction characterized by paradoxical motion (negative shortening). Measured as a percent of baseline segment shortening, anterior wall function in Group I ($n = 8$) and Group II ($n = 5$) at 30 min of reperfusion was $-33 \pm 11\%$ and $-34 \pm 16\%$ ($p = NS$) and at 120 min was $-23 \pm 9\%$ and $-40 \pm 16\%$ ($p = NS$). However, the two groups showed a marked difference in regional myocardial oxygen consumption during reperfusion. Despite the abnormal wall motion, regional oxygen consumption in Group I at 30 and 120 min of reperfusion was unchanged from pre-ischemic levels as measured as a percent of baseline: $104 \pm 20\%$ ($p = NS$) and $111 \pm 21\%$ ($p = NS$). In contrast, regional oxygen consumption in Group II was markedly depressed from baseline at 30 and 120 min of reperfusion: $42 \pm 7\%$ ($p < .01$) and $40 \pm 8\%$ ($p < .01$). To determine whether the dissociation between regional myocardial oxygen consumption and function in Group I was related to mitochondrial uncoupling, six additional dogs were studied. Tissue samples were obtained from post-ischemic myocardium after 120 min of reperfusion following a 15-min coronary artery occlusion, and compared to non-ischemic myocardium. There were no differences in the in vitro mitochondrial respiratory rates or oxidative phosphorylation capacity between the post-ischemic and non-ischemic myocardium. Therefore, in the post-ischemic myocardium, significant depressions in regional contractility may not be associated with falls in oxygen consumption. Following a 15-min coronary artery occlusion, the injured myocardium maintains a paradoxically high oxygen consumption with normal mitochondrial function despite decreased contractility and abnormal wall motion.

Key words: myocardial ischemia, mitochondrial oxidative phosphorylation, regional myocardial dysfunction, reperfusion, oxygen consumption

Introduction

Regional myocardial contractility is usually impaired following a brief coronary artery occlusion. If the period of ischemia is sufficiently brief, function will ultimately recover fully,

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but regional impairment may persist for hours to days. For example, full functional recovery from a 15-min coronary occlusion may not be complete until 1 week after reperfusion (3, 6, 7). Some authors have referred to this dysfunctional post-ischemic reversibly injured tissue as "stunned myocardium" (2).

The etiology of stunned myocardium is unknown. Since active tension production as indexed by regional shortening and wall thickening are markedly diminished (6,7) it has been assumed that this tissue is relatively metabolically inactive. Low intracellular levels of adenosine triphosphate and adenosine diphosphate tend to confirm this metabolic quiescence and suggest that the post-ischemic cells may be incapable of generating sufficient levels of high energy phosphates for normal active contraction (12). Despite these assumptions, no index of metabolic activity has been measured in the post-ischemic myocardium. The purpose of this study was to determine regional myocardial oxygen consumption as an index of metabolic activity in both reversibly injured and irreversibly injured post-ischemic myocardial tissue, and to relate it to regional contractility as indexed by wall motion.

Methods

Part I: Oxygen consumption

Surgical preparation

Male mongrel dogs were anesthetized with pentobarbital (30 mg/kg IV). Respirations were maintained with a Harvard respirator with the respirator rate, tidal volume, and FIO2 adjusted to maintain an arterial oxygen saturation between 94% and 98%, and a pH between 7.36 and 7.44. A surface electrocardiogram was continuously monitored and recorded.

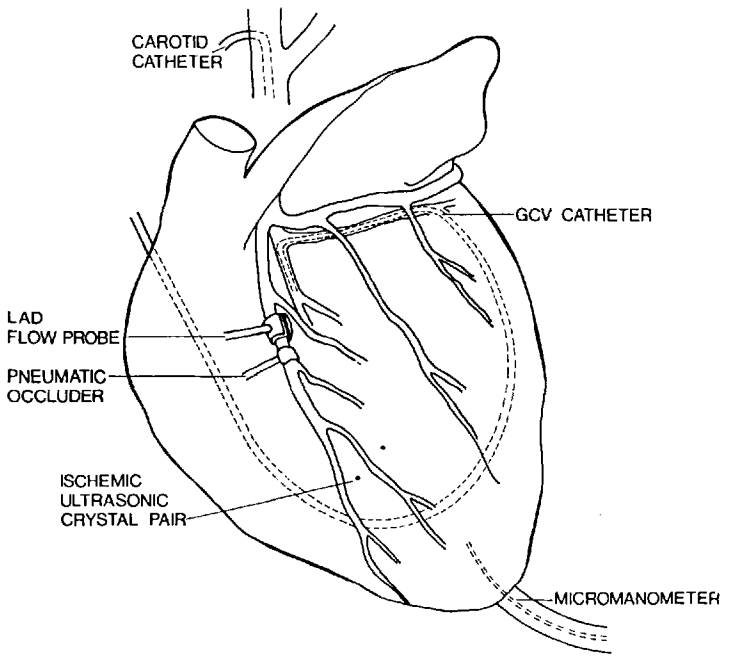

Fig. 1. Schematic representation of the surgical preparation. GCV = great cardiac vein. LAD = left anterior descending artery.

A thoracotomy was performed in the fifth left intercostal space, and the pericardium was opened to form a cradle. One-half centimeter of the left anterior descending artery proximal to the first major diagonal branch was dissected free from the epicardium (Fig. 1). A pneumatic occluder was placed around the artery and an electromagnetic flow probe (Carolina Instruments, Kings, North Carolina) was positioned just proximal to the occluder. A 5-s test occlusion was used to zero the flow meter. A Millar micromanometer (Houston, Texas) was placed into the left ventricle through a stab wound at the apex. Ultrasonic crystals were implanted in the subendocardium of the anterior wall oriented parallel to the minor axis to measure segment length. For venous sampling of the anterior wall, a catheter was placed via the right atrial appendage into the coronary sinus and advanced into the great cardiac vein. The catheter position was confirmed by direct palpation. For arterial sampling and blood pressure monitoring, a catheter was placed in the left common carotid artery and attached to a Statham pressure transducer (Oxnard, California). Oxygen saturation of the carotid artery and great cardiac vein blood was determined on heparinized blood samples which were immediately placed on ice and assayed within 15 min on an ABL3 Acid-Base Laboratory (Radiometer, Copenhagen). Regional myocardial oxygen consumption (RMV02) was calculated by the following formula: RMVO2 = (arteriovenous oxygen saturation gradient) × (left anterior descending coronary artery blood flow) × 1.34 × (hemoglobin concentration)/(risk mass).

Protocol

After the surgical preparation was performed, baseline carotid artery and great cardiac vein blood samples were drawn for oxygen saturation determinations, and hemodynamic data were recorded. Arterial and venous blood samples were withdrawn simultaneously at a rate of 1 cc/30 s. The balloon occluder was inflated around the left anterior descending artery causing total cessation of antegrade flow. Two groups of dogs undergoing reversible and irreversible ischemic injuries were studied (Fig. 2). Group I underwent a 15-min coronary artery occlusion, while Group II underwent a 4-h occlusion. The occluder was then released and sets of blood samples were again drawn 30 and 120 min after reperfusion. Group II underwent an additional 4 h of reperfusion to permit histochemical staining of any irreversible injury. Both groups were sacrificed by infusion of saturated potassium chloride. Risk and infarct size were determined by a previously described in vitro dual perfusion technique using trypan blue and triphenyl tetrazolium chloride (4).

Study population

Twenty male mongrel dogs weighing 23 to 34 kg were instrumented. Eleven of the 20 underwent a 15-min coronary artery occlusion; however, three dogs died with reperfusion following the occlusion leaving eight dogs in Group I. Nine dogs underwent a 4-h coronary artery occlusion. Four of the nine dogs died before completion of the study, two during the occlusion and two with early reperfusion, leaving five dogs to constitute Group II. All deaths were due to ventricular arrhythmias which were unresponsive to defibrillation within 1 min.

Validation of great cardiac vein sampling specificity

To determine the specificity of venous sampling from the great cardiac vein catheter with venous blood from the risk region, five Group I protocol dogs were studied. Between 30 and 120 min of

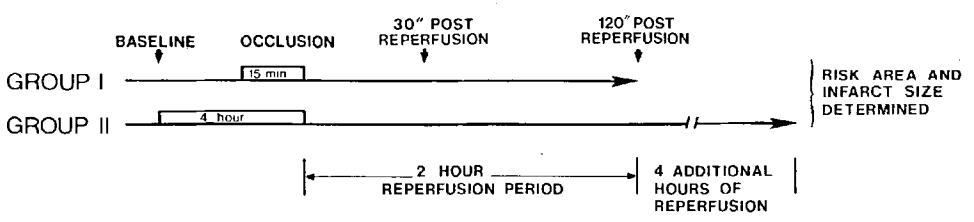

Fig. 2. The experimental protocol. Arrows indicate times when simultaneous arterial and great cardiac venous blood samples were drawn at baseline, 30 min, and 120 min post-reperfusion.

reperfusion, venous samples were randomly drawn from a great cardiac vein branch, which was distal to the first diagonal and close to the center of the post-ischemic bed with a 25-gauge butterfly needle. The oxygen saturation of this sample was compared with a simultaneously obtained sample from the great cardiac vein catheter.

Part II: Mitochondrial function
Surgical preparation and protocol

Six male mongrel dogs weighing 25 to 33 kg were prepared in a manner identical to Part I, except that they were only instrumented with a pneumatic occluder, ultrasonic crystals, and a Millar catheter. The left anterior descending coronary artery was occluded for 15 min and regional myocardial dysfunction was confirmed by the finding of dyskinetic movement of the ultrasonic crystals. After 15 min of occlusion, blood flow was restored and reperfusion continued for 2 h. Following the reperfusion period, the heart was excised quickly and placed in a basin containing normal saline at 4 °C to promptly cool the tissue. While immersed in the cold saline, approximately 1-cubic-centimeter sections were cut from the central area of ischemia between the ultrasonic crystals and from the non-ischemic posterior wall. These sections were then immediately placed in a beaker containing KEA (0.18 M KCl; 10 mM Tris-EDTA; 0.5 % bovine serum albumin, pH 7.40 at 4 °C). Mitochondrial isolation was accomplished using a modification of a previously described method (15) where the mitochondrial pellet was sequentially rinsed, resuspended ("washed") and recentrifuged in modified KEA solutions containing 1.0, 0.1, and 0.0 mM tris-EDTA. Respiratory rates and mitochondrial oxidative phosphorylation capacity were then determined polarographically (15). The mitochondrial subpopulation isolated by this technique is mainly subsarcolemmal in origin.

Analysis

Induction of ischemia was verified by dysfunction of muscular shortening as measured by the piezoelectric crystals in the anterior wall. Systolic function was expressed as the fractional change in segment length from end diastole to end systole. The end of diastole was defined from the dp/dt tracing as the time immediately preceding the upstroke of dp/dt. End systole was defined as occurring .04 s before peak negative dp/dt.

Statistics

Data are presented as mean ± SEM. Intergroup differences were examined using Students *t*-tests, and intragroup differences using paired *t*-tests. All statistical tests were performed with Bonferroni experiment-wise alpha-error protection (18).

Results

Part I: Oxygen consumption

Hemodynamics (Table 1)

Throughout the experiment, neither group demonstrated a significant change in any hemodynamic parameter, except for small increases in left ventricular end diastolic pressure. In Group I, left ventricular end diastolic pressure rose slightly during the coronary artery occlusion ($p < .05$), and remained slightly elevated above baseline ($p < .05$) at 30 min post-reperfusion. In Group II left ventricular end diastolic pressure increased during the occlusion ($p < .05$), at 30 min ($p < .05$), and at 120 min post-reperfusion ($p < .05$).

Regional myocardial function (Table 2)

Both a 15-min and a 4-h left anterior descending coronary artery occlusion caused profound regional myocardial dysfunction during the occlusion and throughout the subsequent 2 h of reperfusion (Fig. 3). Fifteen min after the onset of the coronary artery

Table 1. Hemodynamic data.

	Baseline	Occlusion	30 min post reperfusion	120 min post reperfusion
HR (b/min)				
Group I	151 ± 7	156 ± 7	154 ± 5	154 ± 6
Group II	152 ± 5	144 ± 5	139 ± 7	137 ± 9
MAP (mm Hg)				
Group I	101 ± 4	102 ± 6	103 ± 8	103 ± 9
Group II	119 ± 3	127 ± 5	122 ± 7	123 ± 8
LVEDP (mm Hg)				
Group I	6 ± 1	9 ± 1*	8 ± 1*	8 ± 2
Group II	7 ± 1	11 ± 1*	14 ± 2*	14 ± 2*
CBF (ml/min)				
Group I	52 ± 7	0	53 ± 9	53 ± 7
Group II	67 ± 14	0	58 ± 13	50 ± 14*

Results are expressed as means ± SEM. Group I (n = 8). Group II (n = 5).
Abbreviations: HR = heart rate; MAP = arterial pressure; LVEDP = left ventricular end-diastolic pressure; CBF = coronary blood flow (mean).
Statistically significant intragroup difference from baseline. * $p < .05$.

occlusion, systolic segment shortening, measured as a percent of baseline, was paradoxical and demonstrated negative shortening: $-71 \pm 15\%$ in Group I ($p < .01$) and $-58 \pm 18\%$ in Group II ($p < .01$) (Fig. 4). By the end of the 4-h occlusion in Group II, systolic shortening remained paradoxical at $-46 \pm 14\%$ of baseline ($p < .01$).

The paradoxical lengthening seen during the occlusions persisted in both groups throughout the 2-h reperfusion period. For Group I, systolic shortening was $-33 \pm 11\%$ ($p < .01$) and $-23 \pm 9\%$ of baseline ($p < .01$) at 30 and 120 min post-reperfusion, respectively.

Table 2. Segment length data.

	Baseline	Occlusion	30 min post reperfusion	120 min post reperfusion
EDL (mm)				
Group I	12.7 ± 2.0	14.8 ± 2.4**	14.4 ± 2.2**	14.5 ± 2.3**
Group II	12.6 ± 3.3	15.0 ± 2.9***	14.4 ± 2.8	14.5 ± 2.9
ESL (mm)				
Group I	11.0 ± 1.7	15.9 ± 2.6***	14.9 ± 2.3**	14.9 ± 2.3**
Group II	10.5 ± 2.6	16.2 ± 2.9**	15.3 ± 2.7***	15.5 ± 2.9***
Segment shortening (%)				
Group I	12.4 ± 1.8	−7.4 ± 0.8*	−3.2 ± 0.7*	−2.0 ± 0.7*
Group II	17.4 ± 1.4	−8.4 ± 2.9**	−6.5 ± 3.2**	−7.4 ± 3.4**

Results are expressed as means ± SEM. Group I (n = 8). Group II (n = 5).
Abbreviations: EDL = end diastolic segment length; ESL = end systolic segment length.
Statistically significant intragroup difference from baseline. * $p < .0001$, ** $p < .005$, *** $p < .05$.

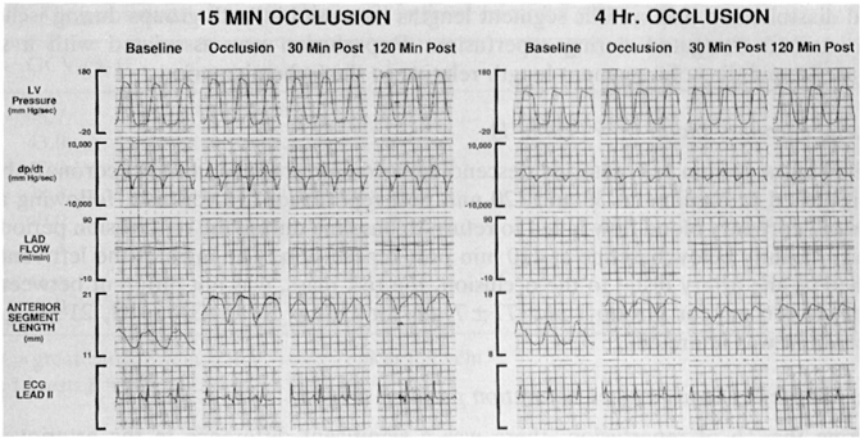

Fig. 3. Left ventricular (LV) pressure, dp/dt, mean left anterior descending coronary artery (LAD) blood flow, anterior wall segment length, and lead II of the surface electrocardiogram in two representative dogs at baseline, at the end of a transient LAD occlusion and after 30 and 120 min of reperfusion. The dog on the left was subjected to a 15-min ischemic period while the dog on the right underwent 4 h of coronary occlusion.

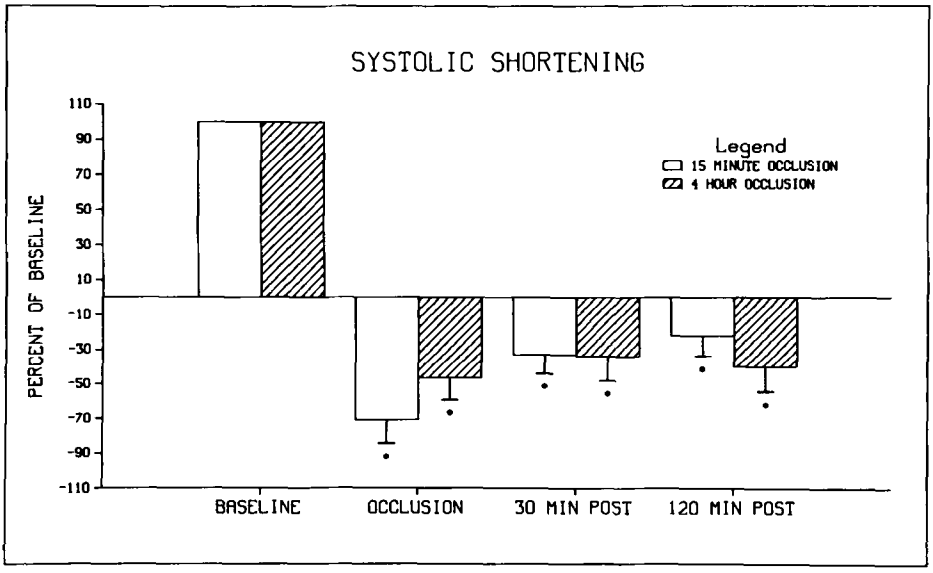

Fig. 4. Regional myocardial function measured as a percent of baseline systolic shortening of ultrasonic crystal pairs for the four experimental periods: baseline, end of occlusion, 30 min, and 120 min post-reperfusion. Group I ($n = 8$) represented by open bars and Group II ($n = 5$) represented by cross-hatched bars. * $p < .01$ difference from baseline.

Systolic shortening, for Group II, was $-34 \pm 16\%$ ($p < .01$) and $-40 \pm 16\%$ ($p < .01$) at 30 and 120 min post-reperfusion. The two groups were functionally indistinguishable at both 30 and 120 min post-reperfusion.

End diastolic and end systolic segment lengths increased in both groups during ischemia and remained elongated during reperfusion. Reperfusion was associated with a small decrease in end diastolic segment length relative to the ischemic period.

Regional coronary blood flow (Table 1)

Following a 15-min left anterior descending coronary artery occlusion, coronary blood flow returned to baseline at 30 and 120 min post-reperfusion. In contrast, following a 4-h occlusion, coronary blood flow failed to return to baseline during the reperfusion period and was significantly below baseline at 120 min post-reperfusion. The mass of the left ventricle supplied by the artery distal to the occlusion, the risk mass, was not different between the groups; 61 ± 6 gm for Group I and 77 ± 7 gm for Group II. In Group II, 21 ± 4 gm of myocardium was infarcted.

Regional arteriovenous oxygen saturation gradient (Fig. 5)

During the 2 h of reperfusion, there was a significant difference in the arteriovenous oxygen saturation gradient between groups. Following a 15-min left anterior descending coronary artery occlusion, the oxygen saturation gradient was $69 \pm 2\%$ at baseline and remained unchanged at 30 min, $67 \pm 2\%$, and at 120 min reperfusion, $68 \pm 2\%$. In contrast, following a 4-h occlusion, the gradient was $65 \pm 2\%$ at baseline and decreased markedly during the 2-h reperfusion period to $31 \pm 51\%$ ($p < .05$) and $34 \pm 6\%$ ($p < .05$) at 30 and 120 min, respectively.

Regional myocardial oxygen consumption

Following a 15-min coronary artery occlusion, regional myocardial oxygen consumption was unchanged from baseline over the 2-h reperfusion period. However, following a 4-h

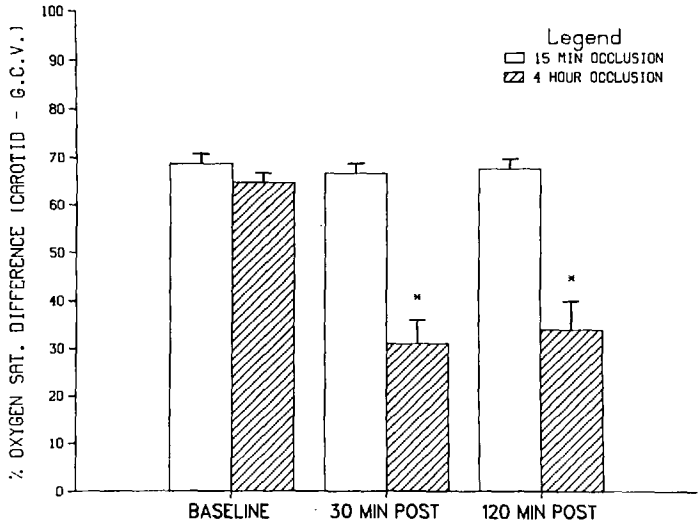

Fig. 5. Regional arteriovenous oxygen saturation gradient. The gradient was measured as the difference in percent oxygen saturation between simultaneously drawn pairs of arterial and great cardiac venous blood samples at baseline, 30 min, and 120 min post-reperfusion. Group I ($n = 8$) represented by open bars and Group II ($n = 5$) represented by cross-hatched bars. * $p < .05$ difference from baseline.

Table 3. Oxygen saturation great cardiac vein vs distal epicardial vein.

	GCV (%)	DEV (%)
	45.7	42.8
	43.0	43.3
	42.0	40.5
	38.3	40.2
	40.0	39.7
	39.3	39.6
Mean	41.4	41.0
SEM	1.0	0.6

GCV = great cardiac vein; DEV = distal epicardial vein.
Paired t-test: P = NS.

occlusion, regional oxygen consumption was profoundly depressed. Measured as a percent of baseline, RMVO2 was 104 ± 20 % at 30 min and 111 ± 21 % at 120 min post-reperfusion in Group I. In contrast, RMVO2 was 42 ± 7 % ($p < .01$) at 30 min and 40 ± 8 % ($p < .01$) at 120 min post-reperfusion in Group II.

Validation of great cardiac vein specificity (Table 3)

The oxygen saturation determinations from the great cardiac vein samples were essentially identical to the more distal great cardiac vein branch samples from the center of the risk region. The mean oxygen saturation for the great cardiac vein catheter samples was 41.4 ± 1.0 % and 40.0 ± 0.6 % for the more distal branch samples.

Table 4. Mitochondrial oxydative phosphorylation.

Substrate	State 3*	State 4*	R.C.R.	ADP:O	O.P.R.
Glutamate + malate					
non-ischemic	227 ± 27	15.7 ± 2.3	13.9 ± 2.2	2.82 ± .05	639 ± 73
post-ischemic	217 ± 25	17.5 ± 2.8	11.7 ± 1.6	2.82 ± .05	612 ± 73
Glutamate					
non-ischemic	207 ± 19	12.7 ± 2.2	15.3 ± 1.8	2.80 ± .02	577 ± 49
post-ischemic	192 ± 16	10.8 ± 1.9	21.9 ± 5.9	2.77 ± .04	529 ± 39
Malate					
non-ischemic	85 ± 7	14.8 ± 2.0	6.2 ± 0.8	2.89 ± .05	245 ± 17
post-ischemic	86 ± 17	14.0 ± 2.5	6.5 ± 1.5	2.97 ± .14	256 ± 50
Succinate + rotenone					
non-ischemic	259 ± 19	55.5 ± 5.2	4.8 ± 0.4	1.59 ± .05	412 ± 34
post-ischemic	239 ± 26	64.2 ± 10.9	4.0 ± 0.5	1.48 ± .07	352 ± 39

R.C.R. = respiratory control ratio (state 3/state 4); ADP:O = oxygen ratio.
O.P.R. = oxidative phosphorylation rate (state 3 × corresponding ADP:O ratio).
Mitochondrial studies were performed at 30 °C. Substrates were prepared as tris salts, and their final concentrations were 5 mM (glutamate, malate) or 9.4 mM (succinate).
The final ADP concentration was 319M. Rotenone concentration was 1 g/mg mitochondrial protein.
P = NS for any parameter non-ischemic vs post-ischemic.
* Oxygen consumption (n atoms O/min/mg protein).

Part II: Mitochondrial function

Mitochondrial oxidative phosphorylation (Table 4)

Mitochondrial function of stunned myocardium after 2 h of reperfusion was normal and not significantly different from that of non-ischemic myocardium. Using four different substrates or substrate combinations, there was no difference in state 3 respiratory rates, state 4 respiratory rates, the adenosine diphosphate:O ratios, the respiratory control ratio or the oxidative phosphorylation rate between tissue derived from post-ischemic bed following 2 h of reperfusion and tissue derived from non-ischemic control myocardium.

Discussion

This study demonstrates that myocardium that has undergone a reversible ischemic insult continues to consume oxygen during the first 2 h of reperfusion at a rate which is equivalent to its pre-ischemic baseline. Thus, despite markedly reduced regional contractility as evidenced by paradoxical wall motion, metabolic activity remains high. In contrast, myocardium having undergone an irreversible injury has both depressed contractility and correspondingly reduced regional oxygen consumption.

The finding that stunned myocardium consumes oxygen at a normal pre-ischemic rate was unexpected since contractility was thought to be a primary determinant of metabolic activity (5, 14, 16, 17). The only previous study of post-ischemic myocardial oxygen consumption was in an isolated non-blood perfused rat heart model subjected to 15 min of partial left ventricular ischemia (9). Although post-ischemic oxygen consumption was not reduced, both the ischemic insult (a 22 % reduction in antegrade coronary flow) and the post-ischemic dysfunction (a 27 % fall in cardiac output) were mild and may not have been sufficient to produce changes in oxygen consumption. The present study using a regional model of severe ischemia producing myocardium with profoundly depressed contractility should have reliably detected any changes in post-ischemic oxygen consumption.

Normal levels of oxygen consumption in stunned myocardium confirm the tight linkage of coronary blood flow to oxygen consumption (1, 14). Previous studies have shown that coronary blood flow in post-ischemic stunned myocardium is not significantly different from baseline pre-ischemic blood flow (6, 7). Although relatively small changes in endocardial to epicardial flow ratios have been demonstrated with microspheres in post-ischemic reversibly injured myocardium, total transmural blood flow has not differed significantly from baseline after 1 h of reperfusion (7). Since blood flow returns to normal in stunned myocardium and blood flow is tightly linked to oxygen consumption, then perhaps it should not have been unexpected that oxygen consumption is normal in stunned myocardium.

Previous studies have shown a marked regional depletion of myocardial adenine nucleotides in this model of stunned myocardium (3, 8, 11, 12), and the endogenous repletion of those adenine nucleotides parallels the time-course of myocardial functional recovery (3, 12). This has suggested that the functional recovery of stunned myocardium is delayed by the slow repletion of adenosine triphosphate stores. This study provides indirect evidence against a central role of depressed adenosine triphosphate precursors as a cause of the mechanical dysfunction of stunned myocardium. If metabolism and, therefore, contractile function is limited by a reduced supply of adenosine triphosphate, then oxygen consumption would be reduced. In contrast, the experimental finding of normal regional myocardial oxygen consumption suggests that reduced adenosine triphosphate levels do not limit metabolism.

The dissociation between regional myocardial oxygen consumption and regional contractility seen in stunned myocardium does not appear to be secondary to mitochondrial

uncoupling. Assuming that an uncoupling agent was not removed during the isolation process, the mitochondrial function of stunned myocardium was not different than that of non-ischemic myocardium (Table 4). In particular, there was no difference in the oxidative phosphorylation rate between the stunned and the non-ischemic myocardium. Although mitochondrial function has not been extensively studied in the canine model of stunned myocardium, Mukherjee and colleagues examined three mongrel dogs and found no difference in state 3 respiration or respiratory control index between myocardium which had undergone a 15-min left anterior descending coronary artery occlusion followed by 90 min of reperfusion and the control non-ischemic myocardium (9). This confirms the present study's findings but does not provide direct evidence about the efficiency of adenosine triphosphate production from the oxygen consumed. Murphy and coworkers studied seven pigs and also found no difference in state 3 respiration or respiratory control index between myocardium having undergone a 15-min left anterior descending artery occlusion and then 2 h of reperfusion and the control non-ischemic myocardium (11). They also failed to see any difference in the adenosine triphosphate/oxygen consumed ratio, indicating that they could not detect a significant decrease in the metabolic efficiency of the mitochondria from stunned myocardium.

Other mechanisms besides mitochondrial uncoupling could explain the normal post-ischemic oxygen consumption. High-energy phosphates produced when oxygen is consumed could be shunted to other metabolic processes besides active contraction. This metabolic energy could be used for maintaining electrochemical intracellular gradients which require more energy because the cellular membranes were damaged during ischemia or early reperfusion. Energy could be required to resynthesize cellular constituents which were either destroyed or lost during the period of ischemia. Besides adenine nucleotides, other intracellular metabolic intermediates, as well as structural and enzymatic proteins may be lost and their resynthesis required. The metabolic energy may be required to maintain wall tension in the regionally dilated segment of myocardium (5). Finally, the supply of high energy phosphates may not be efficiently used to support a variety of cellular functions including active contraction.

The study design assumed that the venous outflow sampling was relatively specific for the ischemic region of myocardium and that the specificity was unchanged between baseline and the reperfusion period. Previous work has shown that nearly 100 % of the blood in the great cardiac vein is derived from the left anterior descending coronary artery in the dog (13). The close correlation between the oxygen saturations sampled from the great cardiac vein branch, provides strong evidence for the specificity of the great cardiac vein sampling (Table 3). Further indirect evidence is the positive control of the experiment where oxygen consumption was reduced in myocardium undergoing infarction (Group II).

An important limitation of this study was that subregional analysis is not possible with the techniques employed. The post-ischemic risk region was likely to be heterogeneous in its consumption of oxygen and the degree of functional depression. For example, myocardial perfusion in the post-ischemic subendocardium was likely reduced (7), yielding a subregional depression in myocardial oxygen consumption (unless the corresponding subregional arteriovenous oxygen gradient was simultaneously increased). Thus, the relationship between contractile function and oxygen consumption may have been preserved in some areas of the post-ischemic myocardium after 15 min of ischemia. Conversely, after a 4-h coronary occlusion some subunits of the post-ischemic myocardium may have developed a relative dissociation between contractile function and oxygen consumption. However, since regional contractile function was depressed following a 15-min coronary artery occlusion while regional oxygen consumption was preserved, then at least some subregions within the post-ischemic myocardium must have had significant dissociations between function and

oxygen consumption. Techniques capable of resolving this heterogeneity on a subregional basis for blood flow, oxygen saturation, as well as contractile function would be required for further analysis.

These results demonstrate that the contractile state of the post-ischemic myocardium is not a primary determinant of oxygen consumption. Myocardium stunned by a reversible ischemic insult can have a marked functional impairment but, paradoxically, normal oxygen consumption. In contrast, myocardium with equally depressed contractility following an irreversible insult will have a reduced oxygen consumption. Although the cellular or biochemical derangements producing this dissociation between contractility and oxygen consumption in the post-ischemic myocardium have not been defined, the observation may have clinical utility in permitting reversibly injured, stunned myocardium to be differentiated from irreversibly injured infarcted myocardium.

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