Myocardial Balance of Inorganic Phosphate and Enzymes in Man

Effects of Tachycardia and Ischemia

By Miguel A. Chiong, M.D., Ph.D., Roxroy West, M.D., and John O. Parker, M.D.

SUMMARY

The effects of atrial pacing on the cardiac balance of inorganic phosphate \((P_i)\) were studied during control, atrial pacing, and recovery periods in 29 patients. Group A \((n = 18)\) who had roentgenographically demonstrated coronary artery disease (CAD) developed angina during pacing, and showed mean myocardial lactate \((L)\) production, abnormal left ventricular end-diastolic pressure \((LVEDP)\) and ST segment depression. Group NA \((n = 11)\), composed of six patients with CAD and five subjects with no demonstrable cardiac disease, had normal lactate metabolism, LVEDP, and ST segments during pacing. In addition, blood levels of two enzymes were determined: creatine phosphokinase \((CPK)\) in nine patients of Group A and six patients of Group NA, and glutamic oxaloacetic transaminase \((GOT)\) in eight patients of each group.

During control, small uptake of \(P_i\) was observed in both groups. During pacing, Group A showed first a fall and then abolition of mean \(P_i\) uptake, and during the early recovery period, a small loss of this ion was observed. Although there was a good correlation between \(L\) and \(P_i\) uptake \((r = 0.86, P < 0.001)\) throughout the study, \(P_i\) loss, which occurred in 55% of patients in Group A, appeared to be a less reliable index of myocardial anaerobiosis than \(L\) production, which occurred in 72%. No consistent changes in \(P_i\) balance were observed in Group NA. The only significant enzymatic change was the small but sudden and significant rise of mean CPK levels in coronary sinus \((CS)\) blood above the arterial levels in five patients of Group A during the first 6 min of pacing. These data show that during pacing-induced angina the human heart loses \(P_i\). In addition, these preliminary observations on the CS CPK levels during pacing in the angina patients suggest that the stress of tachycardia and ischemia may facilitate the escape of this enzyme from the heart.

Additional Indexing Words:
Atrial pacing  Coronary artery disease  Angina  Myocardial anaerobiosis
Creatine phosphokinase  Lactate  Glutamic oxaloacetic transaminase
Left ventricular end-diastolic pressure  ST segments

CARDIAC MUSCLE contains enzymatic systems required for the transformation of substrate-derived energy into the organic phosphate compounds, adenosinetriphosphate \((ATP)\), and creatine phosphate \((CP)\). During myocardial ischemia a fall in the tissue concentrations of these compounds has been reported,\(^1\)\(^-\)\(^3\) as well as an increase in the levels of adenosine di- and monophosphates \((ADP, AMP)\) and inorganic phosphate \((P_i)\).\(^4\)\(^,\)\(^5\) If myocardial ischemia is severe and results in cell death there is not only a release of intracellular enzymes\(^6\) but a decreased cellular content of \(K^+\) and \(P_i\).\(^7\)\(^,\)\(^8\) It is reasonable, therefore, to expect that these ions would escape from the injured myocardium and be detected in the cardiac venous effluent. This has, indeed, been shown in dogs after interruption of the coronary circulation.\(^9\)

It is possible, however, that release of ions and enzymes may occur during a less severe and reversible type of myocardial ischemia. Leakage of \(K^+\) and \(P_i\) ions has been reported in dogs subjected to a gradual reduction of coronary blood flow,\(^10\) and in patients with coronary artery disease \((CAD)\), transient myocardial ischemia induced by atrial
pacing\textsuperscript{11} has been found to be associated with lactate production and K\textsuperscript+ loss.\textsuperscript{18} However, there are no data on the possible release of P\textsubscript{i} and enzymes from the human heart during ischemia, with the exception of one report.\textsuperscript{14} Therefore the present study was designed to explore the possibility that P\textsubscript{i} and two myocardial enzymes, creatine phosphokinase (CPK), and glutamic oxaloacetic transaminase (GOT), may be released in the coronary sinus (CS) blood during the stress of atrial pacing in patients with coronary artery disease.

Materials and Methods

The study was carried out in 29 subjects referred for investigation of suspected CAD (table 1). All patients were free of arrhythmias, cardiomegaly, or clinical evidence of cardiac failure, and none of them was receiving digitalis or diuretics at the time of the study. Mildly elevated arterial blood pressure levels (greater than 150 mm Hg systolic and 90 mm Hg diastolic) were present in three subjects. Hemodynamic and metabolic studies were carried out during an 8 min control period, an 8 min period of atrial pacing, and a recovery period of similar duration. Selective coronary angiography was subsequently carried out and 24 patients were found to have CAD. Eighteen of these developed angina during atrial pacing and constitute the angina group (A). The nonangina group (NA) was composed of six patients with CAD who did not develop ischemic pain during pacing and five patients shown to be free of cardiac disease.

Hemodynamic measurements, which included right and left heart pressures, brachial artery pressure, cardiac output, and heart rate, were obtained by procedures described in detail elsewhere.\textsuperscript{11,13} The

\begin{table}
\centering
\caption{Summary of Patients}
\begin{tabular}{|c|c|c|c|c|c|c|c|c|}
\hline
Patient & Sex & Age & CAD & LV & Angina & Lactate production & Pt. loss & ST depression (>1 mm) & LVEDP\textsubscript{i} (>12 mm Hg) \\
\hline
\multicolumn{9}{|c|}{Group A (n = 18)} \\
\hline
JD & M & 47 & 3 & ↓ & Yes & Yes & No & Yes & Yes \\
GD & M & 47 & 2 & N & Yes & Yes & Yes & Yes & Yes \\
EL & M & 40 & 2 & ↓ & Yes & Yes & Yes & No & Yes \\
RB & M & 47 & 2 & N & Yes & No & Yes & Yes & Yes \\
RC & F & 59 & 1 & N & Yes & Yes & No & Yes & Yes \\
JM & M & 41 & 1 & ↓ & Yes & Yes & Yes & Yes & No \\
FS & M & 53 & 3 & N & Yes & Yes & Yes & Yes & Yes \\
PC & M & 59 & 2 & ↓ & Yes & Yes & Yes & Yes & Yes \\
PMeK & M & 50 & 1 & ↓ & Yes & Yes & No & Yes & Yes \\
HS & M & 41 & 2 & ↓ & Yes & Yes & Yes & No & Yes \\
JG & M & 49 & 2 & ↓ & Yes & No & Yes & Yes & Yes \\
HH & M & 39 & 3 & N & Yes & Yes & No & Yes & Yes \\
WMcC & M & 55 & 2 & ↓ & Yes & Yes & No & Yes & Yes \\
GH & M & 68 & 3 & N & Yes & Yes & No & Yes & Yes \\
NH & M & 37 & 2 & ↓ & Yes & No & No & No & Yes \\
RH & M & 53 & 3 & ↓ & Yes & No & Yes & No & Yes \\
DL & F & 49 & 1 & ↓ & Yes & No & No & Yes & Yes \\
\hline
\multicolumn{9}{|c|}{Group NA (n = 11)} \\
\hline
JV & M & 57 & 1 & N & No & No & — & No & No \\
CS & M & 40 & 1 & ↓ & No & Yes & No & No & No \\
HH & M & 37 & 2 & N & No & Yes & No & No & No \\
GB & M & 47 & 1 & N & No & Yes & No & Yes & No \\
CB & M & 56 & 1 & N & No & No & — & No & Yes \\
GF & M & 36 & 0 & N & No & Yes & Yes & No & Yes \\
WF & M & 43 & 0 & N & No & No & No & No & No \\
GO'D & M & 42 & 0 & N & No & No & Yes & No & No \\
EC & F & 47 & 0 & N & No & No & No & No & No \\
HC & F & 55 & 0 & N & No & No & No & No & No \\
JC & M & 47 & 0 & N & No & No & No & No & Yes \\
\hline
\end{tabular}
\end{table}

Abbreviations: A = angina group; NA = nonangina group; M = male; F = female; CAD = coronary artery disease (0–3 indicates number of vessels with narrowing of more than 75\%); LV = left ventriculogram; Pt\textsubscript{i} = inorganic phosphate; ST = ST segments; LVEDP\textsubscript{i} = left ventricular end-diastolic pressure during interruption of pacing; AA = apical aneurysm; N = normal; ↓ = decreased contractility.
coronary sinus (CS) was catheterized with a No. 8 Gorlin catheter which permitted simultaneous pacing and blood sampling. The first derivative of the left ventricular pressure (dp/dt) was obtained by means of a R-C differentiator with a time constant of 0.5 mm/sec and an output linearly proportional to the input frequency (±5%) up to a maximum of 75 cycles (Hz) (Electronics for Medicine, Model DB12). Left ventricular stroke work index (LVSWI) in g-m/m² was calculated using the formula

\[ \text{LVSWI} = \frac{SI (BAm - LVEDP) \times 13.6}{1000} \]

where SI = stroke work index in g-m, BAm = brachial artery mean pressure in mm Hg, and LVEDP = left ventricular end-diastolic pressure in mm Hg. The modified tension-time index (TTI) was calculated as the product of peak left ventricular systolic pressure and the heart rate.¹⁵

Arterial and CS blood for metabolic studies were drawn simultaneously through a Technicon pump at a rate of 2.5 ml per minute into heparinized tubes placed in a fraction collector set to change every 2 min.¹⁶ Thus, every tube contained an integrated sample of blood drawn continuously over a 2 min period. Plasma was separated by centrifugation at 3°C within 30 min and kept frozen at −30°C for the determination of lactate (L), Pᵅ, CPK, and GOT. Lactate was determined by automated colorimetric and fluorometric methods.¹⁷,¹⁸ There was no difference between these two methods and the lactate results were pooled. Pᵅ was determined by a Technicon automated-method (N-4C I/II) which consistently gave values 20% lower than the SM-12 autoanalyzer system. Recoveries from commercial controls with known amounts of Pᵅ averaged 94.1±3.8% (mean ± se; n = 36). Repeated determinations of pooled plasma gave a standard deviation of 0.02 mg/ml (n = 28). Myocardial uptake of L and Pᵅ were expressed as percent of arterial concentrations according to the formula

\[ \frac{A-CS}{A} \times 100 \]

where A and CS are concentrations in arterial and CS blood, respectively, in mg/100 ml. Enzymes blood levels were determined using a colorimetric method for CPK (Sigma kit No 661; normal values less than 12 units/ml) and a fluorometric automated method for GOT (Technicon Nb8 I/II; normal levels: 10–40 Karman units). Whereas lactate and Pᵅ were determined in all patients, CPK was determined in 15 subjects (nine in Group A and six in Group NA) and GOT in eight patients of each group. This restriction was necessary to minimize blood loss when using the continuous sampling technique.

Results

A clinical summary of the patients included in this study appear in table 1. The angina group (A) was composed of 18 subjects who developed chest pain during atrial pacing. The mean age for the group was 50.4 years (range between 37 and 68 years). Three-vessel disease (more than 75% narrowing) was found in five subjects, two-vessel disease in nine, and one-vessel disease in four patients. Left ventricular contractility during ventriculography was decreased in 12 patients, and one of these had an apical aneurysm.

The nonangina group (NA) included 11 patients with a mean age of 46.1 years (range between 37 and 57 years). Six of the subjects had coronary artery disease and five did not have demonstrable heart disease. Left ventricular contractility was impaired in a patient (CS) with one-vessel disease where the obstruction was located in the proximal portion of the left anterior descending artery.

Metabolic Results

Group NA

This group was composed of patients with CAD who did not develop angina during atrial pacing and normal subjects. No difference was found between these two categories and the time course of the results were pooled and are presented in figure 1 and summarized in table 2.

Arterial and CS lactate levels remained relatively constant during the study. Lactate extraction averaged 19.0 ± 1.4% during control, and 13.7 ± 3.1% during pacing, but there was no significant difference between these two periods. The slight fall in lactate uptake during pacing was due to abnormal lactate metabolism in two subjects with CAD (HH and GB).

Blood levels of Pᵅ also remained constant during the study. There was a small uptake of Pᵅ by the heart during the control period reflected by a mean extraction ratio of 5.4 ± 0.7%. Pᵅ uptake during pacing was quite variable, with mean values somewhat lower than during the control period, but this did not appear to be related to the presence of coronary artery disease. Two patients (one normal and the other with CAD) showed release of Pᵅ during pacing. During the recovery period, Pᵅ levels became more stable and uptake rose toward the control values. There was no correlation between the uptakes of L and Pᵅ at any time during the study (fig. 2).

CPK levels were determined in six subjects of this group. A small but consistent positive A-CS difference, observed during the control and recovery periods, became negative during pacing. These changes, however, were not statistically significant. CS levels of GOT were steady and slightly lower than those in arterial blood and remained unchanged during the study.
GROUP NA

LACTATE (% UPTAKE)  PACING

CS

(% UPTAKE)

Pi (% UPTAKE)  PACING

CS

CPK (units)  PACING

CS

GOT (units)  PACING

CS

Figure 1

Time course of blood levels of L, Pi, CPK, and GOT and mean % uptakes of lactate and inorganic phosphate (Pi) in nonangina group (NA). Each number on the abscissa represents a blood sample taken over a 2 min period. Values are mean ± se. CPK = creatine phosphokinase; GOT = glutamic oxaloacetic transaminase.

Group A

The time course of the metabolic results in the angina patients appear in figure 3 and are summarized in table 2.

During the control period the mean myocardial lactate uptake was 6.9 ± 3.1%. Twelve patients had abnormal lactate metabolism at some time during this period in the absence of chest pain. One of these patients (JD) had a 2 mm ST depression. Atrial pacing was associated with abnormal lactate metabolism. In 13 subjects there was a progressive rise in CS lactate levels leading to a decline of lactate uptake and later to lactate production, which reached a peak of −15.7 ± 5.2% during the last two minutes of pacing. This value was significantly different from the mean control level (P < 0.001). After cessation of pacing, lactate production fell, and finally disappeared during the fifth and sixth minutes of recovery, although myocardial lactate extraction was still abnormal at this time.

The arterial blood levels of Pi remained stable throughout the study. A small positive A-CS difference was seen during the control period, with a mean uptake of 5.7 ± 0.8%, although six patients showed small amounts of Pi loss at some time during this period. When pacing began, Pi uptake gradually decreased and was abolished during the third sample (fifth and sixth minutes of pacing) (P < 0.005). During the last 2 min of pacing and the first 2 min of recovery there were small losses of Pi (−1.0 ± 1.4 and −1.8 ± 1.9 respectively), which were significantly different from the mean control Pi uptake (P < 0.001). In this group, ten patients showed Pi loss with abolition of uptake in another

Figure 2

Correlation between the mean % uptakes of L and Pi during control, pacing, and recovery periods in groups A (angina) and NA (nonangina).
two. During recovery, P1 uptake gradually rose toward control levels. Seven patients had both lactate production and P1 loss during pacing and a high degree of correlation for the entire group was found between these two variables throughout the study (r = 0.86, P < 0.001) (fig. 2).

In nine patients of this group, arterial and CS CPK levels remained fairly constant during the control period with a small positive A–CS difference. Pacing did not influence the arterial levels of this enzyme, but a small and abrupt rise in CS levels was seen immediately after the onset of the tachycardia in five subjects. During the first 6 min of pacing the mean CPK levels in CS blood declined, but remained significantly elevated from control and higher than in arterial blood. It should be noted that the peak of these small but significant changes in CS levels of CPK occurred early in pacing in contrast to the abnormalities in L and P1 uptake which were maximal at the end of pacing and early recovery periods, respectively.

Plasma GOT was determined in eight patients of Group A. There was no difference between the A and CS levels, and these values were not affected by pacing and ischemia.

**Hemodynamic and Electrocardiographic Results**

Comparable mean heart rates were observed in both groups during the control period (84 beats/min) and during atrial pacing (148 beats/min). Since cardiac index remained unchanged during the study, stroke index and left ventricular stroke work index fell significantly and to the same extent in both groups (table 3). During pacing, arterial blood pressure did not change significantly in Group NA. However, in the angina group the systolic blood pressure rose from 140 to 155 mm Hg (+11.6%, P < 0.05) and the diastolic blood pressure from 75 to 89 mm Hg (+20.0%, P < 0.001).

LVEDP was similar in both groups during the control period and fell during atrial pacing to 4.0 ± 0.7 mm Hg (P < 0.001) in Group NA while it remained unchanged in Group A. When pacing was interrupted LVEDP rose to control levels in Group NA, and to a mean value of 21 ± 2 mm Hg in Group A; this latter value was significantly higher than the corresponding level for Group NA (P < 0.001).

There were comparable significant rises in dp/dt and TTI during pacing in both groups. The only electrocardiographic abnormality observed was a significant depression of ST segments (1.7 ± 0.3 mm, P < 0.001) in Group A during interruption of pacing.

**Discussion**

The hemodynamic and electrocardiographic effects of atrial pacing in the angina and nonangina groups confirm the results reported previously from this laboratory.13, 19 The significant increases in systolic and diastolic brachial artery pressures associated with angina may be explained on the basis of an emotional component related to pain, and theoretically to the release of systemic catecholamines. It is interesting that in a recent review20 86% of spontaneous or unprovoked episodes of angina pectoris were preceded by elevation of the

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**Table 2**

**Summary of Metabolic Results**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Lactate uptake (%)</th>
<th>P1 uptake (%)</th>
<th>CPK (A–CS) (units)</th>
<th>GOT (A–CS) (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>(n = 18)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pacing</td>
<td>−15.7 ± 5.2</td>
<td>−1.0 ± 1.4</td>
<td>−1.0 ± 0.4</td>
<td>−0.4 ± 0.5</td>
</tr>
<tr>
<td>Group NA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>(n = 11)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pacing</td>
<td>+19.0 ± 1.4</td>
<td>+2.2 ± 1.8</td>
<td>−0.4 ± 0.7</td>
<td>+0.2 ± 0.3</td>
</tr>
</tbody>
</table>

Control values are the mean of all control samples and pacing values are the peak responses during stress, expressed as mean ± se.

Abbreviations: P1 = inorganic phosphate; CPK = creatine phosphokinase; GOT = glutamic oxaloacetic transaminase; P = significance of comparison between pacing and control values; NS = nonsignificant.
arterial and pulmonary artery pressures. This association strongly suggests that these hemodynamic changes may precipitate spontaneous attacks of angina, and be also an important factor when angina is induced by atrial pacing.

The effects of pacing on myocardial lactate metabolism observed in the present study are not different from those obtained previously. In this experimental situation lactate production is associated with myocardial K⁺ loss and these metabolic abnormalities are related to the production of ischemia during atrial pacing in patients with coronary artery disease.

To our knowledge the myocardial loss of P₁ during pacing-induced angina has not been previously reported. This finding confirms the works on dogs by Owen et al., who observed release of myocardial P₁ after ligation of a coronary artery, and by Case during reversible reduction of coronary blood flow. In addition to ischemia, other factors are capable of releasing P₁ from cardiac muscle. For instance, infusion of ethanol has been shown to induce this phenomenon in dogs and in man.

In animal experiments myocardial losses of P₁ and L appear simultaneously and consistently when coronary flow is reduced below a critical level. In our study these metabolic events were slightly out of phase. While the peak of lactate production occurred during the last 2 min of pacing, the maximum P₁ loss took place during the first 2 min of recovery. The correlation between these two metabolic variables, however, was good, but it seems that P₁ loss is a less reliable indicator of myocardial ischemia than lactate production. Our results show that while 72% of the angina patients produced lactate during pacing, P₁ loss was seen in only 55%, and furthermore, only half of the lactate producers had concomitant P₁ loss. This discrepancy may be explained by the evidence suggesting that P₁ loss from the dog heart during ischemia is approximately only one-fifth of that of lactate. Moreover, one has to keep in mind all the factors which would tend to attenuate this small loss of phosphate ion under the described experimental conditions. While in animal experiments blood flow is reduced in a normal coronary circulation and venous effluent may be collected selectively from the ischemic area, in subjects with CAD the ischemic areas are irregularly distributed and venous blood is sampled from the CS stream which carries a mixed effluent from normal and ischemic myocardium.

The observations on blood enzyme levels reported here are only preliminary. The small but significant increases in CS CPK levels observed in five of the nine angina patients in whom this enzyme was determined occurred always in the presence of tachycardia and myocardial ischemia, and cannot be totally ignored. This change was not
PHOSPHATE & ENZYMES IN MYOCARDIAL ISCHEMIA

Table 3

Summary of Hemodynamic Results

<table>
<thead>
<tr>
<th>Condition</th>
<th>HR mean ± se (beats/min)</th>
<th>CI mean ± se (L/min/m²)</th>
<th>BP mean ± se</th>
<th>LVEDP mean ± se</th>
<th>LVSWI mean ± se</th>
<th>dp/dt mean ± se (mm Hg/sec)</th>
<th>TTI mean ± se (s)</th>
<th>ST mean ± se (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>83 ± 3</td>
<td>2.8 ± 0.1</td>
<td>140 ± 5</td>
<td>75 ± 3</td>
<td>11 ± 1</td>
<td>42 ± 2</td>
<td>1269 ± 87</td>
<td>1162 ± 71</td>
</tr>
<tr>
<td>Pacing</td>
<td>148 ± 2</td>
<td>2.8 ± 0.1</td>
<td>155 ± 7</td>
<td>89 ± 4</td>
<td>10 ± 2</td>
<td>27 ± 2</td>
<td>1898 ± 204</td>
<td>2151 ± 111</td>
</tr>
<tr>
<td>P &lt;0.001</td>
<td>NS</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
<td>(21 ± 2)</td>
<td>&lt;0.001</td>
<td>&lt;0.01</td>
<td>&lt;0.001</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Group A (n = 18)

<table>
<thead>
<tr>
<th>Condition</th>
<th>HR mean ± se (beats/min)</th>
<th>CI mean ± se (L/min/m²)</th>
<th>BP mean ± se</th>
<th>LVEDP mean ± se</th>
<th>LVSWI mean ± se</th>
<th>dp/dt mean ± se (mm Hg/sec)</th>
<th>TTI mean ± se (s)</th>
<th>ST mean ± se (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>85 ± 3</td>
<td>3.1 ± 0.1</td>
<td>131 ± 5</td>
<td>76 ± 3</td>
<td>9 ± 0.4</td>
<td>46 ± 2</td>
<td>1196 ± 93</td>
<td>1107 ± 63</td>
</tr>
<tr>
<td>Pacing</td>
<td>148 ± 2</td>
<td>3.2 ± 0.2</td>
<td>132 ± 5</td>
<td>81 ± 4</td>
<td>4 ± 1</td>
<td>31 ± 2</td>
<td>1842 ± 231</td>
<td>2000 ± 82</td>
</tr>
<tr>
<td>P &lt;0.01</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.02</td>
<td>&lt;0.001</td>
<td>NS</td>
</tr>
</tbody>
</table>

Group NA (n = 11)

Values are mean ± se. The figures in brackets are LVEDP during interruption of pacing.

Abbreviations: HR = heart rate; CI = cardiac index; BP = arterial blood pressure; S = systolic blood pressure; D = diastolic blood pressure; LVEDP = left ventricular end-diastolic pressure; LVSWI = left ventricular stroke work index; TTI = tension-time index; ST = ST segment; P = significance of the change between control and pacing values.

sustained (fig. 3) but declined while pacing was continued and disappeared during the last 2 min of pacing, at a time when the degree of myocardial ischemia was the greatest, as reflected in the peaks of lactate production and P1 loss.

The time course of the CS levels of CPK in comparison with those of L and P1 during myocardial ischemia and tachycardia should be discussed at this point. The possibility that this phenomenon could be due to a heart rate effect alone appears to be supported by the evidence that muscular contraction facilitates the escape of intracellular enzymes during electrical stimulation of the hind-leg of the dog,25 during exercise,26-29 during cardiac pacing in the dog as reflected in the systemic blood enzyme levels30 and in drug-induced cardiac arrhythmias.31 However, the same degree of tachycardia in Group NA was not associated with significant elevations in CS CPK levels. This difference between Group A and NA suggests that myocardial hypoxia, alone or in combination with pacing, may have been responsible for the CPK elevation observed in Group A. This effect is presumably related to an increased permeability of the sarcolemma via the formation of transient pores as postulated by Zierler32 or via an increase in the size or rate of appearance of such pores.30 This hypothesis, however, fails to account for the earlier appearance and decline of the CS CPK levels during pacing since ischemia persisted and even worsened toward the end of the pacing period. It is possible that the myocardial enzyme released may have preferentially escaped via the lymphatics as has been recently discussed.33-35 Our results are at variance with the findings of Amsterdam et al.14 who failed to observe release of the cardiac enzymes CPK, GOT, and LDH during myocardial ischemia induced by catecholamine infusion or atrial pacing. It is likely that this discrepancy could be explained on the basis of our small number of patients and differences in experimental set up and severity of CAD. Obviously further work is necessary to clarify this important issue.

In summary, our results clearly indicate that during angina induced by atrial pacing the human heart loses inorganic phosphate. This P1 loss correlates well with lactate production, but it appears to be a less reliable index of myocardial anaerobiosis. In addition, transient increases in CS CPK levels during pacing in angina patients suggest that this enzyme may also be released during tachycardia and myocardial ischemia.

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References


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MIGUEL A. CHIONG, ROXROY WEST and JOHN O. PARKER

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