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Hepatic blood flow in acute myocardial ischemia[1]

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Summary. Hepatic blood flow was monitored in cats during myocardial ischemia (MI). Increased plasma CPK activity, the S-T segment of the electrocardiogram, and hepatic flow was reduced by 5 h to 40% of control. The results suggest that MI can influence organs distant from the original ischemic episode.

Myocardial ischemia (MI) is a complex disease entity involving a variety of cardiac and extracardiac phenomena[3]. Information regarding the cardiac processes responsible for the spread of ischemic damage in acute myocardial ischemia is becoming better understood[4]. However, extracardiac processes involved in the pathogenesis of acute myocardial ischemia remain poorly understood. The purpose of this study was to determine if myocardial ischemia, uncomplicated by cardiogenic shock, alters liver blood flow. If liver blood flow is compromised it could induce tissue injury resulting in a deficit in energy metabolism, as well as an impairment in phagocytosis of the reticuloendothelial system.

Methods. Male cats (3.8–5.3 kg) were anesthetized with

sodium pentobarbital (30 mg/kg, i.v.). The right carotid artery and left jugular vein were cannulated. Mean arterial blood pressure (MABP) and central venous pressure (CVP) were recorded from the carotid arterial and jugular venous catheters respectively, using a Grass Model 7 oscillographic recorder. Lead III of the scalar electrocardiogram was also monitored. All cats were tracheotomized to allow for positivepressure ventilation after thoracotomy. A mid-line laparotomy was performed with subsequent isolation of the hepatic artery and hepatic portal vein. A noncannulating electromagnetic flow probe (i.d.=1.5 mm) was carefully positioned around the common hepatic artery to ensure that flow through the hepatic artery perfused only the liver. In addition, a cannulating electromagnetic flow probe (i.d.=3.0 mm) was placed in the lumen of the hepatic portal vein for measurement of portal venous flow (PVF). This procedure necessitated ligation of the right gastric and gastroduodenal veins for placement of the flow probe. Heparin (250 U/kg) was administered i.v., and the abdomen was closed.

Subsequently, a mid-sternal thoractomy was performed, and the exposed pericardial sac was incised and retracted. This exposed the left coronary artery and its branches. Myocardial ischemia (MI) was induced via ligation of the left anterior decending (LAD) coronary artery 10–14 mm from the coronary ostium. This ligation was accomplished by passing a 3-0 silk ligature around the LAD coronary artery and tying the vessel securely. Myocardial ischemia was initiated after a 15 min stabilization period. In sham-operated controls, the identical experimental maneuvers were performed except that the LAD artery was not occluded.

Sampling protocol and biochemical assays. 3 ml venous blood samples were drawn just prior to occlusion and every hour thereafter for 5 h. The blood was centrifuged at 2500× g and 4 °C for 20 min. The plasma was collected for the determination of plasma protein concentration, and creatine phosphokinase (CPK) activity. Saline (6 ml of 0.9% NaCl) was given to replace blood lost by sampling. The biuret method of Gornall et al.[5] was used to determine plasma protein concentrations. Plasma creatine phosphokinase activity was determined by the method of Rosalki[6].

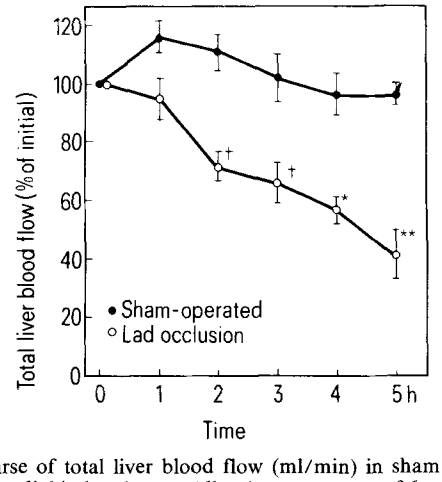
Results. The cardiovascular and biochemical responses of cats subjected to myocardial ischemia and their controls are summarized in the table. In both the sham-operated and myocardial ischemia groups, MABP did not change significantly. In contrast, the plasma CPK activity and the S-T segment of the electrocardiogram increased progressively in the MI group over the 5 h observation period. No significant changes in plasma CPK activity or S-T segment voltage were observed in sham-operated controls. These findings indicate myocardial ischemia existed in cats subjected to coronary artery occlusion, and was not present in sham-operated controls.

Total hepatic blood flow for cats subjected to either acute MI or sham-MI for the 5 h observation period is depicted in the figure. The initial blood flow for both the control and experimental groups was 28.5 and 27.3 ml/kg/min. In the sham-operated control cats, no significant changes in hepatic blood flow were observed over the 5 h experimental period. In contrast, liver blood flow decreased in MI cats within 2 h of coronary artery ligation and progressively declined over the remaining 3 h of the experimental period, so that flow had declined by 60%, 5 h after coronary artery occlusion. Both hepatic portal flow and hepatic arterial flow declined proportionally so that the decreased total hepatic flow was equally distributed between its 2 vascular supplies.

Discussion. Although there is considerable information available on the cardiac adjustments following myocardial ischemia, a paucity of information exists on the extracardiac mechanisms activated in response to acute MI. Our findings indicate myocardial ischemia initiates vascular changes in the liver, an organ distant from the original ischemic episode.

The data presented in the table indicate coronary occlusion resulted in a significant degree of MI after ligation of the left anterior decending coronary artery. The changes noted in plasma CPK activity and the S-T segment of the electrocardiogram are similar to those known to occur in cats following coronary artery occlusion[7,8]. The stable blood pressure observed in the MI group indicates that uncomplicated myocardial ischemia without cardiogenic shock was induced in these cats. In addition, in similar experiments, Spath and Lefer[9] have reported a 35% reduction in aortic blood flow at 5 h of post myocardial ischemia. Thus, the 60% decrease in hepatic blood flow we observed was not a consequence of severely compromised cardiac performance, aortic blood flow or hypotension which occurs in hemorrhagic and other types of shock[10].

The control liver flows obtained in the experiments are comparable to those reported by Nxumalo et al.[11] and Lautt[12]. The reduction in liver blood flow in response to



Time course of total liver blood flow (ml/min) in sham operated and myocardial ischemic cats. All points are means of 6 cats in each group. SEM are shown as brackets.

Myocardial ischemia induced changes in mean arterial blood pressure, S-T segment and plasma creatine phosphokinase activity

Group	N	Time (h) 0			5		
		MABP	CPK	S-T	MABP	CPK	S-T
Sham MI	6	135±11	3.1±0.9	0.01±0.01	116±6	3.8±0.7	0.01±0.01
MI	7	127± 8	2.8±0.7	0.01±0.01	119±5	9.8±0.7*	0.17±0.05*

MABP=mean arterial blood pressure express in mm Hg; CPK=creatine phosphokinase activity of the plasma expressed in IU/mg protein× 10^3; S-T segment change in lead III of EKG expressed in mV. * $p < 0.02$ compared to zero time value.

myocardial ischemia is the first reported observation of hepatic ischemia during acute MI. This 60% reduction in liver blood flow could result in a marked reduction in oxygen availability to the liver and impaired liver function. Previously, it has been demonstrated that prolonged hypoxia or ischemia can result in a loss of liver cellular integrity[13]. In this regard, Dunn et al.[14] noted during congestive heart failure liver injury is often a complicating factor. However, animals experiencing a reduced liver blood flow may be able to compensate for the decreased oxygen delivery by increasing the extraction of oxygen from the blood. Such compensation could mask the effects of an acute reduction in liver blood flow. Furthermore, since the clearance of many substances by the liver is dependent on blood flow[15], a significant decreased flow could compromise the clearance capacity of the liver. In this regard, Lautt[12] has reported that a reduction in hepatic blood flow is accompanied by a decrease in the removal of substances from the blood. Thomson et al[16] reported that in clinical situations associated with reduced hepatic blood flow, the incidence of toxic reactions to lidocaine was increased.

In summary, myocardial ischemia results in a significant reduction in liver blood flow 2 h after coronary artery occlusion. This decrease progresses so that total liver blood flow is only 40% of initial values at 5 h. The resulting ischemia to the liver may contribute to the pathophysiology of myocardial ischemia.

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Fine structural correlations between the muscle pathology of amyotrophic lateral sclerosis (ALS) patients and experimental Ca-Mg deficient rats

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Summary. Nonspecific myofibrillar changes such as streaming of the Z-line, formation of rod-like structures, satellitosis, proliferation of sarcolemmal nuclei and papillary projection of the sarcolemma were recognized as a disorganization of the muscle itself. In addition, fine structural pathology in ALS specimens showed characteristically a pig-tail formation - 'Zopfformation'- which has been considered to have a neurogenic origin.

Although amyotrophic lateral sclerosis (ALS) is a systemic degenerative disease of unknown etiology, involving motor neurons selectively, the possible participation of Ca dysmetabolism in the pathogenetic process of ALS has recently been indicated[1,2]. In relation to this, experimental studies on rats fed a Ca-Mg-deficient diet have been done, with the interesting finding that there was muscle fibre atrophy in white muscle (type II fibre), and a decreased activity of the enzyme succinic dehydrogenase in the gastrocnemius muscle[3, 4]. In this study, myofibrillar changes found specifically in ALS patients and Ca-Mg-deficient rats are demonstrated.

Materials and methods. Human muscle specimens were obtained from biopsied gastrocnemius muscle from 3 cases of ALS. Muscle specimens from experimental animals were obtained from 4 Ca-Mg deficient rats and 5 control rats. 4 experimental rats were fed a Ca-Mg deficient diet for a period of 5-15 weeks. The body weight of the animals continuously decreased during the period of the experiment. Total body weight loss was about 47%. Human muscle specimens were fixed in 1% OsO_4 adjusted with 0.1 M cacodylate buffer (pH 7.4) for 2 h. Experimental animals were perfused with 4% paraformaldehyde-0.5% glutaraldehyde adjusted with 0.1 M cacodylate buffer (pH 7.4) and post-fixed in 1% OsO_4 adjusted with 0.1 M cacodylate buffer (pH 7.4). After fixation, muscle specimens were dehydrated with ethanol and embedded in epoxy resin. Ultrathin sections stained with uranyl acetate and lead citrate were examined under JEOL 100C and T7 model electron microscopes.

Results and discussion. In biopsied muscle specimens from ALS cases, strikingly abnormal features were demonstrated in the sarcolemma and sarcoplasm, as seen in figure 1, showing multiplicative sarcolemmal nuclei (figure 1, a) and papillary projection of the sarcolemma (figure 1, b). In addition, there was proliferation of the satellite cells, and cell wandering at the intermuscular space.

Experimental studies of muscle specimens of Ca-Mg deficient rats revealed papillary projection of the sarcolemma, satellitosis and proliferation of sarcolemmal nuclei, which are similar pathological changes to those observed in the ALS specimens. Besides, infolding or invagination appeared in the nuclear membranes of satellite cells and sarcolemmal nuclei.

Such changes; sarcolemmal papillary projection, and reactive satellite cells and sarcolemma, are commonly described as myopathic changes in skeletal muscle[5]. Satellite cell proliferation in denervated muscle has been frequently observed in hypertrophied muscles rather than in atro-