were prominently elevated, while PaCO_2 , PvO_2 , PvCO_2 and SvO_2 were decreased in all patients. Myocardial oxygen extraction and the coronary arterio-venous oxygen difference was increased, but myocardial oxygen consumption did not change significantly in both groups during HV. Although the coronary sinus blood flow (CSF) was decreased, while the coronary vascular resistance (CVR) was increased significantly in the negative group, CSF and CVR was not significantly changed in the positive group.

It is suggested that decreased PaO_2 might play a preventive role for coronary artery spasm and that no decrease in CSF in positive group was supposed to alter microcoronary circulation smaller than arterioles or to distribution of coronary blood flow.

-57-

CHANGES IN RAT MYOCARDIAL PHOSPHOLIPIDS IN ISOPROTERENOL-INDUCED MYOCARDIAL DAMAGE AND ITS PREVENTION BY PRETREATMENT WITH PHOSPHOLIPASE INHIBITORS

Nobutoshi Takasu, Yutaka Miyazaki, Hidekazu Hashimoto, Takayuki Ito, Kouichi Ogawa and Tatsuo Satake.

The 2nd Department of Internal Medicine, Nagoya University School of Medicine.

To investigate the changes in myocardial phospholipids after administration of isoproterenol (Iso.) and its prevention by pretreatment with several drugs, we determined the content of phospholipid (PL) species in the hearts of female Wistar rats. Iso. (40mg/kg) was administered 24 h before the analyses and chlorpromazine (CPZ, 30mg/kg), mepacrine (Mep., 50mg/kg), nifedipine (Nif., 30mg/kg) and propranolol (Pro., 20mg/kg) were injected intraperitoneally 30 min prior to Iso. administration. Isolation and quantification of PL species were carried out by silica gel rods and hydrogen flame ionization method. Iso. induced significant increases in heart/body weight ratio (HW/BW) [Cont., Iso.; 3.25 ± 0.38 , 3.72 ± 0.33 ($\times 10^{-3}$)], myocardial protein/heart weight ratio (Prot./HW) [91.6 ± 9.6 , 110.1 ± 13.1 ($\times 10^{-3}$)] and lysophosphatidylcholine (LPC), and significant decreases in total phosphorus/myocardial protein ratio (P/Prot.), creatine kinase activity/myocardial protein ratio (CK/Prot.) [581 ± 69 , 522 ± 48 (IU/mg)], phosphatidylethanolamine (PE) and phosphatidylcholine (PC). Although Pro. and Nif. inhibited all these changes, CPZ and Mep. inhibited all these changes except HW/BW and Prot./HW. The result that inhibitors of phospholipases, CPZ and Mep., inhibited only the changes in phospholipids suggests that the activation of phospholipases play a role in the development of myocardial damage induced by Iso.

	Cont.	Iso.	CPZ	Mep.	Nif.	Pro.
P/Prot. (10^{-3})	3.30	2.40	3.18	3.05	2.90	2.95
	± 0.52	± 0.60	± 0.27	± 0.22	± 0.55	± 0.80
PE ($\mu\text{g}/\text{mg}$ Prot.)	30.9	27.1	29.9	30.4	33.3	31.1
PC ($\mu\text{g}/\text{mg}$ Prot.)	± 3.0	± 2.6	± 2.0	± 3.4	± 4.6	± 4.6
	33.3	24.3	30.7	29.0	29.9	30.2
LPC ($\mu\text{g}/\text{mg}$ Prot.)	± 5.3	± 2.8	± 3.6	± 3.1	± 4.4	± 5.1
	2.62	3.32	2.58	2.71	2.89	2.91
	± 0.43	± 0.80	± 0.32	± 0.32	± 0.55	± 0.52
(each group: n=15)						

-58-

EFFECT OF CO Q AND NICORANDIL ON MYOCARDIAL INJURY INDUCED BY CALCIUM PARADOX

-COMPARISON TO THE ACTION OF TAURINE-

Keiko Takihara, Junichi Azuma, Nobuhisa Awata, Akihiko Sawamura, Hisato Harada, Hideyuki Ohta, Tomoyuki Hamaguchi, Yuya Tanaka and Susumu Kishimoto

The Third Department of Internal Medicine, Osaka University Medical School

This study was designed to investigate in chick heart whether pretreatment with taurine or Co Q, or addition of Nicorandil to the perfusate shows any effect upon calcium (Ca) paradox-induced heart failure.

Hearts were removed from 7-day-old chicks and were perfused by conventional Langendorff method. Electrically-paced hearts were stabilized 15 min prior to the 15 min Ca-free perfusion. Subsequently, hearts were reperfused for 10 min under normal condition with Ca (1.8 mM). Ca accumulation and ultrastructural damage resulting from the Ca paradox were significantly reduced in hearts treated with any of the tested agents. The protective effect of taurine is accompanied by attenuation of the elevation of myocardial sodium content during Ca depletion, and reduced the Ca influx during Ca repletion. ATP and total adenine nucleotide contents of the hearts subjected to Ca paradox declined to 25% and 57% of the control value, respectively. Furthermore, Ca paradox resulted in a significant reduction of myocardial CPK, GOT and LDH activities. Co Q significantly protected against the Ca paradox-induced reduction of tissue total adenine nucleotide and LDH content. When Nicorandil (500 μM) was added to the reperfusion medium, CPK content was significantly higher than in control hearts after Ca paradox.

-59-

THE ROLE OF PHOSPHOLIPASE IN THE GENESIS OF REPERFUSION ARRHYTHMIA

Masayoshi Ajioka, Taizo Kondo, Yuuichi Ogawa, Kouichi Ogawa, Tatsuo Satake, Satoru Sugiyama*, Takayuki Ozawa*.

Department of Biomedical Chemistry* and Internal Medicine, University of Nagoya.

The mechanism of reperfusion arrhythmia was investigated. *In vivo* study: Using anesthetized 51 mongrel dogs, the LAD was occluded for 15 min and then released for 5 min. The dogs were divided into two groups depending on the pretreatment with saline or coenzyme Q_{10} (CoQ_{10}), 15 mg/kg, before the ligation, i.e., the control and the CoQ_{10} groups. Reperfusion arrhythmia was observed in 12 out of 38 dogs in the control, whereas in the CoQ_{10} group none developed arrhythmia. In both groups, myocardial plasma membrane were prepared from both the normal and the reperfused areas. Plasma membrane lipids were extracted and the phospholipids content was determined according to Allen's method. Nine species of free fatty acids (FFA) were detected in the plasma membrane in each group by high performance liquid chromatography. In the dogs in the control group with arrhythmia, all species of detected FFA increased, and phospholipid content in plasma membrane decreased. These changes were not observed in the dogs without arrhythmia in both the control and the CoQ_{10} groups. *In vitro* study-1: Incubation of myocardial plasma membrane with phospholipase (PLase) A_2 increased only unsaturated FFA, while PLase C increased all detected FFA. Premedication with CoQ_{10} prevented the increase in FFA caused by PLases. *In vitro* study-2: Using canine papillary muscle of the left ventricle, membrane