2:30

FUNCTION AND PERFUSION IN MYOCARDIAL INFARCTION USING MAGNETIC RESONANCE TAGGING AND MAGNETITE CONTRAST

Susan B. Yeon, Nathaniel Reichek, Barbara Tallant, Joao Lima, Linda C. Palmon, Neil Clark, Deanna Brownson, Eric Hoffman, Leon Axel
Hospital of the University of Pennsylvania, Philadelphia, PA

Magnetic resonance tagging enables noninvasive measurement of myocardial segment shortening. To evaluate spatial relations of function and perfusion, we used magnetic resonance tagging [using spatial modulation of magnetization (SPAMM)] and intravenous magnetite perfusion contrast (which induces signal loss in perfused regions) to image a canine myocardial infarction model (n=9). After short axis SPAMM imaging, we administered 10-20 mg/kg of magnetite colloid and obtained identically located and timed images without SPAMM. At 4 sites per slice, SPAMM stripe separation normal to the endocardium was measured at endocardium, midwall and epicardium and segment shortening calculated. By comparing image sets, we identified measurement sites in magnetite perfusion defects (x). We categorized perfused sites as being within 90 degrees of a perfusion defect on the same slice, between 90 and 180 degrees away from a defect on the same slice, adjacent to a defect on a slice next to the defect, or remote from perfusion defects.

CIRCUMFERENTIAL SEGMENT SHORTENING (%S)

	x	90°	180°	next	remote
n	63	77	10	12	50
mean	-3±29†	11±20*	13±5*	-3±44†	17±8*

†p<0.05 vs. remote, *p<0.05 vs. x

Remote regions showed normal mean %S and transmural gradient in %S. %S was markedly reduced in x and next sites but was nearly normal at sites 90° and 180° from the defect. Greater heterogeneity of %S was found in x, 90°, and next regions compared with remote regions. Dysfunction at next sites may be due to ischemia, as well as stunning and tethering, since magnetite is very sensitive to low level residual perfusion. We conclude that combined SPAMM and magnetite imaging is useful in relating function to perfusion and may be useful in differentiating myocardial stunning from infarction.

3:00

METABOLIC TO MECHANICAL ENERGY TRANSFER AFTER REGIONAL AND GLOBAL MYOCARDIAL ISCHEMIA

John C Lucke, Joseph R Elbeery, Theodore C Koutlas, Stan A Gall, Thomas A D'Amico, R Eric Lilly, Pablo F Soto, J Scott Rankin, Donald D. Glower
Duke University Medical Center, Durham NC

Recent experiments have demonstrated a relative increase in myocardial oxygen consumption (MVO) after ischemia. However, these studies have been less than ideal because they fail to couple coronary perfusion to aortic pressure, employ LV or RV bypass, or utilize incomplete mechanical energy (ME) modeling. The purpose of this work was to better evaluate metabolic to ME transfer after regional ischemia (RI) in conscious dogs and global ischemia (GI) in isolated hearts. In 10 instrumented dogs, paired regional ultrasonic dimension crystals measured LV segment length, while Doppler flow probes and regional venous oximeters measured MVO. In 8 ejecting cross-perfused isolated hearts, ultrasonic crystals measured global LV volume, while coronary sinus effluent sampling assessed MVO. Micromanometers measured LV pressure in both preparations. Total ME was calculated as segmental or global stroke work + (mean ejection pressure x LV end-diastolic segment length or volume) for RI or GI, respectively. In RI, steady state regional MVO at constant ME decreased by 28±20% ($p<0.01$) relative to control after 1 hour of reperfusion following a 15 min LAD occlusion. Similarly, global MVO decreased by 16±10% ($p<0.01$) after 15 min of GI followed by one hour of reperfusion. Thus, reversible ischemic injury reduced MVO relative to ME in both the RI and GI preparations. This finding suggests a fundamental ischemia-induced block in myocardial energy transfer that may play a role in the genesis of stunned myocardium.

2:45

ATTENUATION OF ISCHEMIA-INDUCED INTRACELLULAR CALCIUM INCREASE AND VENTRICULAR DYSFUNCTION BY NISOLDIPINE

Ivo Amende, Lisa A. Bentivegna, Bernard Ransil, William Grossman, James P. Morgan, Harvard-Thorndike Laboratory, Beth Israel Hospital, Boston, MA

To determine the effects of nisoldipine (NIS) on intracellular calcium ($[Ca^{2+}]_i$) handling and LV function during ischemia and reperfusion, $[Ca^{2+}]_i$ and LV isovolumic pressure were recorded in 6 isolated, coronary-perfused ferret hearts loaded with the bioluminescent $[Ca^{2+}]_i$ indicator aequorin. From the aequorin light signals, systolic and diastolic $[Ca^{2+}]_i$ were obtained. After a control period of 3 min ischemia, perfusion with 10^{-6}M NIS was started and 20 min later ischemia repeated for 3 min. NIS 10^{-6}M decreased LV developed pressure (LVP) (109 vs 82mmHg; $p<.001$) and increased LVEDP (11 vs 19mmHg; $p<.002$). Systolic $[Ca^{2+}]_i$ decreased (0.40 vs 0.32 nA; $p<.002$) whereas diastolic $[Ca^{2+}]_i$ was not changed by NIS (0.20 vs 0.18 nA). Results (*$p<.05$ vs control ischemia; S=systolic; D=diastolic; LACT=lactate changes during ischemia; REP=reperfusion) are:

	Ischemia			REP	Ischemia + NIS			REP
Time (min)	0	1	3	1	0	1	3	1
S$[Ca^{2+}]_i$(nA)	0.46	0.71	1.10	0.55	0.32*	0.44*	0.59*	0.33*
D$[Ca^{2+}]_i$(nA)	0.22	0.38	0.79	0.31	0.18	0.25*	0.39*	0.21*
LVP (%Δ)		-67	-94	-29		-54*	-87*	-17*
LACT (mg/dl)			6.5				2.4*	

Conclusions: 1. The negative inotropic effects of NIS on LV function are not associated with changes in diastolic $[Ca^{2+}]_i$. 2. NIS lessens ischemic effects on LV function and myocardial metabolism. 3. NIS attenuates ischemia-induced increase in diastolic and systolic $[Ca^{2+}]_i$, consistent with altered transsarcolemmal $[Ca^{2+}]_i$ influx through the L-type (voltage-dependent) Ca^{2+} channels.

3:15

CONVERSION OF MB CREATINE KINASE ISOFORMS *IN VIVO*

Nelson A Prager, Tadao Suzuki, Allan S. Jaffe, and Dana R. Abendschein, Washington University, St. Louis MO, U.S.A.

Analysis of isoforms of MB CK in plasma may facilitate diagnosis of acute myocardial infarction and detection of coronary recanalization after treatment with thrombolytic agents. Thus far, only 2 isoforms of MB CK have been detected by electrophoresis of plasma samples; presumed to reflect the tissue form and a second isoform attributable to selective hydrolysis of the carboxyl (c-) terminal lysine from M-monomers. However, we have shown that carboxypeptidases remove c-terminal lysines from both M- and B-monomers of MB CK *in vitro* resulting in 4 possible isoforms. To characterize modifications that occur *in vivo*, we separated dimers based on the presence or absence of lysine on the B- monomer by anion-exchange FPLC and then determined the presence of lysine on the M-monomer with a monoclonal antibody. MB CK in pooled plasma from 61 normal subjects lacked c-terminal lysines on 54.3 ± 50.6% of B-monomers and 24.4 ± 24.9% of M-monomers. Early to 20 hours after the onset of acute myocardial infarction, none of the plasma M- or B- monomers were found to lack c-terminal lysines, indicative of release of tissue isoform in which both c-terminal lysines are intact. After 20-30 hours, 57 ± 12% (n=19) of B-monomers lacked c-terminal lysines, but lysine was present on all M-monomers. After 40-50 hours, 86.7 ± 26.5% (n=34) of B-monomers and 53.9 ± 39% of M-monomers lacked c-terminal lysines. Thus, *in vivo* modification of MB CK involves sequential removal of a c-terminal lysine residue from both M- and B-monomers. Hydrolysis proceeds more rapidly for the B-monomer. Accordingly, analyses of plasma samples must account for at least 3 and perhaps 4 isoforms of MB CK. Their separation should facilitate both the early and specific detection of acute myocardial infarction and documentation of recanalization.