965-47 Comparison of Regional Myocardial Blood Flow and Metabolism in Patients with Ischemic and Non-ischemic Cardiomyopathy

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Myocardial viability and recovery of left ventricular (LV) function after revascularization is predicted by the presence of positron emission tomography (PET) defined F-18 deoxyglucose (FDG):blood flow mismatch pattern in patients with ischemic cardiomyopathy (ICM). However, little is known about regional blood flow and metabolism patterns in patients with non-ischemic cardiomyopathy (NICM). Therefore, we studied 10 symptomatic patients (NYHA class II and III) with left ventricular dysfunction; 5 had ICM and 5 NICM. All patients underwent radionuclide angiography, stress thallium scintigraphy, coronary angiography and PET studies with N-13 ammonia and FDG at rest. The myocardial region with the maximum counts on the stress thallium study was used as the normal reference region for relative ammonia and FDG uptake. From matched ammonia and FDG short-axis images, a total of 156 regions were analyzed in ICM patients and 144 regions in NICM patients. Regional blood flow less than 85% in both thallium and ammonia studies was considered abnormal. FDG:ammonia ratio of ≥1.2 was considered to represent metabolism-blood flow mismatch.

	abnormal flow	mismatch	match	LVEF (%)
ICM	89 (57%)*	37 (47%)	52 (53%)	16 ± 8
NICM	37 (26%)*	4 (11%)	33 (89%)	12 ± 5

*$p < 0.001$, **$p < 0.005$

In ICM patients, 57% of all regions demonstrated abnormal blood flow and almost half of such regions exhibited preserved glucose extraction indicative of ischemic but viable myocardium. In contrast, approximately one-fourth of NICM regions had decreased regional blood flow and the majority (89%) of such regions had matched decrease in glucose extraction (nonischemic). Thus, despite the absence of significant epicardial coronary artery stenosis, decreased regional blood flow occurs in patients with NICM and may reflect regions with admixture of viable myocytes and fibrosis.

965-48 Ejection Fraction and Wall Thickness Correlate with Impaired Energy Metabolism in Patients with Dilated Cardiomyopathy

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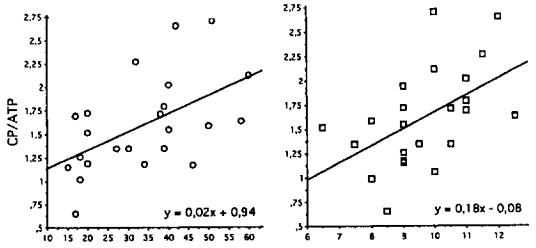
Using 31P-MR spectroscopy, abnormalities of cardiac energy metabolism have been demonstrated in patients with dilated cardiomyopathy (DCM). However, a detailed analysis of the correlations among energy metabolism, cardiac hemodynamics and myocardial hypertrophy obtained from 31P-MR, right and left heart catheterization and echocardiography has not been presented. 23 patients with DCM (left ventricular (LV) EF 34 ± 3%; NYHA class 2.7 ± 0.1; SE) underwent right and left heart catheterization and echocardiography ± 3 days before/after MR spectroscopy. Coronary artery disease was ruled out by coronary angiography. ECG-triggered, localized 31P-MR spectra from the anteroseptal myocardium were acquired at rest (prone position) during 30 min on a 1.5 T Philips Gyroscan MR system using ISIS localization, adiabatic pulses, and a 15 sec repetition time. Peak areas were corrected for T1 effects and for blood contamination, and were determined with Lorentzian line fits in the time domain. Linear correlations between creatine phosphate (CP)/ATP ratios and hemodynamic parameters were calculated.



LV pressures and diameters, cardiac output, stroke volume, pulmonary arterial pressures, right atrial pressure and pulmonary arterial oxygen saturation did not correlate with CP/ATP. Thus, our data demonstrate that in DCM, the extent of high-energy phosphate depletion is related to the extent of mechanical dysfunction as well as to LV wall thickness.

965-49 Abnormal Mitochondrial Respiration in Myocardium of Dogs with Chronic Heart Failure

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We previously showed that abnormalities of mitochondria (MIT) exist in the failing heart and include hyperplasia, reduced organelle size and structural injury. In the present study, we examined MIT respiration in LV tissue obtained from 11 normal (NL) dogs and 8 dogs with heart failure (HF) produced by intracoronary microembolizations (LV ejection fraction 23 ± 3%). Tissue specimen (30 mg) were obtained from the subendocardial (ENDO) and subepicardial (EPI) halves of the LV wall. Basal (V_o) and state 3 (maximal) respiration (V_{ADP}, after addition of 1 mM ADP) were measured with an oxygraph and Clark electrode using saponin skinned fiber bundles (0.2–0.3 mm). Respiratory rate was calculated in ngatoms of oxygen/min/mg of noncollagen protein. The respiration control ratio (RCR) was calculated as V_{ADP}/V_o.

	V_o		V_{ADP}		V_{ADP}/V_o	
	ENDO	EPI	ENDO	EPI	ENDO	EPI
NL	9 ± 2	7 ± 1	46 ± 6	47 ± 1	6 ± 1	7 ± 1
HF	6 ± 1	6 ± 1	20 ± 5	22 ± 5	4 ± 1	4 ± 1
P-value	<0.07	<0.5	<0.001	<0.005	<0.04	<0.004

MIT state 3 respiration is significantly reduced in myocardium of dogs with chronic HF. The observed reduction in the RCR confirms the presence of injury to inner MIT membrane. The abnormalities in MIT oxygen utilization support the concept of low energy production in the failing heart.

965-50 Accumulation of Collagen in the Cardiac Interstitium of Dogs with Chronic Heart Failure is Associated with Decreased Capillary Density and Increased Oxygen Diffusion Distance

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Progressive LV dysfunction is a characteristic feature of the failing heart. The mechanism(s) responsible for this functional deterioration are not known. Progressive accumulation of collagen in the cardiac interstitium termed "reactive interstitial fibrosis" (RIF), occurs in the failing heart but its role in the progression of LV dysfunction remains uncertain. We examined the consequences of RIF severity on capillary density (CD) and oxygen diffusion distance (ODD) in LV myocardium of 11 dogs with heart failure produced by intracoronary microembolizations (LV ejection fraction 26 ± 1%). CD was defined as the index capillary to fiber ratio and ODD as half the distance between two adjoining capillaries. Frozen sections were prepared from LV tissue and double stained with a collagen III antibody to quantitate RIF and with GSI lectin to visualize capillaries. From each section, 5 infarct free fields manifesting severe RIF (volume fraction 16 ± 2%) and 5 fields with little or no RIF (volume fraction 4 ± 1%) were selected for analyses.

	No RIF	RIF	Probability
CD	1.05 ± 0.03	0.92 ± 0.02	$P < 0.003$
ODD (μm)	2.3 ± 0.4	15.3 ± 0.4	$P < 0.001$

Conclusion: In the failed canine heart, CD is decreased and ODD is increased in LV regions manifesting severe RIF. These abnormalities may contribute to the progression of LV dysfunction by promoting hypoxia of the collagen encircled cardiocytes.

965-51 Daily Coronary Microembolization in Awake Dogs Leads to Heart Failure

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Previous efforts to induce heart failure using percutaneous coronary embolization required multiple surgical procedures and a prolonged time course (3–6 months) until heart failure develops. The goal of this study was to create a reproducible and more rapid model of ischemic heart failure in dogs using repeated coronary embolization via a chronically implanted coronary catheter. Dogs (n = 5) were chronically instrumented for measurements of mean arterial pressure (MAP), left ventricular pressure (LVP) and left atrial pressure (LAP). After full recovery, hemodynamic measurements and the response of LV dp/dt to increasing doses of isoproterenol were performed weekly. After control experiments, glass microspheres (90 μm diameter) were injected into coronary circulation daily (50,000–100,000/day) using the implanted coronary catheter for approximately two weeks. The hemodynamic measurements after 3 weeks and a total of 925,000 ± 250,000 microspheres are shown as follows (* < 0.05 from control).