ORAL CONTRIBUTIONS

804 Positron Emission Tomography: Clinical Studies

Monday, March 08, 2004, 9:15 a.m.-10:30 a.m.
Morial Convention Center, Room 243

9:15 a.m.

804-1 ^{18}F-Fluoro-2-Deoxyglucose as a Memory Marker of Transient Myocardial Ischemia

Brian G. Abbott, Yi-Hwa Liu, James A. Arrighi, Yale University School of Medicine, New Haven, CT, VA Connecticut Healthcare System, West Haven, CT

Background: Myocardial uptake of flourine-18 labeled 2-deoxyglucose (FDG) parallels endogenous glucose uptake. Experimental data have shown that glucose utilization increases during acute myocardial ischemia in proportion to its severity and duration, and may persist for up to 24 hours. Whether FDG uptake can be imaged as a memory marker of ischemia in humans is unknown. ***Methods:*** Patients with mild to moderate ischemia on a clinical exercise SPECT myocardial perfusion imaging (MPI) underwent repeat exercise testing within 1-2 weeks, to an equivalent workload after overnight fast. Positron emission tomography (PET) was performed after injection of FDG 60 minutes post exercise. SPECT and PET images were assessed visually and quantitatively using regions of interest for heart:lung ratios and a circumferential profile-based analysis modified for "hot-spot" imaging. A change in regional maximal uptake >10% on SPECT and regional FDG PET uptake >110% was considered as evidence of ischemia. ***Results:*** Ten males with stress SPECT ischemia (mean age 69 years, 7 known coronary artery disease[CAD]) were studied. The mean difference in the rate pressure product between the 2 exercise tests was 1.5±19%. FDG was injected 66±10 min after exercise. Visually, 5 of 10 patients had enhanced regional FDG uptake (mean [range] heart:lung ratio 5.3 [3.5-7.8] in visually abnormal vs. 3.0 [2.5-3.4] without visual uptake, p=0.02 respectively). Using circumferential profiles, 7 patients had maximal FDG uptake >110%; mean FDG uptake in these regions was 120±12%. Overall, 8 of 10 patients studied had evidence of FDG uptake by visual and/or quantitative analysis. All patients with a visually and/or quantitatively positive FDG scan had uptake in either an ischemic SPECT region or a territory with known CAD by angiography. ***Conclusion:*** Regional myocardial uptake of FDG is enhanced even when injected 1 hour post-exercise stress in a subset of patients with ischemia on exercise SPECT MPI. Enhanced FDG uptake localized with regional SPECT ischemia and/or angiographic CAD. The ability to image FDG uptake injected 1 hour after an ischemic episode suggests the potential utility of FDG as a memory marker of transient ischemia.

9:30 a.m.

804-2 Efficacy of Lipid Lowering Therapy in Inducing Arrest or Reversal of Coronary Disease as Assessed With Positron Emission Tomography

Michael E. Merhige, George M. Watson, Joseph G. Oliverio, Victoria Shelton, Shannon N. Frank, Anthony F. Perna, State University of New York at Buffalo, Buffalo, NY

Background: PET myocardial perfusion imaging (PET MPI) identifies coronary disease (CAD) progression and reversal in response to lipid lowering therapy (LLT). Optimal lipid values necessary to reverse CAD have not yet been identified, however, NCEP ATP-III (NCEP) guidelines are used as clinical targets in practice. The purpose of this study was to evaluate the efficacy of aggressive LLT, beyond NCEP guidelines, to induce arrest or reversal of CAD as assessed with PET MPI.
Methods: 128 patients with iv dipyridamole stress induced myocardial perfusion defects at baseline, treated for 1.5 years to beyond NCEP guidelines, underwent follow-up PET MPI and outcome assessments for MI, coronary death, CABG, CVA, and PTCI. Paired stress PET studies were analyzed with automated software to determine the average uptake of 82-Rb in the anterior, septal, inferior, lateral and apical segments normalized to peak myocardial activity. Baseline and follow-up MPI studies were then compared with the paired t-test, to identify significant improvement, worsening, or stabilization in segmental perfusion in each patient.
Results: With LLT: 30 patients demonstrated improvement in myocardial perfusion, 64 patients no change, and 34 progression of CAD despite treatment. At a mean follow-up of 7.5 months after the second PET, coronary events occurred in 3.3%, 10.9%, and 17.7% respectively.
Conclusions: PET MPI identifies 26% of patients with progressive CAD, despite LLT, who have a high-risk of subsequent hard coronary events.

	Baseline	Follow Up	% Change	p-value
Total Cholesterol	168 +/- 38	152 +/- 30	- 10.5	0.0001
LDL	95 +/- 36	83 +/- 23	- 12.6	0.0001
HDL	45 +/- 13	49 +/- 14	+ 8.9	0.03
Triglyceride	137 +/- 74	105 +/- 59	- 23.4	0.0001

9:45 a.m.

804-3 The Effects of Cardiac Resynchronization Therapy on Regional Left and Right Ventricular Energetics and Metabolic Reserve in Patients With Dilated Cardiomyopathy

Juhani M. Knuuti, Jan Sundell, Erik Engblom, Juhani Koistinen, Antti Ylitalo, Kira Q. Stolen, Riikka Kalliokoski, Stephan G. Nekolla, Jeroen J. Bax, Juhani K.E. Airaksinen, University of Turku, Turku, Finland

Background: Cardiac resynchronization therapy (CRT) has been found to enhance on left ventricular (LV) energetics and metabolic reserve in patients with heart failure. The purpose of the study was to investigate the effects of CRT on regional energetics and right ventricle (RV).
Methods: Ten patients with idiopathic dilated cardiomyopathy who had undergone implantation of biventricular pacemaker 8±5 months earlier were studied during 2 conditions: CRT ON and after CRT switched OFF for 24 hours. LV function was measured using echocardiography and oxidative metabolism using [^{11}C]acetate positron emission tomography (Kmono) from both LV and RV. Both measurements were performed at rest and during dobutamine induced stress (5µg/kg/min). Basal and adenosine (140 µg/kg/min) stimulated myocardial blood flow were quantitated using [^{15}O]water.
Results: As found previously when CRT was turned OFF global myocardial efficiency of forward work deteriorated significantly. The regional LV Kmono changes were significant only in the anteroapical regions (p=0.013) while in other regions no changes were seen (p=0.43). CRT has no effect at rest on RV (ON: 0.052±0.014, OFF 0.047±0.018, ns.) but during stress oxidative metabolism was more enhanced when CRT was ON (0.076±0.02 vs. 0.065±0.027, p=0.003). No significant effects were seen in myocardial perfusion.
In 5 patients the response to CRT was striking (mean LV stroke volume increase by 32%) while in the other five no response was seen (+2%). None of the measured parameters except RV oxidative metabolism were associated with the CRT response. In responders RV Kmono at rest was lower than in non-responders (0.036±0.01 vs. 0.058±0.02, p=0.47).
Conclusions: Long term CRT has beneficial effects on LV function and myocardial efficiency in patients with heart failure. However, the change in absolute oxidative metabolism by CRT appears significant only in anteroapical regions of LV. CRT appears to increase RV oxidative metabolism especially during stress likely indicating changes in RV loading. The patients responding to CRT appear to have lower RV oxidative metabolism. This suggests significant role of RV in the response to CRT.

10:00 a.m.

804-4 The Relationship Between Minute Ventilation and the Rate of CO_2 Elimination Reflects the Right Ventricular Oxidative Metabolism in Heart Failure

Heikki Ukkonen, Rob de Kemp, Ross Davies, William Dafoe, Ian Burwash, Haissam Haddad, Karen Mostert, May Aung, Terry Ruddy, Rob Beanlands, University of Ottawa Heart Institute, Ottawa, ON, Canada

Background: The relationship between minute ventilation and the rate of CO_2 elimination (the VE/VCO_2 slope) is strongly related to mortality in patients with congestive heart failure (CHF) and provides complimentary prognostic information to peak oxygen uptake (peak VO_2). The VE/VCO_2 slope has been proposed to reflect pulmonary vascular resistance (PVR) in CHF patients. Therefore, we hypothesized that an increased VE/VCO_2 slope would be associated with elevated right ventricular (RV) oxidative metabolism relative to the left ventricle (LV).
Subjects and methods: 15 patients with CHF (ischemic [n=14], non-ischemic [n=1]; 65±10 yrs; BMI 29±5 kg/m^2; LVEF 30±8 %; NYHA class 2.5±0.5; all pts on ß-blockers and ACE-inhibitors) underwent symptom limited cardiopulmonary exercise testing using a Slow Ramp treadmill protocol. Dynamic ^{11}C-acetate PET was used to simultaneously measure oxidative metabolism (k_{mono}) for both the left (LV) and right ventricle (RV). Corrected RV oxidative metabolism (RVOx) was calculated as: RVOx = RV/LV k_{mono} ratio.
Results: In the 15 CHF pts, mean exercise time was 7:26±2:03 min. Peak VO_2 was decreased at 16.2±3.9 ml/min/kg and the VE/VCO_2 slope was increased at 35.9±4.8 at anaerobic threshold. The mean k_{mono} was 0.043±0.007 min^{-1} for the LV and 0.036±0.007 min^{-1} for the RV. Mean RVOx was 86±17%. There was a good correlation between RVOx and the VE/VCO_2 slope (r=0.63, p=0.013). Exercise parameters did not correlate with LV oxidative metabolism.
Conclusions: VE/VCO_2 slope correlates with RVOx in CHF patients, supporting the hypothesis that PVR is a determining factor for the VE/VCO_2 slope. RVOx derived using ^{11}C-acetate PET may provide a useful prognostic measure in CHF patients.

10:15 a.m.

804-5 Impact of Increased Fatty Acid Delivery on Myocardial Fatty Acid Metabolism in Obese Young Women

Linda R. Peterson, Pilar Herrero, Zulia Kisrieva-Ware, Carmen Dence, JoAnn Marsala, Robert J. Gropler, Washington University, St. Louis, MO

Background: Obesity is associated with an increased risk of heart failure. We have shown that myocardial fatty acid utilization (MFAU) and oxidation (MFAO) are increased in obese young women. Results of studies in animal models of obesity show that high fat diets further increase myocardial fatty acid (FA) metabolism and esterification (MFAE), which contributes to cardiac dysfunction over time. Whether increased plasma FA levels in obese humans cause an increase in myocardial FA metabolism is unknown.
Methods: We studied 6 women (body mass index 40 ± 7 kg/m^2, 21-37 yrs) who were

otherwise healthy. They were studied before and during an infusion of Intralipid and heparin to increase their plasma FA levels (nmol/mL). MFAU, MFAO, MFAE (all in nmol/g/min) and % MFAO were measured with PET and 1-^{11}C-palmitate using well-validated mathematical modeling of the time-activity curves. Paired t-tests were used in the analysis below.
Results: MFAU, MFAO, and MFAE were all higher post-Intralipid. Percent MFAO trended towards being lower post-Intralipid (Table).
Conclusions: Obese women can further increase myocardial FA metabolism in response to increased plasma FA levels, although the capacity to oxidize extracted FA (% MFAO) may be exceeded. These results parallel those of animal models of obesity and support the theory that increased FA delivery increases myocardial FA metabolism. Future studies are needed to determine whether this increase in myocardial FA metabolism in humans contributes to cardiac dysfunction.

	FA	MFAU	MFAO	MFAE	% MFAO
Pre-intralipid	591 ± 179	203 ± 74	182 ± 61	34 ± 38	91 ± 9
Post-intralipid	2118 ± 727	663 ± 216	478 ± 189	247 ± 151	67 ± 17
p value	0.003	0.005	0.02	0.02	0.05

POSTER SESSION

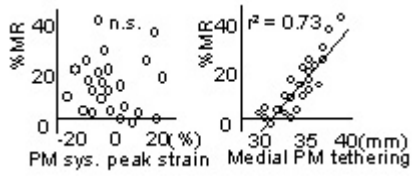
1092 Doppler Imaging of Myocardium

Monday, March 08, 2004, Noon-2:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 1:00 p.m.-2:00 p.m.

1092-161 Ischemic Mitral Regurgitation Is Independent of Papillary Muscle Dysfunction: Insights From Tissue Doppler Strain Imaging in Patients With Inferior Myocardial Infarction

Takeshi UEMURA, Yutaka Otsuji, Toshiro Kumanohoso, Keiko Yuge, Kenichi Nakashiki, Toshinori Yuasa, Akira Kisanuki, Sinichi Minagoe, Robert A. Levine, Chuwa Tei, Kagoshima University, Kagoshima, Japan, Massachusetts General Hospital, Boston, MA

Background: Although the relation between papillary muscle (PM) dysfunction and ischemic MR is controversial, PM dysfunction could be associated with less mitral regurgitation (MR) because of PM elongation, attenuating leaflet tethering. However, associated and variable degree of left ventricular (LV) remodeling to exaggerate leaflet tethering can potentially modify effects of PM dysfunction on the leaflet function.
Method: In 24 patients with prior inferior infarction, LV volume, ejection fraction, mitral annular area, PM tethering distance (PM to annulus), longitudinal PM peak systolic strain and MR fraction were quantified by 2-dimensional and Doppler echocardiography.
Results: 1) MR was not significantly correlated with longitudinal PM peak systolic strain. 2) MR was correlated with LV and mitral annular dilatation, and increased tethering, with the strongest independent contribution by multivariate analysis from increased medial PM tethering.
Conclusions: Ischemic MR is independent of PM dysfunction but is related to geometric changes with medial PM tethering from LV remodeling in patients with inferior MI.



1092-162 Myocardial Strain and Displacement Following Cardiac Resynchronization Therapy

Dean Notabartolo, John Merlino, Andrew L. Smith, David B. DeLurgio, Fernando V. Mera, Randolph P. Martin, Angel R. Leon, Carlyle Fraser Heart Center, Emory University School of Medicine, Atlanta, GA

Background: Cardiac Resynchronization Therapy (CRT) improves left ventricular (LV) function in heart failure patients. Tissue Doppler imaging (TDI) measurements of strain and displacement, may help clarify the mechanisms of LV improvement and remodeling.
Methods: We enrolled forty-five patients with various etiologies of heart failure, a QRS duration ≥ 120ms and EF ≤ 35%. Baseline and 3 months testing included 2-D echocardiogram (GE, Vivid 7) with TDI to assess strain and displacement. From the apical 4, 3, and 2 chamber views, strain and displacement were recorded at the base, mid and apical segments of 6 LV regions at the closure of the aortic valve. Using standard techniques, we calculated the ejection fraction (EF), mitral regurgitation area (MR), end systolic (ESD) and diastolic dimensions (EDD), and end systolic (ESV) and end diastolic volumes (EDV).
Results: CRT improved EF (23.6% ± 9.1 vs. 34.1% ± 12.8, p<0.01), decreased MR (7.4 cm^2 ± 5.6 vs. 4.2 cm^2 ± 3.3, p<0.01), ESD (5.8 cm ± 1.3 vs. 5.3 cm ± 1.6, p<0.01), EDD (6.7 cm ± 1.2 vs. 6.4 cm ± 1.5, p=0.05) and ESV (121.5 ml ± 56.7 vs. 102.1 ml ± 61.0, p<0.01). EDV did not change (158.1 ml ± 59.0 vs. 147.0 ml ± 66.8, p=0.11) but showed a trend towards improvement. Strain and displacement did not consistently improve after CRT. Table.
Conclusions: Despite improvements LV function and remodeling by 2-D echo measures, strain and displacement do not change after 3 months of CRT and do not give further information about LV mechanics.

Segment	N	Strain at AVC (%)			Myocardial displacement at AVC (mm)		
		Baseline	3M	p-value	Baseline	3M	p-value
IS-Base	43	-5.7 ± 8.0	-10.6 ± 10.2	0.01	2.3 ± 2.5	3.0 ± 2.6	0.08
IS-Mid	42	-6.1 ± 8.0	-3.7 ± 8.1	NS	1.5 ± 2.3	1.5 ± 2.6	NS
IS-Apex	38	-2.3 ± 4.3	-4.3 ± 8.1	NS	0.8 ± 2.0	0.3 ± 1.3	NS
Lat-Base	44	-6.6 ± 10.1	-7.4 ± 12.9	NS	3.0 ± 2.3	3.8 ± 2.6	0.05
Lat-Mid	38	-6.3 ± 7.9	-2.3 ± 7.2	0.02	1.3 ± 1.9	1.8 ± 2.2	NS
Lat-Apex	29	-3.8 ± 7.9	-4.8 ± 7.5	NS	0.1 ± 1.5	1.4 ± 2.1	0.001
Inf-Base	43	-6.4 ± 9.5	-7.7 ± 13.2	NS	3.2 ± 2.9	4.9 ± 2.9	<0.001
Inf-Mid	41	-3.1 ± 6.4	-4.8 ± 7.7	NS	1.9 ± 2.7	2.2 ± 2.5	NS
Inf-Apex	32	-5.6 ± 6.9	-6.2 ± 7.6	NS	1.2 ± 1.9	1.0 ± 1.7	NS
Ant-Base	40	-8.5 ± 9.4	-10.1 ± 12	NS	2.4 ± 1.6	3.4 ± 2.1	0.002
Ant-Mid	29	-2.1 ± 7.0	-5.3 ± 9.7	0.08	1.0 ± 1.2	1.6 ± 1.4	NS
Ant-Apex	19	-2.1 ± 2.6	-6.3 ± 8.9	0.05	0.2 ± 0.6	0.8 ± 1.1	0.04
Pos-Base	29	-6.7 ± 12.6	-9.3 ± 16.3	NS	3.6 ± 2.5	4.0 ± 2.5	NS
Pos-Mid	28	-5.5 ± 5.7	-6.3 ± 7.4	NS	1.7 ± 1.9	2.1 ± 2.0	NS
Pos-Apex	23	-4.9 ± 7.9	-4.0 ± 8.5	NS	0.5 ± 1.6	1.0 ± 1.5	NS
AS-Base	22	-3.8 ± 7.4	-4.9 ± 8.7	NS	1.6 ± 1.5	2.3 ± 1.7	0.08
AS-Mid	16	-2.2 ± 4.7	-4.9 + 5.5	0.05	1.0 ± 1.8	0.8 ± 0.9	NS
AS-Apex	5	-4.5 ± 5.9	3.6 ± 3.9	0.06	0.3 ± 0.8	-0.3 ± 0.8	0.06

AVC = Aortic valve closure, 3M = 3 month, IS = Inferior Septum, Lat = Lateral, Inf = Inferior, Ant = Anterior, Pos = Posterior, AS = Anteroseptal.

1092-163 Tissue Doppler Analysis of Nonuniform Transmural Recovery of Myocardial Contractility in Cardiac Raynaud's Phenomenon in Sclerodermic Cardiomyopathy

Shinichi Fujimoto, Reiko Mizuno, Yoshihiko Saito, Shinobu Nakamura, Nara Medical University, Kashihara, Japan

Background: Cardiac Raynaud's phenomenon (C-Raynaud) is reversible myocardial ischemic change introduced by cold provocation and is often detected in progressive systemic sclerosis (PSS). This study investigated transmural differences of myocardial contractile recovery in cardiac Raynaud's phenomenon using tissue Doppler analysis. Methods: We studied 21 PSS patients with C-Raynaud and induced C-Raynaud by cold provocation. Using tissue velocity imaging, peak systolic myocardial velocities (PVs) were measured in inner, mid, and outer layers of left ventricular wall at base line, during and after cold provocation. Results: Under baseline, PVs was significantly greater in inner layer than mid and outer layers. During cold provocation all patients had transmural hypokinesis exhibiting reduced PVs in all layers. At 10 minutes after cold provocation, increase of PVs was significantly depressed in inner layer compared with mid and outer lyers. At 20 minutes after cold provocarion, PVs in mid and outer layers recoverd to base line, whereas PVs in inner layer was still depressed. At 40 minutes after cold provocation PVs in inner layer recovered to base line. Conclusion: This study demonstrates nonuniform transmural recovery of myocardial contractility in C-Raynaud using tissue Doppler analysis and indicates that recovery of myocardial function after transient ischemia is slower in inner layer than outer layer.

1092-164 Echocardiographic Tissue Synchronization Imaging Predicts Acute Response to Biventricular Pacing Therapy

Hideaki Kanzaki, Bazaz Raveen, Kaoru Dohi, Donald A. Severyn, David Schwartzman, John Gorcsan, III, University of Pittsburgh, Pittsburgh, PA

Background: Cardiac resynchronization therapy (CRT) can be beneficial to patients with heart failure (HF) and abnormal electrical activation. However, prospective identification of patient responders to CRT remains unclear. Our objective was to test the hypothesis that the novel color-coding system with tissue Doppler, tissue synchronization imaging (TSI), may assist prediction of patients with acute response to CRT.
Methods: Twenty-nine HF patients (age 65 ± 10 yrs, ejection fraction 26 ± 6%, QRS duration 175 ± 34 ms) were studied before and < 48 hrs after CRT with Vivid 5 or 7 (GE Vingmed). TSI consisted of real time color-coding of time-to-peak velocities detected automatically: green (20-100 ms), yellow (100-300 ms) through red (300-500 ms) in default. Tissue velocity plots of basal and mid LV segments from 3 apical views were assessed after averaging for 3 cardiac cycles.
Results: Fifteen patients (52%) had an acute response to CRT defined as a ≥15% increase in LV stroke volume. Defferences in baseline TSI time-to-peak velocity between opposing LV walls were greater in responders than non-responders: 120 ± 148 vs. 35 ± 153 ms (p<0.05). A ≥ 65 ms delay from anteroseptum to posterior wall from the apical long-axis view had 87% sensitivity and 100% specificity for predicting acute response.
Conclusion: TSI quantified LV dyssynchrony which was associated with acute response