9:00

735 Increased Myosin Heavy Chain Turnover in Compensatory Hypertrophy Due to Chronic Aortic Regurgitation

Norman M. Magid, Roderick K. King, Jeffrey S. Borer. *Cornell Medical Center, New York, NY*

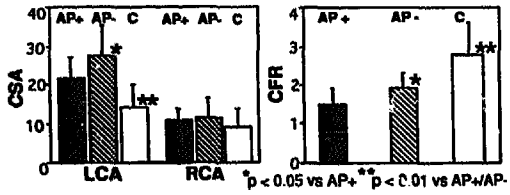
We previously demonstrated dynamic alterations in protein turnover at 3 days and 1 month after surgical induction of aortic regurgitation(AR). To characterize protein fractional synthesis(Ks) and degradation(Kd) during the long-term plateau phase, we performed [^{3}H]-leucine infusions 2 1/2 years after induction of AR in 10 New Zealand White rabbits and 12 sham-operated controls. Ks was obtained by analysis of plasma and protein hydrolysate samples, growth rates(Kg) were determined from protein concentrations and heart weights, and Kd was calculated by subtraction of Kg from Ks. AR (regurgitant fraction 25 ± 11%) caused a 57% increase in left ventricular weight in comparison with controls (7.4 ± 1.7 vs 4.7 ± 0.6 g, $p < 0.001$) and no evidence of heart failure. Although concentrations of total cardiac protein(TCP), myosin heavy chain(MHC) and actin were similar, the enlarged AR hearts had increased amounts of TCP (1,009 ± 312 vs 682 ± 120 mg/LV, $p < 0.05$), MHC (148 ± 91 vs 81 ± 29 mg/LV, $p < 0.05$), and actin (73 ± 42 vs 44 ± 16 mg/LV, $p < 0.06$). Individual protein Ks and Kd were closely balanced. However, MHC fractional turnover rates were 152% ($p < 0.01$) greater than those of TCP in AR animals, while only 52% ($p < 0.05$) greater in controls (AR vs controls, $p = 0.05$). Variations in actin turnover between AR and control animals did not attain statistical significance. MHC and actin Ks values correlated closely in AR rabbits ($R = 0.81$, $p < 0.02$), but not among controls ($R = 0.41$, NS). Thus, a relative increase in myosin heavy chain turnover contributes to the maintenance of increased myofibrillar protein content in the "compensatory" left ventricular hypertrophy of chronic AR.

9:15

735-4 Inadequate Hypertrophy as a Cause for Angina Pectoris in Patients With Aortic Valve Disease

Barbara K. Julius, Martin Spillmann, Bruno Villari, Giuseppe Vassalli, Franz R. Eberli, Otto M. Hess. *Department of Internal Medicine, Cardiology, University Hospital, Zurich, Switzerland*

Background: 40–50% of all patients (pts) with aortic valve disease (AVD) have anginal symptoms despite normal coronary arteries. *Patients and Methods:* 85 pts with severe AVD and normal coronary arteries and 33 controls were included in the present analysis. There were 39 pts with (AP+) and 46 pts without AP (AP–). Coronary cross-sectional area (CSA) was determined by quantitative coronary angiography and coronary flow reserve (CFR) by coronary sinus thermodilution. *Results:* Peak systolic stress was significantly higher in AP+ whereas left coronary CSA, CFR and left ventricular muscle mass were significantly smaller in AP+ when compared to AP–.



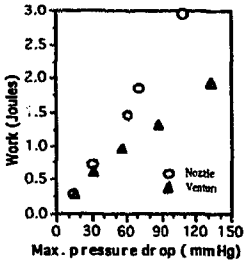
Conclusions: In pts with aortic valve disease left coronary arteries are significantly smaller in pts with than without AP suggesting an inadequate growth of the epicardial vessels Thus, the occurrence of myocardial ischemia may be explained by inadequate left ventricular hypertrophy with an increased wall stress, small coronary arteries and a reduced coronary flow reserve.

9:30

735-5 Pressure Recovery, Not Maximal Orifice Pressure Drop, Influences Left Ventricular Work in Aortic Stenosis

Russell S. Heinrich, Arnold A. Fontaine, Randall Y. Grimes, Aniket Sidhaye, Serena Yang, Robert A. Levine, Ajit P. Yoganathan. *Georgia Tech, Atlanta, GA; Mass. General Hospital, Boston, MA*

The severity of aortic stenosis is widely assessed by Doppler ultrasound in terms of the maximal pressure drop at the orifice. Pressure recovery of varying degrees, however, has been shown to occur downstream of stenotic valves and could potentially affect the workload on the left ventricle. The purpose of this study was to determine whether, for comparable degrees of maximal pressure drop at the orifice, pressure recovery influences pump work. Pulsatile flow (cardiac output = 2–7 l/min) was pumped through a stenotic nozzle or a tapered Venturi shape designed to maximize pressure recovery. Cardiac work was calculated by measuring pressure, flow and velocity at the boundaries of a control volume surrounding the stenosis and applying conservation of energy. The results showed that for comparable maximal orifice pressure drops, the pump work varied with model type and paralleled pressure recovery; the nozzle required the most work (average = 0.99 Joules), while the Venturi required the least (average = 0.69 Joules). Energy loss correlated best with pressure drop after recovery: Energy Loss = −0.04 + 0.006(orifice ΔP), $R = 0.63$; Energy Loss = −0.02 + 0.02(recovered ΔP), $R = 0.97$.



Conclusion: Pressure recovery alters the work needed to pump blood across a stenosis for a given orifice pressure drop, and therefore influences the physiologic impact of stenosis on the pumping ventricle.

9:45

735-6 Diminished Contractile Reserve in Latent Left Ventricular Dysfunction in Mitral Regurgitation: Evidence From a Simplified Model of Pressure-Volume Loop

Dominic Y. Leung, Brian P. Griffin, Brian Haluska, William J. Stewart, James D. Thomas, Thomas H. Marwick. *Cleveland Clinic Fdn, OH*

To assess left ventricular (LV) function at rest and at exercise (Ex) in mitral regurgitation (MR), we performed preoperative Ex echo in 64 pts with no coronary disease and normal resting LV function undergoing valve repair for isolated MR (age 54 ± 13 years, 51 men). These were compared with 10 controls matched for age, sex and resting systolic blood pressure (SBP). LV end diastolic and end systolic volume were measured at rest and after Ex. To construct simplified, rectangular-shaped pressure-volume (PV) loops at rest and Ex, LV systolic pressure was taken to be SBP and LV diastolic pressure was assumed to constant at 10 mmHg. Stroke work (SW) is the area within the PV loop. *Results:* 21 pts (33%) with post repair (postop) ejection fraction (EF) ≤ 50% were considered to have latent LV dysfunction preoperatively.

	EF_{REST}(%)	SW_{REST}(gm)	SW_{EX}(gm)	$\Delta SW_{EX-REST}$(gm)
Postop EF ≤ 50%(A)	60 ± 10	147 ± 43	188 ± 70	41 ± 51
Postop EF > 50%(B)	65 ± 7	154 ± 37	252 ± 81	98 ± 60
p value (A vs B)	0.08	0.5	0.003	<0.001
Controls	69 ± 5	104 ± 19	184 ± 52	80 ± 37

SW_{REST} was higher in pts than in controls ($p = 0.001$). $\Delta SW_{EX-REST}$ was not different in controls and in pts with postop EF > 50% but was significantly lower in pts with postop EF ≤ 50%. *Conclusions:* 1) Ability of LV to increase SW at exercise (contractile reserve) is diminished in MR pts with latent dysfunction, 2) Resting EF and SW_{REST} were not different between pts with and without latent dysfunction, 3)SW_{EX} and $\Delta SW_{EX-REST}$ may be used to identify pts with latent dysfunction.

736 Pretransplant Evaluation

Tuesday, March 26, 1996, 8:30 a.m.–10:00 a.m.
Orange County Convention Center, Room 230B

8:30

736-1 Non-Invasive Determination of Transpulmonary Gradient and Pulmonary Vascular Resistance in Potential Heart Transplant Candidates: Can Right Heart Catheterization Be Avoided?

James H. Stein, Alex Neumann, Lynn M. Preston, Jeffrey S. Soble, Susan M. Quinn, Maria R. Costanzo, Joseph E. Parrillo, Maryl R. Johnson, Richard M. Marcus. *Rush Medical College, Chicago, IL*

Transpulmonary gradient (TPG) and pulmonary vascular resistance (PVR)

are important determinants of suitability for orthotopic heart transplantation (OHT) that are conventionally assessed by serial right heart catheterizations. The feasibility of obtaining accurate, non-invasive (NI) estimates of these parameters has not been evaluated. *Methods:* Invasive (INV) measurements of TPG and PVR were compared with Echo/Doppler NI estimates in 15 OHT candidates (age range 29–59 years, 12 males). NI data included: RA pressure by IVC size and respirophasic change, PA systolic pressure = 4[peak TR velocity]^2 + RA, PA diastolic pressure = 4[pulmonary insufficiency end-diastolic velocity]^2 + [illegible], PA mean pressure = PA diastolic + 1/3 [PA systolic – PA diastolic], pulmonary capillary wedge pressure (PCW) = diastolic BP – 4[MR velocity at aortic valve opening]^2, TPG = PA mean – PCW, cardiac output = [transaortic velocity-time integral][aortic annular area][HR], PVR = TPG/cardiac output.

Results:

	INV range	Mean Δ (INV – NI)	± 95% confidence	r
TPG(mmHg)	3–14	−3.45	4.38	0.93
PVR(Wood U)	0.69–4.36	−0.85	1.52	0.95

Both TPG and PVR could be NI determined in 11 patients (73%) and were *never* underestimated. An algorithm (NI TPG < 13 *and* PVR < 4) identified 80% of patients that were hemodynamically suitable for OHT and excluded 100% of patients with INV TPG > 12 *or* PVR > 3 ($p < 0.02$). *Conclusion:* Accurate NI determination of TPG and PVR is feasible and may obviate the need for serial right heart catheterizations in many patients awaiting OHT.

8:45

736-2 Simplified Assessment of Pulmonary Hypertension in Heart Transplant Candidates

Randall C. Starling, Garrie J. Haas. *The Ohio State University, Columbus, Ohio*

Elevated pulmonary vascular resistance [PVR] is associated with poor outcome due to right heart failure after cardiac transplant [TX]. Acute administration of vasodilators are typically utilized to assess PVR. The purpose of this investigation was to determine the effectiveness of sublingual nitroglycerin [NTG] to evaluate PVR in prospective candidates for TX. Twenty-six patients [pts] mean age 55 years with congestive heart failure [CHF] referred for TX evaluation with pulmonary artery [PA] systolic pressure [sys] > 50 mm Hg received NTG while being hemodynamically monitored. Comparisons were made with 23 CHF pts mean age 52 years that received sodium nitroprusside [SNP]. Mean SNP dose was 2.9 ± 2.1 mcg/kg/min and mean NTG dose was 0.55 mg. The mean duration of the studies was 50 min. for SNP versus 23 min. for NTG.

	NTG base	NTG peak	SNP base	SNP peak
PA Sys	67	48 [28]	71	49 [31]
PA Mean [PAM]	44	34 [24]	48	34 [29]
PA Wedge [PAW]	30	22 [26]	34	22 [32]
(PAM-PAW) [TPG]	14	12 [14]	14	12 [12]
PVR WOOD UNITS	2.7	2.2 [12]	3.0	1 5 [46]*
SVR dynes-sec-cm^{-5}	1383	1200 [12]	1404	713 [45]*
CARDIAC OUTPUT l/min	5.5	5.7 [5]	5.2	8.1 [35]*
MAP	88	86 [2]	84	71 [16]*
HEART RATE	84	84 [0]	94	94 [0]

*% change NTG vs SNP $p < 0.01$. [ ] percent change.

Similar declines in PA sys, PAM and TPG were observed with both drugs. However, SNP resulted in significantly greater changes in cardiac output, SVR, MAP and WOODS units. We conclude that NTG provides a rapid and effective alternative for assessing the reactivity of CHF pts with PA hypertension. NTG has minimal systemic effect in CHF pts. The TPG is reduced but significant reductions in TSVR and MAP are avoided.

9:00

736-3 Development and Prospective Validation of a Clinical Index to Predict Survival in Ambulatory Patients Referred for Cardiac Transplant Evaluation

Keith D. Aaronson, Tze-Ming Chan, J. Sanford Schwartz, Donna M. Mancini. *Columbia-Presbyterian Medical Center, New York, NY*

Selection of cardiac transplant (TXP) candidates is based on measurement of prognostic variables in CHF and secondary exclusion factors. We derived an objective preTXP risk-stratification system from multivariable analyses performed on 268 patients referred to the U of Penn (HUP) from 7/86–1/93, and validated this on 204 patients referred to Columbia (CPMC) from 7/93–9/95. Over 80 variables were prospectively collected: history & physical, chemistries, catheterization data, exercise testing with respiratory gas analysis, MUGA and ECG. Patients were followed to death; UNOS 1 TXP (analyzed as death); UNOS 2 TXP (censored) or alive. Kaplan-Meier 1- and 2-year survivals were 74 ± 3% and 61 ± 4% (HUP) and 60 ± 4% and 39 ± 6% (CPMC). Cox modeling was performed on the HUP data set to develop "noninvasive only" and "unrestricted" (i.e., best combination of noninvasively & invasively determined variables) models. The noninvasive model included ischemic etiology, LVEF, HR, mean BP, QRS ≥ 120 ms, peak VO_2, serum sodium; the unrestricted model was the same except PCW was used instead of serum sodium. Model discrimination was determined by calculating the area under receiver operating characteristic curves for 1-year survival and were as follows:

Model	Cross-Validation (HUP)	Validation (CPMC)
Noninvasive model	0.79 ± 0.03	0.76 ± 0.04
Invasive model	0.81 ± 0.03	0.73 ± 0.05

In conclusion, a model incorporating seven noninvasively obtained clinical variables was prospectively validated with good discrimination. Addition of invasively determined information did not improve model discrimination. This model provides a practical method to improve the objective selection of TXP candidates.

9:15

736-4 Cost Effectiveness of Positron Emission Tomography (PET) in the Management of Ischemic Cardiomyopathy Patients Who Are Referred for Cardiac Transplantation

Tao H. Duong, Gregg Fonarow, Hillel Laks, Pooneh Hendi, Johannes Czernin, Michael Phelps, Heinrich Schelbert, Jamshid Maddahi. *UCLA School of Medicine, Los Angeles, CA*

Cardiac transplantation (TX) in patients (pts) with advanced ischemic cardiomyopathy (ICM) and heart failure is limited by a high cost, donor availability, and a high mortality of wait listed candidates. Since Positron Emission Tomographic (PET) pattern of myocardial perfusion-metabolism "mismatch" has been shown to be predictive of the potential for improvement of LV dysfunction, heart failure symptoms, and survival after CABG; we hypothesized that a PET based decision algorithm in TX candidates identifies a subgroup of ICM pts who would be referred to CABG as a less costly alternative to TX. Accordingly, 112 pts with ICM (LVEF ≤ 35%) and heart failure who were referred to UCLA for TX evaluation underwent PET. In 38/112 pts, 2 or more areas of mismatch were identified. Of these 38 pts, 30 received CABG rather than TX and 8 underwent medical therapy (MRx) because they had either poor coronary targets or refused surgery. Of the 74 pts without PET mismatch, 33 had TX and 41 received MRx. Perioperative mortalities were similar for CABG and TX (10% vs. 6.1%, p = ns). Of note, the 5-year actuarial survival rates for pts who received CABG and TX were also similar (71.4% vs. 80.1%, p = ns) and were both significantly higher than that of MRx pts (42.4%, $p < 0.05$). Based on the average cost for PET, CABG, and TX (including the initial and follow-up costs) at our institution ($1,900, $50,000, and $200,000, respectively), the PET driven decision algorithm in management of our 112 TX candidates incurred $212,800 cost for PET studies but, resulted in diverting 30 pts to CABG ($1,900,000 cost) from potential TX ($6,000,000 saving); a net total saving of $3,887,200 or $34,707 per TX candidate. Thus, a PET based decision algorithm in the management of cardiac transplant candidates identifies a subgroup of pts who could undergo CABG rather than TX, at a substantial cost saving and with similar peri-operative and five year survival results.

9:30

736-5 Does Pre-Existing Donor Heart Atherosclerosis Lead to More Transplant Coronary Artery Disease? A Prospective Study Using Morphometric Analysis of Intracoronary Ultrasound

Jay A. Johnson, Jon A. Kobashigawa, Lawrence Yeatman, Jeffrey G. Carr, Kevin D. Trosian, Alejandro Sabad, Lianne S. Wener, Davis Drinkwater, Hillel Laks. *University of California, Los Angeles, California*

Due to donor shortages in heart transplantation, older donor are being used more frequently, yet the role of pre-existing coronary artery disease (CAD) in the development of transplant coronary artery disease (TCAD) has not been well established. Previous studies with intracoronary ultrasound (ICUS) have been done using ≤ 3 sites/patient and may not accurately assess TCAD. We identified and followed 17 transplant patients (Group 1) with a baseline (6–8 weeks after transplant) mean maximal intimal thickness (MIT) ≥ 0.3 mm using intracoronary ultrasound (ICUS, 2.9 F or 4.3 F, 30 Mhz). Quantitative ICUS was done using morphometric analysis (10 random sites/patient) of the left anterior descending artery at baseline and 1 year. This group was compared to 31 transplant patients (Group 2) with a baseline MIT < 0.3 mm. Computerized planimetry was done to obtain the following measurements: