1042-44 Can a Simple Score Predict Significant and Severe Coronary Disease Better Than Physicians and Other Scores?  
Nikael J. Lipsen, Katherine Schelter, Dan Du, Edele Almond, Lara Oesterling, Barry Franklin, Jeffrey West, Vidor Frecilhuez. Stanford-VA/SHC, Palo Alto, CA, William Beaumont Hospital, Royal Oak, MI

A variety of treadmill scores are available to aid physicians in determining whether a patient has significant or severe angiographic coronary artery disease (CAD). However, the incorporation of the scores into practice has been hampered by their complexity. There is now a simple score available that can be calculated by adding together a set of variables. We compared the simple exercise test scores to physician and scores estimates of disease severity. METHODS: 882 consecutive male patients with a mean age of 59 were considered for the analysis of severe disease and 599 without prior MI were considered for significant CAD. With significant CAD defined as any coronary lumen occlusion >50%, 56% had CAD. Severe CAD was defined as >50% luminal occlusion in 3 vessels, proximal LAD and another vessel, or left main, with 24% having severe CAD. The clinical/treadmill test reports were sent to expert cardiologists and to other groups including randomly selected cardiology interns and internists who classified them as high, low or intermediate probability of CAD in addition to estimating a numerical probability from 0 to 100% for both significant and severe CAD. RESULTS: A total of 882 physicians estimates were returned with the largest group being the expert cardiologists that returned 489 reports. When probability estimates were compared, the simple score was superior at predicting significant CAD (0.75 area under the curve of an ROC) to all the physician groups (0.70 for the experts, 0.65 for the cardiologists and 0.61 for the internists: p<0.01). The simple score also predicted severe CAD better than all the physician groups (0.74 AUC of simple, 0.67 for experts, 0.60 for cardiologists, and 0.59 for internists). The simple score also placed far fewer patients with significant and severe CAD at low probability of disease than the physicians (EC 12% to Simple 3%, RC 15% to 9%, and internists 12% to 4%). The simple score performed as well as the Consensus of scores and better than the Duke Treadmill Score. (AUC of ROC for simple .75, Consensus .75, and the DTS .71). CONCLUSION: The Simple Score performs better than the physician groups and the Duke Treadmill Score in all areas and performed as well as the Consensus of Scores.

1042-73 Validation of the Accuracy of Pretest and Exercise Test Scores in Women With a Low Prevalence of Coronary Disease: The National Heart Lung and Blood Institute-Sponsored Women’s Ischemia Syndrome Evaluation (WISE) Study  
Anthony Morse, Marian B. Olson, C. Noel Bairey Merz, Nathaniel Reichek, William J. Rogers, Carl J. Pepine, Steven E. Reis, Barry L. Shand, George Stupke, Jarnett F. Lewis, WWU, Morgantown, WV

Background: Pretest and Exercise Test Scores derived for use in women without known coronary disease have not been tested in women with a low prevalence of coronary disease. Methods: We evaluated 434 women undergoing coronary angiography for suspected myocardial ischemia with an overall low (28%) prevalence of angiographic coronary disease, defined as >50% stenosis in ≥1 epicardial vessel. Overall, 115 underwent treadmill exercise testing. Pretest Score incorporated age, symptoms, exercise status, and 6 other coronary risk factors. Exercise Test Score incorporated age, symptoms, electrocardiographic findings, and 5 exercise test variables (ST depression, Duke angina score, peak heart rate). Using previously defined cutpoints, women were placed into low, intermediate and high probability groups. We compared the scores to angiographic results. RESULTS: The prevalence of any coronary disease in each subgroup was as follows: Low probability (4%), intermediate probability (15%), and high probability (41%). Subgroup coronary disease prevalences, expressed as %, are shown below (Table).  

<table>
<thead>
<tr>
<th>Pretest</th>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
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</thead>
<tbody>
<tr>
<td>Pretest</td>
<td>10/119 (8.5%)</td>
<td>42/189 (22%)</td>
<td>6/37 (17%)</td>
</tr>
<tr>
<td>Exercise</td>
<td>7/14(49%)</td>
<td>17/68 (25%)</td>
<td>17/33 (52%)</td>
</tr>
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</table>

P<0.001 for both rows. When both scores were considered together, the best stratification by Exercise Test Score was in the intermediate Pretest Score group: low Exercise Test Score 19 (11%), intermediate Exercise Test Score 10/43 (23%), high Exercise Test Score 4/7 (57%) (p=0.009).

Conclusion: Both Pretest Score and Exercise Test Score perform well in stratifying women with a low prevalence of coronary disease. Exercise Test Score appears particularly useful in women with an intermediate Pretest Score, consistent with American College of Cardiology/American Heart Association guidelines.

Does ST Depression in Premature Ventricular Contractions Predict Ischemia?  
Margaret Leila Rasouli, Myrvin H. Elstad. Long Beach Memorial Medical Center, Long Beach, CA, University of California, Irvine, Irvine, CA

Background: Patients with coronary artery disease frequently have premature ventricular contractions (PVCs) at rest and during exercise. The vagal and coronary artery configuration or these ectopic beats vary a good deal and, to our knowledge, the ST segment depression in these complexes have not been correlated with the presence or absence of ischemia. If changes in the ST segment of PVCs were a consistent finding during ischemia, this would provide one more marker that would be useful when doing exercise testing. Methods: We searched our stress testing database for all patients who had had PVCs at rest during exercise AND had undergone a coronary angiogram within a few months of the stress test. There could be no intervention between the two procedures. We were able to identify 94 patients; 64 had significant coronary artery obstruction more than or equal to 50% or at least one vessel as detected by angiography. These 64 nonischemic subjects and an additional 10 ambulatory normals were selected to make a sample group of 100 total subjects. We examined the PVCs of all 100 patients, at rest and during exercise and calculated a ratio: ST depression amplitude divided by the R wave amplitude. Measurements were performed by an investigator blinded to angiographic results. Comparisons of data between ischemic and nonischemic patients were performed by using the ANOVA and the Fisher exact test. Results: We compared 12 lead electrocardiographic changes during exercise in 100 patients with PVCs. 38 were nonischemic and 64 had coronary artery disease. ST depression in PVC's more than 10% of the R wave amplitude when measured in leads V4-V6 significantly identified ischemic (P<0.001). This comparison of predicting ischemia with this method is 95%, and specificity is 67%. It is most reliable with 5 vessel disease (100%), but does not markedly diminish for 1 or 2 vessel disease (91.0%). Conclusion: We believe ST segments observed in PVCs may be another way to identify ischemia. We report a sensitivity of 95%. We predict that when present, PVC analysis in conjunction with classic ST depression may considerably diminish the false negative response rate in stress testing.

1043 Get Physical: Mechanical and Electrical Means to Treat Heart Failure  
Sunday, March 18, 2001, Noon-2:00 p.m.  
Orange County Convention Center, Hall A4  
Presentation Hour: Noon-1:00 p.m.

1043-45 Changes in Left Ventricular Shape and Cavity Area After Myocardial Splicing in a Dog Model: A Real-Time 3-Dimensional Echocardiographic Study  
Jin Xin Qiu, Takahiro Shikita, Masami Takagaki, Lisa A. Cantor, Yoshih Ochiai, Tomotogu Tabata, Patrick M. McCarthy, Cynti J. Schenck, Todd J. Morfill, Jr., Richard F. Schroeder, James D. Thomas. The Cleveland Clinic Foundation, Cleveland, OH, Myocor Inc, Plymouth, MV

Background: The Myocor Myosplint is designed to reduce left ventricular (LV) volume and wall stress in dilated cardiomyopathy (DCM), but its impact on LV geometry is unknown.

Methods: Seven dogs with heart failure (ejection fraction < 25%) induced by rapid ventricular pacing were studied. Three Myosplint devices were implanted perpendicular to the LV long axis at base, mid and apical level and tightened to produce an estimated 20% reduction in wall stress. Real-time three-dimensional echocardiography (RT3DE) was performed operatively pre-implantation, post tightening and at one month follow-up. The LV cavity areas and the area of LV cavity (AC) and myocardial (AM) were measured at mid LV, which was recognized by moving the image plane in 3D space with RT3DE. The ratio of LV diameters (antero-septal/antero-posterior) were calculated.

Results: Three Myosplint devices were visualized clearly in 3D space (Figure). The LV shape was consistently changed from globose to globular and the ratio of LV cavity areas were significantly decreased from 0.83 ± 0.03 to 0.60 ± 0.10 at end-diastole (p<0.0002), from 0.65 ± 0.05 to 0.64 ± 0.11 at end-systole (p = 0.0001) and remained during follow-up (0.54 ± 0.08 and 0.56 ± 0.03 at end-diastole and end-systole, respectively). The AC was significantly decreased after Myosplint implantation and remained smaller during follow-up (16 ± 2 cm³, 12 ± 2 cm³, 13 ± 2 cm³, respectively, p < 0.001) while there was no significant change in AM after Myosplint implantation.

Conclusion: The Myocor Myosplint device consistently produced unique LV shape changes and decreases in LV cavity arena, throughout the cardiac cycle, immediately after implantation and at pacing one month follow-up. Each a device may allow LV volume reduction in DCM without myectomy.
2.8 + 0.6). 17 patients had concomitant valve repair or replacement (15 mitral), and 12
Of
diastolic dimension (EDD), end-systolic dimension (ESD), and Uniscale (quality of life
ventricular recovery. Brain natriuretic peptide (BNP) is produced in the myocardium in
concentration of BNP, echocardiographic findings and the clinical outcome to determine
echocardiographic data and blood chemistry. They were divided into patients who were
the assist device who did not require transplantation (Group 2, n = 4) and patients who
were successfully transplanted (Group 1, n = 8). patients who were successfully weaned off
concentrations decreased significantly after initiation of mechanical circulatory support
orly io fit the ventricles Results: There were no intra-operative complications A 10% rate
weaned off the system wiii without requiring a heart transplantation.

Results}

To evaluate the potential of BNP as a predictor of cardiac recovery in patients supported by mechanical circulatory assist

The present study was designed to examine the safety of the Acorn Cardiac Support Device (SCD) in patients with non-ischemic cardiomyopathy. The Acorn Cardiac Support System is a fully implantable, percutaneous device that provides ventricular assist by applying balanced pressure to the anterior and septal wall in 12 patients (65 ± 8 years). During and in a period of 6 months after implantation, the medication remained unchanged. End-diastolic pressures were significantly lower in patients who received BNP with the Acorn Cardiac Support System (p < 0.01, Wilcoxon’s signed rank test). Furthermore, the changes of BNP plasma concentrations were significantly different between patients who died before transplantation or before weaning (Group 3) and patients who died before transplantation or before weaning (Group 3).

Initial Efficacy Trends With the Acorn Cardiac Support Device in Patients With Advanced Heart Failure

Background: Chronic therapy with the Acorn Cardiac Support Device (SCD) is a novel, fully implantable, percutaneous device that provides ventricular assist by applying balanced pressure to the anterior and septal wall. The device is designed to provide ventricular support without the need for systemic anticoagulation. The Acorn Cardiac Support System is a fully implantable, percutaneous device that provides ventricular assist by applying balanced pressure to the anterior and septal wall in 12 patients (65 ± 8 years). During and in a period of 6 months after implantation, the medication remained unchanged. End-diastolic pressures were significantly lower in patients who received BNP with the Acorn Cardiac Support System (p < 0.01, Wilcoxon’s signed rank test). Furthermore, the changes of BNP plasma concentrations were significantly different between patients who died before transplantation or before weaning (Group 3) and patients who died before transplantation or before weaning (Group 3).

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Background: Tetrahydrobiopterin (BH4) is an absolute cofactor required for the enzyme nitric oxide synthase (NOS 3) and the subsequent generation of nitric oxide (NO) from L-arginine. BH4 group (p<0.05). Conclusion: These data uncover, for the first time, novel beneficial effects on these parameters (Table). Myocytes from water treated rats were hypertrophied compared to sham, water treated Ml rats had a 47% increase in CT-1 mRNA levels. Enalapril treatment tended to reduce myocyte hypertrophy (Leng 169*9 and width 261*2) but not significantly. As compared to sham, water treated rats had a 47% increase in C1 mRNA levels. Enalapril reduced this to 37%; candesartan to 12% and combination normalization levels the same.

1044-53 Novel Cardioprotective Effects of Tetrhydrobiopterin: An Experimental Model of Global Ischemia and Reperfusion

Sudhir Gupta, Linder S. Anand, VA Medical Center, Minneapolis, MN, University of Minnesota, Minneapolis, MN

Background: Cardioprotein-1 (CT-1) has been shown to induce hypertrophy in cardiac myocytes, characterized by assembly of sarcomere in series resulting in eccentric hypertrophy, as seen in post MI hearts. Methods: We investigated the role of the ACE inhibitor (ACE-I), enalapril, AT1 blocker (AT-I-B), candesartan, and their combination on left ventricular CT-1 expression and myocyte hypertrophy in 6 week MI and sham operated rats. Results: Hearts from both groups were excised and studied using the modified Langendroff procedure. In equilibration, the hearts were subjected to 30 minutes of ischemia followed by 30 minutes of reperfusion. Following treatment, the hearts were frozen and malondialdehyde levels were increased in MI rats as compared to sham. ACE-I (10mg/kg), AT-I-B (10mg/kg) or combination in drinking water. Treatment was started 2 weeks after MI and continued for 6 weeks, when rats were sacrificed. Results: Hemodynamic, echo, and morphometric parameters confirmed significant remodeling and LV dysfunction in MI hearts. All treatments had significant effects on these parameters (Table). Myocytes from water treated rats were hypertrophied compared to sham (length 185±10 vs 185±6; width 26±6; vs. 26±2; p<0.01).

1044-52 Role of Cardiotrophin-1 In Postinfarct Myocyte Hypertrophy: Effects of ACE Inhibitors and AT1 Blockers

Sudhir Gupta, Linder S. Anand, VA Medical Center, Minneapolis, MN, University of Minnesota, Minneapolis, MN

Background: Cardiotrophin-1 (CT-1) is a potent pro-hypertrophic cytokine. Studies from this laboratory have demonstrated decreases in both collagen type I (associated with tensile strength) and collagen type III, and angiotensin converting enzyme was determined by North-Taylor tissue culture assay. Results: Hemodynamic, echo, and morphometric parameters confirmed significant remodeling and LV dysfunction in MI hearts. All treatments had significant effects on these parameters (Table). Myocytes from water treated rats were hypertrophied compared to sham (length 185±10 vs 185±6; width 26±6; vs. 26±2; p<0.01). Treatment with sodium iodide and combination reduced myocyte length (124±10 and 124±8 respectively) but increased myocyte width (38±2 and 30±2 respectively; p<0.01) as compared to water treated animals. Enalapril treatment tended to reduce myocyte hypertrophy (Length 169*9 and width 261*2) but not significantly. As compared to sham, water treated rats had a 47% increase in C1 mRNA levels. Enalapril reduced this to 37%; candesartan to 12% and combination normalization levels the same.

1045-03 VEGF cDNA gene therapy post myocardial infarction: New strategy to reduce adverse ventricular remodeling

Masoud Sadreddini, Fayez Dawood, Duncan Stewart, Anne O’Rapsky, Sam Sier, Peter Liu, Heart & Stroke/Richard Lewar Centre of Excellence, Toronto, ON, Canada

We have demonstrated previously that the coronary microvasculature (MV) is not only compromised in the presence of cardiac injury and heart failure, but is also a critical determinant of the fate of cardiac remodeling. To determine whether this abnormality is potentially reversible, we created a rat model of MI via LAD ligation with or without microvascular damage using dilute Triton-X (Tri-X) injected in the aortic root (Tri+ or Tri-).

1044-55 VEGF cDNA Gene Therapy Post-myocardial Infarction: New Strategy to Reduce Adverse Ventricular Remodeling

Elizabeth Vermaa, Selah P. Rijavec, Aaron S. Dumoulin, Annapurna Mahindra, Khairul Ahamed, Todd J. Anderson. University of Calgary, Calgary, AB, Canada

Background: Tetrhydrobiopterin (BH4) is an absolute cofactor required for the enzyme nitric oxide synthase (NOS 3) and the subsequent generation of nitric oxide (NO) from L-arginine, in the endogenuem in the present study we hypothesized that BH4 may protect the myocardium, against ischemia-reoxygenation induced cardiac dysfunction through increasing NO production and/or availability. Methods: Male Wistar rats were divided into two groups (n=10 per group). Group 1 received BH4 (25mg/kg/d, iv, 5 days) while group 2 was injected with saline and served as the control group. Following treatment, the hearts were excised and studied using the modified Langendorff procedure. The hearts were paced and perfused at a constant flow rate of 7 ml/min. LVDP, LVPat and LVEDP were determined using a latex balloon inserted into the left ventricle. In addition, coronary perfusion pressure (CPP) was determined. Following 30 minutes of equilibration, the hearts were subjected to 30 minutes of ischemia followed by 30 minutes of reperfusion. A separate group of saline treated rat hearts were consecutively perfused for a period of 90 minutes. Following this protocol, the hearts were frozen and malondialdehyde (MDA) levels, an index of myocardial injury, were determined. Data were analyzed using ANOVA followed by a Newman Keuls test for post hoc comparisons. Results: In the control group, ischemia with subsequent reperfusion resulted in myocardial dysfunction as evidenced by a decrease in LVPat and an increase in CPP and LVEDP (p<0.05). Hearty exhibited protection against ischemia-reperfusion induced cardiac dysfunction (LVPat 74±5 vs. saline 42±5 mmHg, p<0.002; LVEDP 10±3 vs. saline 34±8 mmHg, p<0.05). A 3 fold increase in MDA levels following ischemia-reperfusion was apparent in the saline treated rats which was attenuated in the BH4 group (p<0.05). Conclusion: These data uncover, for the first time, novel beneficial
Background: Congestive heart failure (CHF) may be associated with combined systolic and diastolic dysfunction in elderly patients. Elderly patients with cardiovascular disease differ in clinical presentation, management, and outcome from younger patients. The present study examined the association between alcohol consumption, moderate alcohol consumption and risk of heart failure has not been established.

Methods: The study population included 2282 persons aged 65 years and older who were enrolled in the Epidemiological Study of the Elderly (EPESE) program. Persons with heart failure at baseline were excluded from analyses. Alcohol consumption in the month prior to the baseline interview was assessed by self-report. The multivariable adjusted relationships between alcohol consumption and subsequent risk of heart failure were analyzed using Cox proportional hazards regression.

Results: During an average of 8.6 years of follow-up, 292 persons developed heart failure. Among those consuming no alcohol, 1-30 ounces of alcohol, and >30 ounces of alcohol in the month prior to baseline, the crude heart failure event rates per 1000 person-years of follow-up were 16.3, 11.0 and 6.6 respectively. In multivariate Cox regression models that controlled for age, sex, race, education, history of myocardial infarction, hypertension, and results of alcohol consumption and risk of heart failure have not been established.

Conclusions: IRAD provides an opportunity to study elderly with AAD in the current era. Our investigation shows significant differences in demographics, comorbidities, clinical features, and test findings in elderly patients with AAD as compared to younger cohort. Further, our data indicates that elderly patients are more often managed conservatively in the setting of heart failure compared to younger patients. Further research is needed to better understand the risk factors and management of heart failure in elderly patients.
1046A ABSTRACTS - Cardiac Function and Heart Failure

Cardiac Function and Heart Failure

1046-60 Age Related Differences in Underlying Pathophysiology of Suspected Vasovagal Syncope

Anvinder S. Kerbàn, Nevin Wijesekera, Ann-Christine Fransen, Timothy Sorak, Gita Mathur, David Heavan, Richard Sitten, Chelsea & Westminster Hospital; London, United Kingdom, London Chest Hospital; London, United Kingdom

Background: In this and other populations, a large proportion of cases were asymptomatic and a minority of all cases were receiving adequate treatment. This supports the need for screening programmes for left ventricular systolic dysfunction in the community.

Conclusions: BNP and NT-proBNP have similar sensitivity and specificity for the diagnosis of symptomatic and asymptomatic LVSD for the 2 assays. The area under the curve (AUC) for all LVSD was 0.82 for both NT-proBNP and for BNP (sensitivity of 94% for both and specificity of 56% and 63%, respectively at relevant cut-offs). Both tests had high negative predictive values of 99% at cutoffs, but low PPVs of 11% and 13%, respectively.

Conclusions: BNP and NT-proBNP have similar sensitivity and specificity for the diagnosis of LVSD in a community setting. These performance is superior to routine screening tests such as mammography (AUC 0.85) and PAP smears (AUC 0.70). Despite delays in transport, processing and analysis of samples (routine in primary care), NT-proBNP and BNP remain useful predictors of LVSD. NT-proBNP/ELISA may offer technical advantages.

1045-52 The Prevalence and Aetiopathological Associates of Left Ventricular Dysfunction in the Population of North Glasgow, Scotland, Aged 55 to 74 Years

Stephen D. Robb, Theresa A. McDonagh, Caroline E. Morrison, Henry J. Dargie. University of Glasgow, Glasgow, United Kingdom

Background: The epidemiology of heart failure has been previously well described but less is known about the epidemiology of its major contributor, left ventricular (LV) systolic dysfunction.

Methods: We studied 1009 individuals aged 55 to 74 years randomly selected from the urban population of North Glasgow, Scotland. Each person completed questionnaires regarding demographics, past medical history, the symptom of breathlessness, and current medication. Their blood pressure was measured and a resting 12 lead ECG was recorded and coded according to the Minnesota coding system. A full echocardiogram was performed on an L.V. ejection fraction (L.V.E.F.) calculated using a biplane Simpson's method.

Results: L.V.E.F. was able to be calculated in 750 people and the median L.V.E.F. was 59.7%. Based on a subgroup considered to be free from evidence of cardiovascular disease and its major risk factors left ventricular (L.V.) systolic dysfunction was taken to be represented by an L.V.E.F. of < 35%. L.V. systolic dysfunction was present in 50 people (6.7%) and its prevalence rose with age: being higher in men than in women (9.4% vs 4.6%, P<0.004) in each five year age band. The proportion of L.V. systolic dysfunction which was considered to be symptomatic (associated with cardiovascular breathlessness or being treated with a loop diuretic) was 46% with no age or gender effect evident. Only 10% of individuals with L.V. systolic dysfunction were currently receiving treatment, with an angiotensin converting enzyme inhibitor. The principle aetiological associate of L.V. systolic dysfunction was ischemic heart disease (based on questionnaire and E.C.G. findings) with it accompanying 78% of all cases. Neither isolated hypertension nor diabetes mellitus were more prevalent in individuals with L.V. systolic dysfunction than in individuals with normal L.V. function.

Conclusion: This study found a higher prevalence of L.V. systolic dysfunction than previously described in this and other populations. A large proportion of cases were asymptomatic and a minority of all cases were receiving adequate treatment. This supports the need for screening programmes for L.V. systolic dysfunction in the community.
Background: Heart failure (HF) is a major cause of mortality and morbidity. Treatment improves prognosis in left ventricular systolic dysfunction (LVSD), the main cause of HF. Unfortunately diagnosing heart failure on clinical grounds is difficult and echocardiography is not routinely available to primary care in many parts of the world. Assays of natriuretic peptides (particularly BNP) may prove useful as screening tests for HF. Previous studies have mainly been in hospital, with samples taken under lab conditions, from unrepresentative populations. Objectives: To establish the performance characteristics of BNP assays in the diagnosis of heart failure in the general population. Methods: 591 patients were randomly selected from community populations stratified for socio-economic status assessed as part of the ‘ECHOES study of HF prevalence. 52 were diagnosed using the presence or absence of LV dysfunction using echocardiography. Conclusions: BNP and NT-proBNP (Roche Diagnostics) were subsequently performed at a central lab. Results: Receiver Operator Characteristic (ROC) curves were plotted for diagnosis of heart failure for the 2 assays. The area under the curve (AUC) was 0.69 for NT-proBNP and 0.83 for BNP (sensitivity of 89% and specificity of 65% at 20 pg/ml). Both tests exhibited very similar ROC curves, with better sensitivity at high cutoff values. Conclusions: BNP and NT-proBNP have been shown to be sensitive and specific for the diagnosis of HF in a community setting. Despite delays in transport, processing and analysis of samples (routine in primary care) NT-proBNP and BNP remain useful pretests of HF. These data suggest BNP may be utilized in echocardiography to rule out and confirm clinical testing.

The Use of B-Natriuretic Peptide (BNP) in Assessing Cardiac Function in Patients with Diabetes Mellitus

Victoria A. Epelboyn, Kathrin Morrison, Padma Krishnaswamy, Radmila Kazanegra, Men B. Maasik. WADPHCS, Van Doga, CA

Background: Diabetic patients are at significant risk for cardiovascular events. Routine screening of diabetic patients with echocardiography is not feasible due to its limited availability, high cost, as well as the relatively asymptomatic nature of cardiac dysfunction in diabetic patients. Brain Natriuretic Peptide (BNP) is secreted predominantly from left ventricle (LV) in response to both volume expansion and pressure overload and may be elevated early in the course of both systolic and diastolic cardiac dysfunction. We therefore asked whether BNP levels can be used to screen diabetic patients for cardiac dysfunction. Methods: The subjects were 111 diabetic patients referred for echocardiography to evaluate the presence or absence of LV dysfunction. Plasma levels of BNP were measured by a point-of-care immunoassay (BioMerieux Diagnostics). The results of BNP levels were blinded to cardiologists making the assessment of LV function. Results: In 51 patients with LV function, BNP = 30 ± 9 pg/ml. This is significantly less than patients with systolic dysfunction (n = 13) BNP = 379 ± 118 pg/ml, diastolic dysfunction (n = 33) BNP = 474 ± 106 pg/ml, and systolic plus diastolic dysfunction (n = 22) BNP = 586 ± 189 pg/ml (P < 0.001). All group comparisons were made on log transformed BNP levels. BNP levels over 80 pg/ml were seen in only 5.3% of patients with normal LV function, compared to 54.0% of patients with abnormal ventricular function (P < 0.001). A receiver-operating characteristic (ROC) curve showing the sensitivity and specificity of BNP against echocardiographic diagnosis revealed the area under the curve to be 0.92 (95% confidence interval 0.86 to 0.98). Conclusions: BNP is a specific and sensitive test for detecting the presence or absence of LV dysfunction using echocardiography. Conclusion: A simple and rapid assay for BNP can be employed to reliably screen diabetic patients for presence or absence of LV dysfunction. This test may be especially useful for detecting early LV dysfunction in asymptomatic patients.

N-Terminal Pro Brain Natriuretic Peptide Plasma Level is Dependent of Age and Gender: A Survey of a Large Urban Population Aged Older Than Fifty Years

Ian Raymond, Bjorn A. Greinert, Frants Pedersen, Jeanett Dimth, Matthias Raue. Starbeck Hospital. Copenhagen, Denmark, Integrated Health Care Solutions, F. Hohmann-Le Roche Ltd, Basel, Switzerland

Background: N-terminal pro brain natriuretic peptide (NT-proBNP) has in several [BG] studies been reported to be a useful diagnostic of congestive heart failure (CHF). The aim of the present study was to examine the influence of age and gender on NT-proBNP. Methods: A total of 603 unrelated subjects (mean age 66 years, range 50-90) were examined. The participants were answered a questionnaire on symptoms, previous heart disease and cardiovascular risk factors and ECG and blood samples were obtained. Results: We found a significant increase with age in the level of NT-proBNP. A similar pattern was found in 'normal' subjects without history of myocardial infarction or diastolic dysfunction. NT-proBNP levels over 44 pg/ml in normal ECG, blood pressure ≤140/90, no diabetes or lung disease (n=135). The mean concentration of NT-proBNP in the entire study population was higher than in normal subjects (42±19 (NS) versus 19±14 pmol/l; p<0.001). NT-proBNP was significantly higher in females than in males in both study populations.
Evaluation of N-terminal Pro-Brain Natriuretic Peptide as Marker of Impaired Left Ventricular Function After Myocardial Infarction
Andreas Luchner, Christian Hongsteng, Hannesloe Loewel, Juergen Trawinski, Matthias Baumgart, Heribert Schunkert, Guenter A. J. Riegger, Stefan R. Holmer, Klinikum Innenmedizin II, Augsburg, Germany, Roche Integrated Health Care Solutions, Basel, Switzerland

Background: Plasma concentrations of N-proBNP were found to be increased early after acute myocardial infarction (MI), we tested whether N-proBNP can serve as predictive marker for left ventricular (LV) dysfunction late after MI.

Methods: In 635 MI patients (MONICA-Munich, Augsburg, time after MI 1-10 years, mean 5.6) we assessed the association between N-proBNP, LV ejection fraction (EF) (left and mass, and anthropometric, hemodynamic, and metabolic variables. In addition, 465 of their siblings without MI (no MI) were studied. N-proBNP was measured by non-enzymatic, chemiluminescent homogeneous immunoassay (Muench Diagnostics).

Results: N-proBNP was elevated in patients (56±13.3 pmol/ml vs. noMI 31.2±8.1, p<0.001). Particularly elevated N-proBNP was found in MI patients with severe LV dysfunction (LVEF<25%, 18.0±4.19 pmol/ml, p<0.01 vs. controls and vs. MI without LV dysfunction, LV hypertrophy [LHV], 214.6±167.1 pmol/ml, p=0.01 vs. control and vs. MI without LHV), and renal dysfunction (ReDo, 210.3±51.4 pmol/ml, p<0.01 vs. control and vs. MI without ReDo). Multiple regression analyses revealed that N-proBNP was correlated with LV mass index, glucagon receptor, history of MI, gender, and diastolic blood pressure. prognostic parameters are shown in the table.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Area (%)</th>
<th>Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-proBNP</td>
<td>29.9</td>
<td>95.9</td>
</tr>
<tr>
<td>LVEF&lt;25%</td>
<td>24.3</td>
<td>93.0</td>
</tr>
<tr>
<td>LHV</td>
<td>22.6</td>
<td>92.3</td>
</tr>
<tr>
<td>ReDo</td>
<td>21.2</td>
<td>92.0</td>
</tr>
</tbody>
</table>

Conclusion: Plasma NT-proBNP appears to represent a biochemical diagnostic tool for the detection and particularly the exclusion of LV dysfunction with or without concomitant LVH or renal dysfunction.

1046-09
CHF Severity and Neurohormonal Activation in a Large International Population With Chronic Heart Failure Enrolled in Vat-HeFT
Roberto Latini, Inder Anand, Serge Masson, Dianne Judd, Monica Sileo, Gabriella Baldi, Roberti Reiser, Darrick R. Spornick, Aldo R. Maggioni, Gianni Tonetti, Jay N. Cohn, on behalf of the Vat-HeFT Investigators, Institute of Rickettsial and Protozoal Pathology, Milano, Italy, University of Minnesota, Minneapolis, MN

Background: Chronic heart failure (CHF) is associated with progressive activation of various neuroendocrine systems that may relate to the progression of the disease. The relation between baseline plasma hormones and CHF severity (NYHA functional class and echo LV dysfunction) was assessed in a large (n=8,011 patients; 59% on ACE-I, 36%, on beta-blockers) international clinical trial (Vat-HeFT) which is evaluating the efficacy of the Ang II receptor antagonist valsartan. Methods: Blood samples were to be collected at entry and plasma brain natriuretic peptide (BNP, pg/ml), renal activity (PRA, ng/ml/h), aldosterone (Aldo, pg/ml), big endothelin (Big ET-1, pm), and endothelin-1 (ET-1, pm) were assessed by specific immunoassays, and neuropeptide (NE, pg/ml) with HPLC in core labs. The population was stratified according to NYHA class (I [62%] vs. III-IV [38%]), median value of LVEF (27%) and LV internal dimension (LVIDd) (3.57 cm/m2).

Results: Baseline BNP was not different in the placebo and bucindolol groups. At 3 months, patients treated with bucindolol had lower Big-ET and NE levels than patients receiving placebo (10.6±3.0 vs. 13.6±3.2, p<0.05; and 435±126 vs. 487±126, p<0.003, respectively). These differences were not present at 12 months. None of the other neurohormones were different between groups at any time point. Correlations of Big-ET and BNP correlate with NYHA Class and LV in patients with advanced heart failure. Bucindolol therapy was associated with an early decline in Big-ET and NE, but these changes did not persist at 12 month follow-up.

1046-07-71
Effect of Nesiritide on Endothelin-1 Levels in Patients With Decompensated Congestive Heart Failure
Donna Aronson, Andrew J. Burger. Beth Israel Deaconess Medical Center, Boston, MA, Harvard Medical School, Boston, MA

Background: Endothelin-1 (ET-1) is elevated in congestive heart failure (CHF) and has been implicated in mediating elevation of cardiac filling pressures, pulmonary hypertension, and the progression of circulatory failure. Brain natriuretic peptide (BNP) is produced in ventricular myocytes and its levels are substantially augmented in response to ventricular overfilling in CHF, promoting a decrease in cardiac filling pressures. In several studies have shown that BNP strongly inhibits ET-1 production. We hypothesized that the administration of nesiritide (BNP) would reduce ET-1 levels in patient with CHF.

Methods: The study population includes a subset of 32 patients with decompensated CHF enrolled in the VESPERTEN (Vasopressin Suppression Through Endothelin Inhibition in Congestive Heart Failure) study. Patients were randomized to receive dobutamine (minimal dose 50μg/kg/min, n = 27), low-dose (0.015 μg/kg/min) nesiritide to randomized to dobutamine (minimal dose 50μg/kg/min, n = 27), low-dose (0.015 μg/kg/min) nesiritide and placebo (n = 20). Plasma levels of nephrilinpeptide (NEP), ET-1, tumor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6) were obtained in each patient immediately prior to administration of study drugs and following 15 minutes of treatment.

Results: There was no significant change in ET-1 levels with dobutamine therapy (8.5 ± 0.79 to 8.1 ± 0.72 pg/ml, p = 0.63). By contrast, both low-dose (8.6 ± 0.69 to 6.8 ± 0.58 pg/ml, p = 0.001) and placebo (17.7 ± 1.3 to 9.0 ± 1.1 pg/ml, p = 0.04) nesiritide therapy resulted in a significant drop in plasma ET-1 levels. In patients receiving nesiritide, baseline ET-1 predicted the magnitude of the decrease in ET-1 at 24h (r = -0.52, p = 0.0001). No significant change was observed in NE, TNF-α, or IL-6 levels during dobutamine or nesiritide therapy.

Conclusions: In patients with decompensated CHF, acute BNP infusion induces a rapid reduction in plasma ET-1. This effect may account, in part, for the beneficial hemodynamic and clinical effects of nesiritide in the setting of heart failure.

1046-72
Resting Cardiac Production of Natriuretic Peptides Determines the Effects of Infusion of Brain Natriuretic Peptide in Heart Failure
Hans P. Brumm-Lu-Ricca, David M. Kaye, Robby L. Woods, Jacqueline Herschings, Florentina Socaciu, Murray D. Esler. Baker Medical Research Institute, Melbourne, Australia, Howard Florey Institute, Parkville, Australia

Background: Natriuretic peptides (NPs) possess beneficial effects in heart failure (HF). Intravenous infusion of brain NP (BNP) and inhibition of degradation of NP have been proposed as novel therapies. However, it is unknown whether there are determinants of NP production. We tested whether there were determinants of NP production that could explain efficacy of infusion of NP.

Methods: In 625 MI patients (MONICA Ml-register, Augsburg; time after MI 1-10 years, n=279, 38% with advanced heart failure. Bucindolol therapy was associated with an early decline in Big-ET and NE, but these changes did not persist at 12 month follow-up.

Results: Baseline BNP was not different in the placebo and bucindolol groups. At 3 months, patients treated with bucindolol had lower Big-ET and NE levels than patients receiving placebo (10.6±3.0 vs. 13.6±3.2, p<0.05; and 435±126 vs. 487±126, p<0.003, respectively). These differences were not present at 12 months. None of the other neurohormones were different between groups at any time point. Correlations of Big-ET and BNP correlate with NYHA Class and LV in patients with advanced heart failure. Bucindolol therapy was associated with an early decline in Big-ET and NE, but these changes did not persist at 12 month follow-up.

Conclusions: In patients with decompensated CHF, acute BNP infusion induces a rapid reduction in plasma ET-1. This effect may account, in part, for the beneficial hemodynamic and clinical effects of nesiritide in the setting of heart failure.
There were no adverse effects of IET SCINT or ECHO as initial test were required in Harpreet Johl, Samuel D. Turnipseed. University of California, Davis, Sacramento, CA Orange County Convention Center, Hall A4 Sunday, March 18, 2001, 3:00 p.m.-5:00 p.m.

Impact of Magnesium on Exercise Duration at Study Entry and Exit

<table>
<thead>
<tr>
<th>Magnesium (n=94)</th>
<th>Placebo (n=93)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entry exercise duration (min+SD)</td>
<td>8.1±2.7</td>
<td>7.9±2.9</td>
</tr>
<tr>
<td>Exit exercise duration (min+SD)</td>
<td>8.7±2.1</td>
<td>7.9±2.9</td>
</tr>
<tr>
<td>p-value</td>
<td>0.0104</td>
<td>0.1024</td>
</tr>
</tbody>
</table>

Quality of life was significantly improved in the magnesium group by one month and continued to be improved compared to no significant improvement obtained in the placebo group (p<0.01). Conclusion: Magnesium supplementation significantly improves functional capacity measured by exercise duration and quality of life in stable CAD patients.

Impact of Magnesium on Exercise Duration and Quality of Life in Patients With Coronary Artery Disease

Michael Shuchter, C. Noel Butany, Marz, Hans S. Shulinger, Michael Shanh, Shironi Meletsky, Othmar Pachinger, Jorg Bley, Babet Bahniwitz, The Heart Institute, Sheba Medical Center, Tel Aviv University, Tel Hashomer, Israel, Cedars-Sinai Medical Center, Los Angeles, CA

Background: Coronary artery disease (CAD) patients are often relatively magnesium depleted. The impact of magnesium supplementation on exercise duration and quality of life in CAD patients has not previously been assessed. Methods: In a multicenter, randomized, and double-blind, trial, 187 stable CAD patients (151 men, 36 women, mean age of 63±10 years, range: 42–83), were randomized to receive either magnesium oxide orally (Magnosolv, 30 mmoliday, Asta Medica, Vienna, Austria) (n=94) or placebo (n=93) for 6 months. Entry and after 6 months exit symptom-limited exercise testing (Bruce protocol) were performed and quality of life questionnaires were filled out. Results (Table):

Conclusions: IET is safe and accurate for initial assessment and short-term prognostic evaluation of a majority of low risk pts presenting with chest pain. For the remainder of these pts, who comprise a substantial minority, cardiac stress imaging is required as the initial test.

Heart Rate Recovery and Functional Capacity as Predictors of Mortality in Very Old People

Barbara Masling-Report, Eugene Blackstone, Claire Snader, Michael S. Laufer, Cleveland Clinic, Cleveland

Background: The prognostic value of exercise testing in very old adults has not been well-defined. Methods: Consecutive adults aged >75 years without a history of heart failure, valve disease, or pacemaker implantation underwent symptom-limited exercise testing and were followed for 4 years. Impaired functional capacity was defined as a peak exercise workload <5 METS in men and <4 METS in women. An abnormal heart rate recovery was defined as a failure of the heart rate to fall by >12 beats during the first minute after exercise. Results: There were 1108 patients eligible for analyses (mean age 78, range 75–92, 32% female). Abnormal heart rate recovery was found in 440 (40%) and impaired functional capacity in 291 (26%). During follow-up 229 patients (21%) died. In univariate analyses, death was predicted by an abnormal heart rate recovery (38% vs. 16%, hazard ratio [HR] 1.9, 95% CI 1.5–2.5, P<0.0001) and by impaired functional capacity (30% vs. 15%, HR 2.7, 95% CI 2.1 to 3.5, P<0.0001). The only other strong predictor was >5 predicted fatal risks of age were (P<0.001), smoking (P=0.008), history of myocardial infarction (P=0.02), and non-use of aspirin (P=0.0002). Also of note, the use of beta-blockers (n=41), (26% of the cohort) had significant impact on the association of heart rate recovery.

ABSTRACTS - Cardiac Function and Heart Failure 149A

Robert H. Fiedler, Ismar Fiedler, Michael Fiedler, William Fieck, Arnold Pfeiffer, Michael Fiedler. University of St. Louis, MO, CV Therapeutics, Palo Alto, CA

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ACh concentrations, respectively. This enhanced vasorelaxation was abolished in the mals served as controls. Compared to sham rats, untreated animals had a decreased (P < 0.05) vasorelaxation in Ml rats by 84% and 86% at 10^-4 and 10^-5 M.

Ml untreated animals had a decreased (P < 0.05) vasorelaxation in Ml rats by 84% and 86% at 10^-4 and 10^-5 M.

**Poster Session**

**1056 Mechanism Targeted Treatment of Heart Failure**

Sunday, March 18, 2001, 3:00 p.m.-4:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 3:00 p.m.-4:00 p.m.

**1056-45 Cardiovascular Actions of Chronic Oral Omapatrilat Are Superior to ACE Inhibition in Experimental Heart Failure**
Shing-Chun Lee, John C. Burnett. Mayo Clinic, Rochester, MN

**Background:** Omapatrilat (OMA) is a vasopeptidase inhibitor which simultaneously inhibits angiotensin converting enzyme (ACE) and neutral endopeptidase (NEP) which degrades the cardiac peptides ANP and BNP which function via cGMP. Studies report that OMA is superior to ACE inhibition (ACE-I) in reducing symptoms of congestive heart failure (CHF), yet the cardiovascular actions of chronic OMA versus ACE-I remain poorly defined. We investigated the cardiovascular and humoral actions of oral OMA versus ACE-I in a canine pacing-induced model of CHF with a third untreated group as Control.

**Methods:** Groups (n = 5, each) received OMA (100 mg/kg/d), the ACE-I Fosinopril (FSN, 1 mg/kg/d), or vehicle control, and compared to sham-operated animals without pacing (SHAM) and YMC 3 micron 4.6mm x 15cm Guanine adducts column.

**RESULTS:** Data (means + SE) for tissue total aldehyde levels (pmol/lOOmg) and LVEDP.

**Conclusion:** Our study demonstrates for the first time that in canine pacing-induced CHF, there is a marked increase in LV tissue aldehyde levels, indicative of severe oxidative stress in the failing heart. Both AT, and ETA receptor blockade ameliorates oxidative stress. The disproportionate reduction in LV aldehyde levels by AT, receptor blockade suggest that increased endogenous angiotensin II induces oxidative stress in the failing heart.

**1056-47 Elevated Cardiac Tissue Aldehyde Levels in Heart Failure: Marker of Increased Oxidative Stress and Amelioration by Neurohormonal Blockade**
Gordon W. Moe, Methesh Dossanaplan, Andrea Konig, Marina Romanova, Porter Liu. St Michael's Hospital, Univ of Toronto, Toronto, ON, Canada

**Background:** Oxidative stress is known as an important regulator of cardiac remodeling and function. Aldehydes are products of peroxidation of polyunsaturated fatty acids (PUFA) and contribute to many downstream processes that lead to oxidative stress and chronic heart failure. Cardiac aldehyde levels have been shown to correlate with adverse cardiac outcomes and higher mortality. Studies have shown that inhibition of angiotensin-converting enzyme (ACE) and neutral endopeptidase (NEP) decreases cardiac aldehyde levels. This study compared cardiac tissue aldehyde levels in a canine model of heart failure (CHF) treated with OMA vs. ACE-I vs. control groups.

**Methods:** Groups (n = 5, each) received OMA (100 mg/kg/d), the ACE-I Fosinopril (FSN, 1 mg/kg/d), or vehicle control, and compared to sham-operated animals without pacing (SHAM) and YMC 3 micron 4.6mm x 15cm Guanine adducts column.

**Results:** Data (means + SE) for tissue total aldehyde levels (pmol/lOOmg) and LVEDP.

**Conclusion:** Our study demonstrates for the first time that in canine pacing-induced CHF, there is a marked increase in LV tissue aldehyde levels, indicative of severe oxidative stress in the failing heart. Both AT, and ETA receptor blockade ameliorates oxidative stress. The disproportionate reduction in LV aldehyde levels by AT, receptor blockade suggest that increased endogenous angiotensin II induces oxidative stress in the failing heart.
Effects of Combined Endostatin A Receptor Blockade Plus ACE-Inhibition in Rats With Chronic Heart Failure

Daniela Fraccarolio, Johann Bauersachs, Paolo Galuppo, Markus Kellner, Georg Ertl.

Background: Heart failure is related to left ventricular (LV) remodeling and heart failure. We investigated the effects of the ET(A) receptor antagonist LU 138252 (LU), the ACE-inhibitor Trandoiapril (T), and the combination of LU+T in rats with chronic heart failure (CHF), LV end-diastolic pressure > 15 mm Hg on LVH, LVH, cardiac ratio of beta-Myosin Heavy Chain (MHC) to alfa-MHC mRNAs and LV dilatation.

Methods: Seven days after coronary artery ligation, rats were allocated to treatment with LU (25 mg/kg/d), T (0.6 mg/kg/d), or LU+T in drinking water for 11 weeks.

Results: Compared to T alone, LU+T prevented the increase in RV beta-MHC:alfa-MHC mRNAs. LU and T appear to be complementary option in chronic heart failure in addition to an ACE-inhibitor.

Conclusion: The combination of LU+T is beneficial in chronic heart failure.

Poster Session

1057 Myocarditis: Various Aspects and Myocardial Hypertrophy in Athletes

Sanjay Sharma, Sami Firooz, Brian Mist, Perry M. Elliott, Greg Whyte, William J. McKenna, St. George's Hospital Medical School, London, United Kingdom

Background: A number of studies have suggested that athletes have a greater risk of sudden cardiac death (SCD) than their age-matched peers. An increased left ventricular wall thickness (LVWT) is a risk factor for SCD. Myocarditis is associated with an enlarged left ventricle. A LVWT > 12 mm is exceptionally rare. Therefore, an athlete's heart can be normal. The diagnosis of myocarditis in athletes is challenging. A number of studies have reported that athletes may have cardiac hypertrophy (LVH).

Methods: We examined 5,680 athletes, 72% male, aged 9 to 55 years (median 23), participating in 38 different sports. Of those, 1,211 athletes were referred for evaluation of suspected cardiac abnormalities detected at preparticipation screening protocol (group A, positive), and 4,469 athletes, who had previously been cleared with screening protocol (group B, negative).

Results: Cardiac abnormalities were detected in 97 (8%) of the 1,211 athletes in group A, and in 41 (1%) of the 4,469 athletes in group B (p=0.001). In particular, hypertrophic cardiomyopathy was identified in 10 athletes (0.8%) in group A and none in group B (p<0.001); Marfan syndrome in 5 athletes (0.4%) in group A and in 2 (0.04%) in group B (p<0.001); dilated cardiomyopathy in 5 (0.4%) in group A and in none from group B (p<0.001). Instead, arrhythmogenic right ventricular cardiomyopathy was detected less frequently (2% in athletes in each group).

Conclusion: The Italian preparticipation screening protocol, with the 12-lead ECG, proved to be efficient in identifying most of the athletes with cardiac disease at risk of sudden death: only a relatively small proportion [1%] were subsequently identified by other echocardiographic or electrocardiographic diagnosis. In particular, athletes with cardiac disease are more consistently detected, i.e. hypertrophic cardiomyopathy, dilated cardiomyopathy and Marfan syndrome. Instead, arrhythmogenic right ventricular cardiomyopathy may not be uncommonly missed.

Tissue Factor Expression in Atrial Myocarditis Associated With Nonrheumatic Atrial Fibrillation: A Possible Cause of Cardiogenic Thromboembolism

Yasuy Nakamura, Kengo Kuroara, Kazufumi Nakamura, Tetsuo Emori, Hiroshi Morita, Chisato Yukita, Tatsuama Hamuro, Hironi Matsubara, Toshih Oh, Osakaya University Medical School, Osaka, Japan

Background: Recent myocardial infarction has been detected in some patients with aortic valve disease or atrial fibrillation. It was demonstrated that expression of tissue factor, which plays a key role in the extrinsic coagulation pathway, is induced by inflammatory cytokine. To elucidate the mechanism of thrombogenesis in non-rheumatic atrial fibrillation, we investigated tissue factor expression on the endothelia of atrium obtained from patients with nonrheumatic atrial fibrillation. To elucidate the mechanism of thrombogenesis in non-rheumatic atrial fibrillation, we investigated tissue factor expression on the endothelia of atrium obtained from patients with nonrheumatic atrial fibrillation and compared with those from normal atria.

Methods: We studied 7 patients with nonrheumatic atrial fibrillation and compared with those from normal atria.

Results: Tissue factor expression was more frequently observed in the atrial fibrillation group than in the normal group.

Conclusion: Tissue factor expression was more frequently observed in the atrial fibrillation group than in the normal group.

Poster Session

1057-51 Peak Oxygen Consumption Measurement Differentiates Physiological Left Ventricular Hypertrophy in Junior Athletes From Pathological Hypertrophy in Adolescents With Hypertrophic Cardiomyopathy

Sanjay Sharma, Sami Firooz, Brian Mist, Perry M. Elliott, Greg Whyte, William J. McKenna, St. George's Hospital Medical School, London, United Kingdom

Background: Hypertrophic cardiomyopathy (HCM) is the commonest cause of sudden cardiac death in adolescents (14-18 year olds). A large study of junior elite athletes showed 5% to have substantially increased left ventricular wall thickness (LVWT) ranging between 12-14 mm. Our experience of 95 adolescent patients with HCM suggests that 8% of patients have a LVWT in the same range. Many patients are highly active but remain at high risk of sudden death. Some junior athletes therefore, fall into the "gray zone" where distinction between physiological and pathological left ventricular hypertrophy (LVH) is crucial but may be difficult with echocardiography alone. This study evaluated the role of peak oxygen consumption (pVO2) measurements in differentiating physiological LVH from HCM.

Methods: Asymptomatic adolescents (off medication) with genetically proven non-rheumatic HCM and mild LVH (LVWT 12-14 mm), male athletes matched for age, LVWT, and a respiratory quotient > 1 indicating adequate stress.

Results: Each athlete with a LVWT exceeding predicted normal limits also had a greater than predicted left ventricular hypertrophy size (LVH) (range 2-5 mm).

Conclusion: pVO2 has a high discriminatory power in adolescents with LVH.

1057-55 Efficacy of the Preparticipation Screening for the Detection of Cardiovascular Abnormalities at Risk of Sudden Death in Competitive Athletes: The Italian Experience

Pelliccia Antonio, Di Paolo F.M., De Luca R., Bucoferri C., Maron B.J., Institute of Sport Science, Rome, Italy, Minneapolis Heart Institute Foundation, Minneapolis, MN

Background: There is substantial interest in preparticipation cardiovascular screening in athlete populations, and cost-effective strategies for identification of the potentially lethal cardiac diseases are still debated. The 12-lead ECG, in addition to medical history and physical examination, is relied upon extensively in the systematic preparticipation screening of Italian competitive athletes. The aim of our study was to assess the efficacy of this protocol in identifying cardiovascular diseases at risk for sudden death.

Methods: We examined 5,680 athletes, 72% male, aged 9 to 55 years (median 23), participating in 38 different sports. Of those, 1,211 athletes were referred for evaluation of suspected cardiac abnormalities detected at preparticipation screening protocol (group A, positive), and 4,469 athletes, who had previously been cleared with screening protocol (group B, negative).

Results: Cardiac abnormalities were detected in 97 (8%) of the 1,211 athletes in group A, and in 41 (1%) of the 4,469 athletes in group B (p<0.001). In particular, hypertrophic cardiomyopathy was identified in 10 athletes (0.8%) in group A and none in group B (p<0.001); Marfan syndrome in 5 athletes (0.4%) in group A and in 2 (0.04%) in group B (p<0.001); dilated cardiomyopathy in 5 (0.4%) in group A and in none from group B (p<0.001). Instead, arrhythmogenic right ventricular cardiomyopathy was detected less frequently (2% in athletes in each group).

Conclusion: The Italian preparticipation screening protocol, with the 12-lead ECG, proved to be efficient in identifying most of the athletes with cardiovascular disease at risk of sudden death.

1057-56 Tissue Factor Expression in Atrial Myocarditis Associated With Nonrheumatic Atrial Fibrillation: A Possible Cause of Cardiogenic Thromboembolism

Yasuy Nakamura, Kengo Kuroara, Kazufumi Nakamura, Tetsuo Emori, Hiroshi Morita, Chisato Yukita, Tatsuama Hamuro, Hironi Matsubara, Toshih Oh, Osakaya University Medical School, Osaka, Japan

Background: Recent myocardial infarction has been detected in some patients with atrial fibrillation. It was demonstrated that expression of tissue factor, which plays a key role in the extrinsic coagulation pathway, is induced by inflammatory cytokine. To elucidate the mechanism of thrombogenesis in non-rheumatic atrial fibrillation, we investigated tissue factor expression on the endothelia of atrium obtained from patients with nonrheumatic atrial fibrillation. To elucidate the mechanism of thrombogenesis in non-rheumatic atrial fibrillation, we investigated tissue factor expression on the endothelia of atrium obtained from patients with nonrheumatic atrial fibrillation and compared with those from normal atria.

Methods: We studied 7 patients with nonrheumatic atrial fibrillation and compared with those from normal atria.

Results: Tissue factor expression was more frequently observed in the atrial fibrillation group than in the normal group.

Conclusion: Tissue factor expression was more frequently observed in the atrial fibrillation group than in the normal group.

Poster Session

1057-52 Physiological Limits of Left Ventricular Hypertrophy in Elite Junior Athletes: Relevance to Differential Diagnosis of Athlete's Heart From Hypertrophic Cardiomyopathy

Sanjay Sharma, Sami Firooz, Greg Whyte, Perry M. Elliott, William J. McKenna, St. George's Hospital Medical School, London, United Kingdom

Background: Regular intensive physical training in some sports may cause an increase in left ventricular wall thickness (LVWT) creating uncertainty regarding the differential diagnosis with hypertrophic cardiomyopathy (HCM). The distinction between physiological hypertrophy in athletes and HCM is crucial since HCM is responsible for about one third of all sudden cardiac deaths in young athletes. Available data defining the athlete's heart are limited to senior athletes. Therefore, a paucity of data in junior athletes (aged 16 or less) in whom sudden death due to HCM is most prevalent.

Methods: 95 junior elite athletes (74% male), aged 15-16.4 years (range 14-18 yrs) and 250 healthy non-athletic controls of similar age, gender and body surface area (BSA) underwent 2-D echocardiography. Long- or high-level training amongst athletes (regional or national) was 4.3(1.5) yrs.

Results: Compared with controls, trained athletes had an increased LVWT (9.1(1.6)mm; range 6.4-11.4mm; p<0.001). The LVWT exceeded the predicted upper limits in 35 (3.5%) athletes. However, in only 1 athlete (0.15%) was the absolute LVWT > 12 mm. Each athlete with a LVWT exceeding predicted normal limits also had a greater than predicted left ventricular hypertrophy size (LVH) (range 2-5 mm).

Conclusion: Junior athletes have a greater LVWT compared with non-athletic controls. In an important minority (5%) the LVWT exceeds predicted upper limits and is always associated with an enlarged left ventricle. A LVWT > 12 mm is exceptionally rare. Therefore, a diagnosis of HCM should be considered in any junior elite athlete with a LVWT > 12 mm and a non-dilated left ventricle.
1057-1058 Coronary Vasomotor Response in Cardiac Transplant Recipients. A Detailed Analysis in 286 Investigations
Michaela Weiss, Simon Panitkovski, Bruno Moser, Wolfgang von Steinau. University Hospital Gussenhoven, Munich, Germany. Stanford University Medical School, Stanford, CA

Endothelial activation is an early event in the process leading to cardiac allograft vasculopathy (CAV). Invasive vasomotor dysfunction occurs early after heart transplantation (HTx). However, the causal prevalence of this specific entity of CAV over time is still unknown and, therefore, was investigated in a large patient cohort. 286 investigations were performed in 100 HTx patients without angiographic disease. Patients were divided in 3 groups according to time after HTx: group 1: 1-6 months after HTx (n=81); group 2: 12-24 months after HTx (n=75); group 3: >24 months after HTx (n=114). Endothelium-dependent (S and 150ug/15 min i.c. Ado) and -independent (Adenosine; 800 ug/15 min ic Ado) vasomotor function was determined in epicardial (proximal and distal QCA) and microvascular (capillary Doppler) compartments. Normal vasomotor endothelial function was defined by a 10% diameter constriction to Ado, moderate epicardial endothelial dysfunction (mMED) as >10% diameter constriction to Ado, respectively. Normal microvascular endothelial function (mMEF) was defined as coronary flow velocity increase to Ado (Ado) was >105% (>170%) and was independent of basal coronary flow. A strong correlation between Ado and Ado response occurred in conduit and resistance vessels (r=0.24 and r=0.16; p<0.0001), whereas epicardial and microvascular measurements in response to Ado were not significant. Conclusion: Coronary flow velocity increase to Ado was strongly associated with early endothelial dysfunction in both compartments, with a trend towards significance in microvascular compartments.

1058-56 Progression of Intimal Thickening is Greatest Early After Cardiac Transplantation and Not Directly Related to Changes in Vessel Size (Remodeling): A 4-Year Serial Intravascular Ultrasound Study
Hiroshi Tsutui, Khalid M. Zafar, Paul Schoenhagen, Timothy D. Crowe, William A. Maguire, Alexander J. Dong, Donnica Scarduffa, Michael A. Virvo, Guillermina Tancio, Steven E. Nissen, E Murat Tuzcu. The Cleveland Clinic Foundation, Cleveland, OH

Background: In native vessel atherosclerosis, remodeling is described as an adaptive change in vessel size that occurs to accommodate plaque volume. However, in transplant vascularopathy, there is limited data to describe the relationship between intimal thickening and coronary artery remodeling. Methods: In 23 cardiac transplant recipients, serial intravascular ultrasound (IVUS) imaging was performed within 36 weeks of transplantation and annually for 4 years. In 23 imaged LAD arteries, 54 segments were matched between baseline to follow-up. For each patient, 12.5-59.9 mm long matched segments were analyzed using still images 1 mm apart. External elastic membrane (EEM) area, lumen area and intimal area (IA) were measured and %IA was derived [%IA/EEM area x100]. A mean value for each segment was calculated. Segments were defined as showing “progression” if mean intimal area increased >10% of EEM area in one year and “non-progression” if the change was <10%. Positive and negative remodeling of coronary artery were defined as >10% change in EEM area in one year. Results: During the 1st and 2nd years, intimal area increased rapidly from 1.8±1.1 (baseline) to 3.1±2.1 (1 year) to 5.9±2.8 (2 year) mm² (p<0.001, r=0.41). Progression was more common in 1st and 2nd years post-transplant (34/54 segments) than in years 3 to 4 (7/54), p<0.001(Table). However, both positive and negative remodeling were observed in progression and non-progression segments. Conclusion: In transplant vascularopathy, intimal thickening occurs primarily early after transplantation and can be associated with positive or negative remodeling. Additional, changes in vessel size were observed in segments without significant intimal thickening, indicating that this phenomenon is not solely determined by the degree of disease progression.

1058-57 Modulation of Cyclosporin-induced Coroary Artery Dysfunction by Tetrahydrobiopterin: A Novel Mechanism of Protection
Satish R. Raj, Aaron S. Dumont, Khalid Al-Faraidy, Andrew Mattland, Subodh Verma. University of Calgary, Calgary, AB, Canada

Background: Cyclosporin A (CyA) impairs endothelial function and enhances vascular reactivity via the production of superoxide anions. Since enhanced superoxide production has been implicated in the pathogenesis of CyA-induced endothelial dysfunction, we tested the effect of CyA on the production of NO and superoxide anions in isolated coronary arteries from rats. Method: CyA was added to the incubation medium and the release of superoxide anions was measured in isolated coronary arteries (n=10) using the lucigenin-enhanced chemiluminescence technique. Results: CyA (100-500 nmol/L) caused a dose-dependent increase in superoxide anion production (p<0.001). Since NO production was not affected, we hypothesized that CyA-induced endothelial dysfunction is due to the increased production of superoxide anions. We investigated the effect of NOS activators (tetrahydrobiopterin, pyruvate, and adenosine triphosphate) on CyA-induced endothelial dysfunction. Conclusion: CyA-induced endothelial dysfunction is mediated by the production of superoxide anions. Since enhanced superoxide production may serve to inactivate NO, an effective therapeutic strategy for CyA-induced endothelial dysfunction may be the prevention of CyA-induced superoxide production in order to improve endothelial function.

1059-52 Expression of the Signal Transduction Protein 14-3-3 Gamma in Injured Arteries and Stimulated Human Vascular Smooth Muscle Cells
Michael V. Astilean, Christopher Carbona, Howard Eisen. Temple University School of Medicine, Philadelphia, PA

Background: Cellular proteins induced by vascular injury which play a role in activation of medial vascular smooth muscle cells for antirestenotic therapy and for translation arteriopathy. The 14-3-3 family of proteins are thought to play a role in this pathway (with tetrahydrobiopterin) may improve CyA-induced endothelial dysfunction. Methods: In 14-3-3 protein expression in rat aortic smooth muscle cells in vivo and in vitro. Results: 14-3-3 expression was significantly increased in rat aortic smooth muscle cells in vitro compared to control cells. Conclusion: 14-3-3 proteins may be a potential target for antirestenotic therapy and for translation arteriopathy.

1059-54 The 14-3-3 gamma protein is expressed in rat aortic smooth muscle cells in vivo and in vitro. Results: 14-3-3 expression was significantly increased in rat aortic smooth muscle cells in vitro compared to control cells. Conclusion: 14-3-3 proteins may be a potential target for antirestenotic therapy and for translation arteriopathy.
null
Inotropic Effect of Glucose-Insulin-Potassium infusion: Comparison With Low Dose Dobutamine

Lucas J. Klein, Linda C. M. C. van Clampon, Garntin T. Tzeleva, Otto Kamp, Cees A. Visser, Frans C. Visser. University Hospital VU, Amsterdam, The Netherlands

Background We previously observed that glucose-insulin-potassium (GIK) infusion recruits contractile reserve in dysfunctional segments in patients shortly after acute myocardial infarction (AMI) to a similar extent as low-dose dobutamine (LDD) infusion. We hypothesized that GIK infusion would also result in improved global ventricular function.

Methods Thirty patients underwent GIK echocardiography 5.2±3 days after AMI. The GIK protocol consisted of a fixed insulin infusion rate (100 mU/kg/h) and a variable dose of glucose/KR, to maintain euglycemia. Four additional patients received an infusion of saline instead of GIK. Echocardiograms were made at baseline and after 80 min of infusion. In all patients LDD echocardiography was performed with echocardiographers at baseline and at 15 min after infusion. Echocardiograms were analyzed off-line and end-diastolic (ED) and end-systolic (ES) volumes were determined. From these values, stroke volume (SV) and ejection fraction (EF) were calculated, as well as cardiac output (CO).

Results During LDD infusion, both EDV and ESV decreased, with an increase in EF, SV and CO (see Table). During GIK infusion, EDV did not decrease whereas ESV did. Also, SV and EF increased, without an increase in heart rate (HR) or rate-pressure product (RPP). Saline infusion had no effect on EDV, ESV or CO.

LDD Base LDD 15 mg GIK Base GIK 60 min

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LDD Base</th>
<th>LDD 15 mg</th>
<th>GIK Base</th>
<th>GIK 60 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV (ml)</td>
<td>135±30</td>
<td>123±30</td>
<td>0.0105</td>
<td>135±30</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>63±28</td>
<td>54±19</td>
<td>&lt;0.001</td>
<td>64±24</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>72±20</td>
<td>70±23</td>
<td>0.130</td>
<td>71±16</td>
</tr>
<tr>
<td>EF (%)</td>
<td>54±11</td>
<td>64±40</td>
<td>&lt;0.001</td>
<td>52±10</td>
</tr>
<tr>
<td>CO (l/min)</td>
<td>4.9±1.6</td>
<td>6.1±5.9</td>
<td>0.959</td>
<td>4.7±1.2</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>88±11</td>
<td>83±13</td>
<td>&lt;0.001</td>
<td>86±12</td>
</tr>
<tr>
<td>RPP (mmHg)</td>
<td>23.6±4.3</td>
<td>10.0±2.5</td>
<td>0.001</td>
<td>6.7±1.9</td>
</tr>
</tbody>
</table>

Conclusion GIK infusion has a similar inotropic effect as low-dose dobutamine infusion, with a comparable increase in EDV and ESV but a larger increase in EF. CO and LVEF increase without the RPP increase in contrast to dobutamine, GIK may be particularly suited to use in the setting of (subacute) myocardial infarction in order to improve ventricular function.

Myocardial, Metabolic and Endothelial Effects of Trimetazidine in Diabetic Patients With Ischemic Dilated Cardiomyopathy

Gabriele Fragasso, Pietramaria Platti, Ludicla Monti, Gianpietro Varriano, Riccardo Carrucia, Emmauroe Savel, Sangio Cunniff, Informat Sci. University San Raffeile, Milan, Italy

We assessed whether the addition of trimetazidine (TMZ) to standard current therapy, in the treatment of diabetic patients (pts) with severe ischemic cardiomyopathy, can effectively improve exercise, symptoms, tolerance and resting left ventricular function as well as skeletal muscle metabolism and release of endothelin-1 (ET-1). Ten such pts (6 males) on conventional therapy were randomly assigned in a double blind placebo to either placebo or TMZ (20 mg tid), each arm lasting 15 days. At the end of each period, all pts underwent 2-endocardiographic, exercise testing, hyperinsulinaemic/euglycaemic clamp and forearm indium-111 macroaggregate, maximal exercise time (ET), ET-1 levels, M value (index of total body glucose disposal) and CO (see Table). During TMZ, ET-1 levels, M value and ET increased, while basal ET-1 (13.6±2.7 pg/ml) vs 11.3±2.6 pg/ml, p<0.05) decreased during TMZ. In conclusion, short-term TMZ treatment improves left ventricular function and glucose metabolism in pts with diabetes and dilated ischemic cardiomyopathy. Additionally, TMZ reduces the release of ET-1. These beneficial effects are likely to depend on the fact that TMZ inhibits myocardial oxidative phosphorylation and shifts FFA oxidation to glucose oxidation. These effects may operate in both the heart muscle and the vascular endothelium.

Clinical Determinants of Benefit in Patients With a Biventricular Pacemaker for Heart Failure

Charan Varma, Peter O’Callaghan, Sami Firoozi, Anne Bradford, Stephen Brecker, Philippe Mabo, Claude Daubert, Department of Cardiology, CHU, Rennes, France

Biventricular pacing may improve symptoms and exercise tolerance in patients with chronic LV systolic dysfunction and intraventricular conduction delay. The aim of this study was to compare the long-term effects of biventricular pacing in patients with dilated cardiomyopathy (DCM) or ischemic origin (ICM) and patients with ischemic left ventricular assist device (LVAD) vs ICM. The study included 90 patients consecutively implanted with a Biventricular pacemaker between August 1994 and February 2000. Patients were retrospectively divided into two groups (ischemic and nonischemic) according to the results of a more recent coronary angiography. Symptoms and objective data were assessed before PM implant (pre-I M) and 6 months (M-I M) after and compared between the 2 groups. Results are summarized in this table.

Comparison With Low Dose Dobutamine

Yves Etienne, Philippe Guillo, Jacques Mansourati, Abdelkader Touiza, Martine Gilard, Yves Bizais, Jean-Jacques Blanc, University Hospital of Brest, Brest, France

Background: Biventricular pacing improves exercise capacity and left ventricular function in patients with heart failure (HF). The aim of the study was to evaluate the effects of permanent LV-based pacing on LV contraction heterogeneity in such patients.

Methods: Twenty-three patients (mean age: 68±7 years) with severe HF (NYHA class 3.2±0.4 vs 3.8±0.4, p=0.038) and LV systolic dysfunction (EF 22.7%±8.2% vs 26.0%±6.5%, p=0.028) were prospectively evaluated 6 months after implantation of a LV-based permanent pacemaker (LV-PM, n=13), and an LV lead without pacing (LVP, n=10) by nuclear magnetic resonance (NMR) imaging at 1.5 T. The LV myocardium was divided into 12 segments and segmental LV longitudinal strain (LS), inotropic effect, and end-systolic pressure-volume (P-V) relation were measured.

Results: Baseline LS, inotropic effect, and P-V relation were similar in the two groups. In response to dobutamine, LS increased by 10±5% in both groups. In response to isoproterenol, LS increased by 14.9±5.6% in the LV-PM group and by 7.5±5.3% in the LVP group (p<0.05). There was no significant difference in LV global EF (20.6%±7.0% vs 22.0%±5.4%, p=0.06). LV-PM pacing was associated with a significant increase in LV global EF (23.7%±7.0% to 32.7%±8.0%, p<0.001), whereas LVP pacing did not (22.4%±9.7% to 24.3%±10.4%, p=0.16). Conclusion: Biventricular pacing provided significant and sustained improvement in LV function, exercise tolerance and LVEF in both idiopathic and ischemic DCM patients.
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1058-72 Dialysis in Diuretic Resistant Congestive Heart Failure: Pilot Experience

Amir L. Pohwani, Guy A. MacGowan, Dennis M. McNamara, Warren D. Rosenblum, Shiva Shirani, Vanderbilt University and Harper Hospital, Nashville, TN

Background: Diuretic resistance is frequently encountered in patients (pts) with chronic congestive heart failure (CHF), and is characterized by declining symptoms, progressive renal failure, frequent hospitalization and high mortality. Objective: To determine whether dialysis reduces hospitalization, and improves NYHA class in diuretic resistant CHF patients. Methods: 9 CHF patients (6 male, 3 female), mean age 66.4 years (range 52-83), NYHA class II 0% 0% 25%

% of Patients on lnotropic Therapy 80% 20% 0% 0%

BUN (mg/dl) 89.9 58.6 64 31.3

Creatinine (mg/dl) 2.1 3.6 2.8 3.3

% of Patients on Inotropic Therapy 60% 20% 0% 0%

NYHA Class III 0% 0% 25

NYHA Class III 0% 80% 0% 75%

NYHA Class IV 100% 100% 0% 0%

# of Hospitalizations within 6 months 2.4 0 3.2 0.25

P<0.05 after dialysis vs. baseline

GROUP B

GROUP A

Dialysis Dialysis

Baseline After Dialysis Baseline After Dialysis

BUN (mg/dl) 89.9 58.6 64 31.3

Creatinine (mg/dl) 2.1 3.6 2.8 3.3

% of Patients on Inotropic Therapy 60% 20% 0% 0%

NYHA Class III 0% 0% 25

NYHA Class III 0% 80% 0% 75%

NYHA Class IV 100% 100% 0% 0%

# of Hospitalizations within 6 months 2.4 0 3.2 0.25

P<0.05 after dialysis vs. baseline

1059-71 Internal Cardiovrsion of Permanent Atrial Fibrillation in Serious Heart Failure is Effective and Leads to Long Term Functional Improvement

Gaetano De Ferrari, Maurizio Landolina, Francesco Cantil, Michela Casella, Barbara Novacek, Carlo Campagna, Stefano Ghio, Luca Lazzaroni, S Matteo Hospital - IRCCS, Pavia, Italy

Among patients with heart failure (HF), atrial fibrillation (AF) is very common and associated with worsened mortality and morbidity. Effective external cardiac defibrillation (CV) is infrequently successful, recurrences rate high and an improvement in left ventricular function has never been shown. This study assessed the effects of amiodarone treatment and of internal cardioversion in 25 pts with advanced HF evaluated for heart transplantation, with permanent AF and no prior experience of CV. Mean age was 57 ± 8.7 years, NYHA class 2.5 ± 0.5. All pts had a very dilated LV (mean ED and ES volume were 275 ± 182 and 197 ± 90 ml), and LA (30 ± 11 mm diameter [A]). Amiodarone 400 mg for 4 weeks before CV and 200 mg after CV and warfarin were given to all pts. CV was performed via a coronary sinus lead. The success rate was 21 ± 9 shocks/patient, and 1 shock/patient in 14 pts (54%),<br>2 shocks in 6 pts (23%), 3 shocks in 4 pts (15%) and 4 shocks in 2 pts (8%). The mean delivered energy of successful shock was 13.9 ± 3.2 joules. No side effect from amiodarone treatment was observed. No after effect from amiodarone treatment was observed. No after effect from amiodarone treatment was observed. Thus, the combination of internal CV and amiodarone treatment is safe and effective in restoring and maintaining sinus rhythm in pts with advanced HF and permanent AF, leading to a significant improvement both in symptoms and in cardiac function.

1059-71-1059-72

1059-73 Thermal Vasodilation Therapy Improves Vascular Endothelial and Cardiac Function in Patients With Chronic Heart Failure

Takashi Kihara, Sadaoishi Bin, Masakazu Iinami, Shiro Yosihko, Kunitoku Takaseki, Yukana Shih, Shinchi Inage, Masayoshi Toyama, Chukai Tei, First Department of Internal Medicine, Kagoshima University, Kagoshima, Japan

Background: We previously reported that repeated 60 degrees C sauna, a thermal vasodilation therapy, improves hemodynamics and clinical symptoms in patients with chronic heart failure (CHF) (Circulation 1995;91:1332-36). But the underlying mechanism was unclear. Since thermal vasodilation therapy was found effective in patients with CHF, we hypothesized that sauna restores endothelial function, then improves cardiac function. Patients and Methods: Twenty patients (62 ± 15 years) with CHF in New York Heart Association functional class II or III were studied. Their medication had not been changed for the weeks before and during the study. They had 60 degrees C for infrared-ray dry sauna for 15 min and were kept at bed rest with blankets for 30 min once a day. The effect of the sauna was evaluated before and at the day after 2-week sauna therapy. With high-resolution ultrasound, we measured the diameter of brachial artery at rest and during reactive hyperemia (flow mediated dilation, %FMD) as an endothelium-dependent dilation, and after sublingual administration of nitroglycerin (%NTG) as an endothelium-independent dilation. We also measured plasma levels of brain natriuretic peptide (BNP), nitric oxide, and tumor necrosis factor alpha (TNF-


dl). Results: All patients responded well to the sauna therapy. Plasma levels of BNP were significantly shortened (from 321±128 pg/ml to 141±30 pg/ml, P<0.01). Plasma levels of nitric oxide and tumor necrosis factor alpha did not change. Conclusion: Repeated sauna therapy improves vascular endothelial function, resulting in the improvement of cardiac function in patients with chronic heart failure.

1059-74 Prognostic Indicators in Congestive Heart Failure

Monday, March 19, 2001, 9:00 a.m.-11:00 a.m.

Orange County Convention Center, Hall A4

1059-74-1059-75

1059-75 Forced Vascular Vital Capacity in Severe Heart Failure: A Powerful Predictor of Adverse Outcome

Mansoef F. Mehr, Patricia A. Uber, Myung H. Park, Robert L. Scott, Carl J. Levis, Nicholas V. Milani. Ochsner Cardiomyopathy and Heart Transplant Center, New Orleans, LA

Background: Forced Vital Capacity not only reflects pulmonary restriction but also respiratory muscle dysfunction. We hypothesized that use of Forced Vital Capacity as a marker of peripheral muscle kinetic aberrations might allow better outcome discrimination in patient cohorts characterized by low peak aerobic capacity. Methods: In order to investigate this issue, we prospectively analyzed a consecutive group of 144 heart failure patients (52±11 years,jection fraction 20±8%, 78% men, 76% white, 1-5 years follow-up) listed for heart transplantation (VO2max 14±5ml/kg/min), and evaluated baseline Forced Vital Capacity % predicted as a marker for survival. Results: Regression analysis for significant correlates of Forc capacity % predicted included: left ventricular ejection fraction (r=0.57, p<0.01; serum sodium (r=0.58, p<0.01; bilirubin (r=0.4, p=0.03), uric acid (r=-0.7, p=0.0002). Forced Expiratory Volume 1% (FEV1) (r=-0.5, p=0.0001). New York Heart Association class, pulmonary vascular resistance, use of amiodarone, peak aerobic capacity, and hemodynamic measurements were not significant predictors. Moreover, a very simple algorithm using only Forced Vital Capacity % predicted distinguished between survivors (n=103) and non-survivors (n=41) with high accuracy (ROC area under the curve = 0.86, p<0.0001). Conclusions: Forced Vital Capacity is a powerful independent predictor of survival in heart failure patients, with a better outcome discrimination in patients characterized by low peak aerobic capacity.
cure correlate. Survive analysis of patients with a Forced Vital Capacity % <50% was significantly lower than in those with a normal FVC, and the presence of left ventricular systolic dysfunction had not been well established.

Methods: We studied 6797 patients: 2569 in the Treatment Trial (left ventricular dysfunction in heart failure) and 4228 in the Prevention Trial (left ventricular dysfunction without heart failure) of the Studies of Left Ventricular Dysfunction (SOLVD). We evaluated hospitalization for heart failure over an average follow-up of 4.1 years in the Prevention Trial and 3.7 years in the Treatment Trial, comparing patients who were current smokers to non-smokers at baseline. Cessation rate was factored in for heart failure. In both trials, the 1-year mortality was 23.5% in the Prevention Trial and 23.5% in the Prevention Trial.

Results: After adjusting for age, gender, race, ejection fraction, atrial fibrillation, alcohol consumption, NYHA class, chronic obstructive pulmonary disease, hypertension, diabetes mellitus, previous myocardial infarction, angina, and history of left ventricular dysfunction, rehospitalizations and medications, smokers had significantly higher hospitalization rate in all patients in the Combined Trials (RR=1.17, p<0.05). The effect was even more pronounced for patients with left ventricular dysfunction in both the Combined Trials (RR=1.27, p<0.005) and the Prevention Trial (RR=1.44, p=0.002).

Conclusion: Smoking was associated with increased hospitalization rate for heart failure in SOLVD. This effect was most pronounced in patients with ischemic cardiomyopathy in the Prevention Trial.

**1008-04** Serum Total Cholesterol, High-Density Lipoprotein, and Prognosis in Patients With Chronic Heart Failure


Background: We have recently identified low cholesterol to be predictive for increased mortality in chronic heart failure (CHF). The aim of this study was to prospectively validate this finding.

Methods: In 114 CHF patients (age 62±13 years, mean±SD, 62% ischemic etiology), we performed a prospective study, enrolling patients in stable condition, with a median follow-up of 4.9 years. A cholesterol level of 5.5±1.0 mmol/l, LDL of 3.5±1.0 mmol/l, HDL of 1.2±0.4 mmol/l, triglycerides of 1.7±0.9 mmol/l, and tumor necrosis factor receptor 1 (TNFR1) of 45±9.9 pg/ml were measured. Severity of CHF was assessed with NYHA class (I/II/III/IV: n=11/34/54/15), MVO2 (7.2±0.8 ml/kg/min), and ejection fraction (EF: 28±11%). With the low cholesterol hypothesis in mind, a second independent CHF population (n=11, age 60±5 years) was predicted mortality. TNFR1 (p<0.0001), age (p=0.001), and low cholesterol (p=0.006) remained related to mortality in both the combined Trials (RR=1.27, p<0.005) and the Prevention Trial (RR=1.44, p=0.002).

Conclusion: Smoking was associated with increased hospitalization rate for heart failure in SOLVD. This effect was most pronounced in patients with ischemic cardiomyopathy in the Prevention Trial.

**1008-05** The Independent Prognostic Impact of Decreased High Density Lipoprotein Levels in Severe Heart Failure

Manfred R. Mehta, Patricia A. Uher, Myung H. Park, Robert L. Scott, Richard V. Milani. *Cincinnati Cardiology and Heart Transplant Center, Cincinnati, OH*

Background: High Density Lipoprotein is known to interact with cytokine induced adhesion molecule expression and in influencing the generation of prostacyclin via cyclooxygenase stimulation, both pathophysiological events that are implicated in the natural history of chronic heart failure.

Methods: We have recently identified low cholesterol to be predictive for increased mortality in chronic heart failure (CHF). The aim of this study was to prospectively validate this finding.

Results: Smoking was associated with increased hospitalization rate for heart failure in SOLVD. This effect was most pronounced in patients with ischemic cardiomyopathy in the Prevention Trial.

Conclusion: Smoking was associated with increased hospitalization rate for heart failure in SOLVD. This effect was most pronounced in patients with ischemic cardiomyopathy in the Prevention Trial.

**1008-06** Right Ventricular Function is a Predictor of Outcome in Patients With Left Ventricular Dysfunction After Myocardial Infarction. The Survival and Ventricular Enlargement Trial

Leonardo Zannoli, Hicham Ski, Marin St. John, Sutton, Jean Rouleau, Gervasio Lamas, Gandos Lewis, Tod Mastrap, Jacques Rouleau, Lorne Mayes, Marc Peer, Scott Solomon. Brigham and Women’s Hospital, Boston, MA

Background: Right ventricular function has been shown to predict exercise capacity, ambulatory survival, and survival in patients with advanced heart failure. The aim of this study was to determine whether right ventricular function in patients following myocardial infarction. Methods: The Survival and Ventricular Enlargement Study consisted of 2291 patients with acute myocardial infarction and left ventricular dysfunction (ejection fraction <40%), who were randomized to treatment with captopril or placebo. Nineteen 2-dimensional echocardiograms were obtained in 416 patients from the echo ancillary study (mean 11.1±3.2 days post-infarction). Right ventricular areas from the apical 4-chamber view were digitized at end-diastole and end-systole. Right ventricular function was assessed as percent change in cavity area from end-diastole to end-systole (fractional area change) and related to outcomes in univariate and multivariate analyses. Results: Right ventricular function correlated weakly with left ventricular ejection fraction (r=-0.02; p>0.15). In univariate analyses, right ventricular fractional area change was a predictor of mortality, cardiovascular mortality, and congestive heart failure (p < 0.0001), but not recurrent myocardial infarction (p=0.7154). After adjusting for age, gen-
A Prediction Model for Mortality and Hospitalizations Based on a Cohort of 7274 Patients With Congestive Heart Failure

Centre hospitalier de l’Université de Montréal, Montreal, PQ, Canada

Background: Congestive heart failure (CHF) is a leading cause of patient morbidity and mortality but reliable models to predict patient outcomes in the angiotensin converting enzyme (ACE) inhibition era are lacking. Methods: Multivariate statistical modelling of the 7,274 patients who were taking ACE inhibitors on entry into the loox on the remaining beats. Temporal and spectral parameters were assessed

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graphic left ventricular ejection fraction, peak creatine kinase, cigarette use and total mortality, cardiovascular mortality and congestive heart failure in patients with left ventricular dysfunction after myocardial infarction.

1098-69

Lifetime Risk Through Age 60

1098-70

Increasing Pulse Pressure Contributes to Lifetime Risk of Congestive Heart Failure

Donald M. Lloyd-Jones, Martin G. Larson, Aruna Bilsara, Ralph B. D’Agostino, Framingham Heart Study, Framingham, MA, Massachusetts General Hospital, Boston, MA

Background: Lifetime risk calculation allows estimation of the absolute risk of developing a given disease before dying of another cause. With the aging of the population, congestive heart failure (CHF) is becoming a major public health concern, and pulse pressure (PP) appears to be a risk factor for CHF. However, there have been no estimates of the lifetime risk based on PP levels. Methods: We included all subjects in the Framingham Heart Study who were examined from 1971-1996 and were free of CHF at baseline. Each subject was classified according to the average of all PP measurements in the 6 years prior to index ages of 50, 60, and 70 years, disregarding treatment status. Subjects were classified into groups based on PP as follows: Group 1 (PP ≤ 45 mmHg); Group 2 (PP 45-64 mmHg); and Group 3 (PP > 65 mmHg). Lifetime risk of CHF was calculated for each group, with death free of CHF as a competing event. Results: We followed 3,303 men and 3,918 women; 616 developed CHF and 2,056 died free of CHF. The remaining lifetime risk of CHF at each index age is shown in the Table, by sex and baseline PP group. There was a stepwise increase in lifetime risk of CHF with increasing PP at all ages, resulting in approximately 2-fold risk for subjects in the highest versus lowest PP group. At age 60, subjects in the highest PP group had a remaining lifetime risk of nearly 1 in 3 for the development of CHF. Conclusions: Lifetime risk of CHF increases with increasing PP for men and women at each age. Thus, elevated PP may identify patients at high risk for CHF in the long term, who may benefit from aggressive therapy aimed at blood pressure reduction.

1098-71

The Beneficial Effect of Spironolactone on Heart Rate Variability in Severe Congestive Heart Failure

Ali R. Bilge, Badreddine Ahmadou, Pierre Block, Daniel Duprez, Agnieszka Babiyants, Luc A. Piérard, University hospital cardiology department, Liège, Belgium, Université Libre de Bruxelles, Brussels, Belgium

Background: Improvement of parasympathetic activity is one of the potential mechanisms explaining the results of RALES study. Classical and non-linear analysis of heart rate variability was performed in the Belgian RALES population. Methods: 24-hour Holter recordings were obtained before randomization and after 3 and 6 months. We performed temporal, spectral and non-linear analysis. The latter evaluates successive RR intervals and 2 measures were defined: 1. the regularity index R, the percentage of RR intervals not exceeding 16 msec of difference between 3 consecutive beats. 2. The variability index V, which is the ratio of the systemic increase and decrease of three consecutive RR intervals over the remaining beats. Temporal and spectral parameters were assessed during both 24 hours and a 4 hour night period (from 0 to 4 a.m.) where hourly premature beats rates was reduced. Results: 66 patients were studied at baseline and 18 died during the study period. The 5 Holters were obtained in 42 patients (23 in the spironolactone group and 19 in the placebo group). The results show the different p values of the HRV variables in 3 different categories: death vs. alive and comparison between treatment groups spironolactone (SP) vs. placebo (PL) at 3 and 6 months. Conclusion: The V index increased significantly in the spironolactone group at 3 and 6 months. However, the effect of spironolactone on heart rate variability was not statistically significant in the placebo group. The V index may be a novel and promising parameter to evaluate the effects of spironolactone on heart rate variability.
Heart Failure in a Veteran Cohort: Predictors of Outcome

Maria N. Ansari, Ali Tutar, Jean Bullard, John R. Teerlink, Barry M. Massie. San Francisco VAMC/L EST, San Francisco, CA

Background: Survival estimates in CHF patients are highly variable depending upon the population studied and methodologies used. Most data derived from epidemicologic studies, in which limited information is available about pertinent characteristics, or clinical trials that have highly selective entry criteria. Therefore, we examined survival rates in a well-characterized unselected outpatient cohort.

Methods: Charts of consecutive VA outpatients (n=417) with a CHF diagnosis from 7/94-12/98 were reviewed and survival was examined through 5/2000. 42 were excluded because of lack of CHF by Framingham criteria or lack of follow-up within the VA system. Determinants of survival were assessed by proportional hazards models that included 5 clinical and 2 treatment variables.

Results: In 375 patients (mean age 72, 96% male), EF was reduced (<45%) in 66%, preserved (>45%) in 27%, and unknown in 7%. Survival in the total cohort was 79.5% after a mean of 29 months, and was not significantly different in the low and preserved EF subgroups (79.8% and 80.2%, respectively). Significant predictors of mortality and the associated hazard ratios are shown in the table.

<table>
<thead>
<tr>
<th>Determinant</th>
<th>Total Cohort</th>
<th>EF &lt;45%</th>
<th>EF &gt;45%</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per decade increase)</td>
<td>1.6 (1.1-2.2)</td>
<td>1.4 (1.1-1.9)</td>
<td>1.2 (1.1-1.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP (per 10mm Hg increase)</td>
<td>1.04 (1.01-1.07)</td>
<td>1.04 (1.01-1.1)</td>
<td>1.07 (1.01-1.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ACE I use</td>
<td>1.3 (1.1-1.7)</td>
<td>1.4 (1.1-1.8)</td>
<td>1.3 (1.1-1.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Warfarin</td>
<td>1.4 (1.0-2.0)</td>
<td>1.5 (1.1-2.0)</td>
<td>1.3 (1.0-2.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiology Provider</td>
<td>0.5 (0.4-0.6)</td>
<td>0.4 (0.3-0.6)</td>
<td>0.6 (0.4-0.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: Mortality in this cohort was similar to class II-IV trial patients with low EF, and surprisingly was similar in low and preserved EF groups. Severe renal dysfunction was the most significant adverse predictor. Interestingly, low SBP was an adverse predictor in low EF patients, whereas high SBP was associated with higher mortality in preserved EF patients. Treatment with a cardioselective beta-blocker was associated with improved survival. ACE inhibitor therapy, but not beta-blocker treatment was associated with better survival in low EF patients.

Significant Predictors of Survival and Hazard Ratios with 95% Confidence Intervals

Poster Session

Exercise on Valvular Heart Disease and Arrhythmias

Monday, March 19, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 9:00 a.m.-10:00 a.m.

Implications of Symptomatic, Hemodynamic, and EKG Changes During Exercise Stress Testing in Patients With Aortic Stenosis: Relationship to Coronary Artery Disease

Luc M. Beauchesne, Kwan L. Ghan, Kathy J. Ascah, Ian G. Bumash. University of Ottawa Heart Institute, Ottawa, Canada

Background: Recently, exercise stress testing (EST) has been increasingly utilized in the assessment of patients with aortic stenosis (AS). However, in AS patients, the relationship of the EST responses to CAD is unclear. Methods: In 47 consecutive pts with moderate or severe AS (AVA or <1.6 cm2, AI >4), undergoing treadmill EST and coronary angiography, we investigated whether any symptomatic, hemodynamic or EKG response during treadmill EST predicts obstructive CAD (> or =70% stenosis in > or =1 large or medium-sized epicardial artery). Results: One pt was excluded because of resting LBBB. Of the remaining 46 pts, 31 pts (66%) had echocardiographic A2 + A3 > or =0.84 cm2, were free of obstructive CAD (non-CAD). CAD and non-CAD groups were similar for age (70.4 vs 66.1 ± 11.9 years, p=NS), valve area (0.79 ± 0.18 vs 0.78 ± 0.20 cm2, p=NS), history of angina (48 vs 84%, p=NS) and use of negative coronary marks (67 vs 44%, p=NS). Analysis of ST-segment depression during the recovery period (48 ± 3 vs 45 ± 3, p=NS). The development of systolic hypotension during exercise (BP fall >10 mmHg) did not predict coronary status (26% CAD vs 16% non-CAD, p=NS). No adverse events occurred with treadmill EST. Conclusions: Treadmill EST can be safely performed in patients with moderate or severe AS. However, symptomatic, hemodynamic and EKG responses during EST provide no information on the presence or absence of concomitant obstructive CAD.

Effects of Atrial Flutter on Exercise Tolerance in Adult Congenital Heart Patients

Wei Li, Michael Y. Henein, Jane Somervill. Royal Brompton Hospital, London, United Kingdom

Background: Atrial flutter (AF) is a frequent complication in adult congenital heart patients and leads to deterioration of patients’ effort tolerance and Ability Indices. Methods: Exercise tests using modified Bruce protocol were performed in 20 consecutive such patients during AF and again during 20-40 hours after DH conversion to sinus rhythm (SR). Basic abnormalities of the patients were one ventricle 9 (5 with Fontan type surgery), transposition of great arteries 4 (3 had Mustard and 1 arterial switch), hypertrophic cardiomyopathy (HCM) 6, closed atrial septal defect 5 and others 0. Age of study was 01 to 62 years, 11 female, AF postled for 2-21 (mean 7) days; first attack in 4 and subsequent in 16 who were on antiarrhythmics. Results: Exercise test AF vs SR predictor therapies/month during the 6 months prior to enrollment in CR was 0.5 ± 0.7 compared to 6.2 ± 0.7. Further study is needed to determine if exercise training reduces the frequency of AFL.
A Randomised and Controlled Trial of Beta Blockers for the Treatment of Recurrent Syncope in Patients With A Positive or Negative Response to Head-Up Tilting Test

Rodolfo Ventura, Rewie Maas, Daniel Ziedler, Andreas Schuchert, Thomas Meinertz. Department of Cardiology, University Hospital Eppendorf, Hamburg, Germany.

Background: The efficacy of beta-blockers in preventing syncope is controversial. Previous trials with beta-blockers only assessed patients (pts) with a positive result of head-up tilting test (HUT). Thus, the value of HUT in predicting the efficacy of therapy has not been ascertained yet. Methods: 56 pts (36 female, 44±18 years) with recurrent syncope (>1 event in the last 6 months) of suspected neurocardiogenic origin were included in the study. Independently from the response to HUT pts were randomised to metoprolol or propranolol (46 pts, group A) or the maximal tolerated dose (20±11 mg, 12±3 mg, respectively) or to no pharmacotherapy (28 pts, group B). Pts of group B were requested to drink sufficiently, to wear elastic stockings, and in case of prodromal symptoms to assume a supine position with the feet elevated. Primary endpoint was the first recurrence of syncope. Results: During 1 year of follow-up 20 pts of the group A had no recurrence while 8 experienced further syncopal events. Conversely, in the group B 20 pts had recurrences and 8 remained free of symptoms. In the group A, of 8 pts with recurrences 5 had a positive and 3 a negative response to HUT while of 20 pts without recurrences 12 had a positive and 8 a negative HUT result. In the group B of 20 pts with recurrences 10 had a positive and 10 a negative HUT result while of 8 pts without recurrences 4 had a positive and 4 a negative response to HUT. Conclusions: Background-A Glycine for Arginine substitution in codon 389 (G>C) has been associated with heart failure (HF) and cardiac intracellular calcium release channel (ryanodine receptor, RyR2) dysfunction in patients with familial atrioventricular block. Here we tested the hypothesis that this glycine to arginine substitution might modulate the effects of selective beta-blockers in canine RYR2. Methods—We studied 297 CHF patients enrolled in the MERIT-HF trial. DNA was isolated from blood cells. We analyzed the relation between BAR1 genotype and clinical characteristics and response to beta-blockade. Results—There were 156 patients with the CC, 110 with the GC, and 21 with the GG genotype. We compared survival was improved by metoprolol in all genotypes Conclusions—In this exploratory study patients with CHF, the G6 variant of the BAR1 may be of relevance in CHF and that patients homozygous for the hypofunctional Gly389 variant may particularly benefit from beta-blockade.

ABSTRACTS - Cardiac Function and Heart Failure 159A

1100 Basic Mechanisms Underlying Therapeutic Effects of Beta-Blockers

Monday, March 19, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 9:00 a.m.-10:00 a.m.

1100-48 Enhanced Efficacy of Metoprolol in Patients With Heart Failure Homozygous for the Hypofunctional Gly389 Variant of the Beta1-Adrenergic Receptor: A Substudy of the MERIT-HF Trial

Rudolf A. Da Boit, Yigal M. Pinto, Corine Volkers, Robert H. Hunning, Edith Celtev, Albrecht B. Hult, Wolf H. Van Gits, Neefeld Kruiz, DSt J. Van Ypohof, University Hospital, Thoracenter, Department of Cardiology, Groningen, The Netherlands, University of Groningen, Department of Clinical Pharmacology, Groningen, The Netherlands

Background—A Glycine for Arginine substitution in codon 389 (G>C) has been associated with heart failure (HF) in patients with familial atrioventricular block. Here we tested the hypothesis that this glycine to arginine substitution might modulate the effects of selective beta-blockers in CHF. Methods—We studied 297 CHF patients enrolled in the MERIT-HF trial. DNA was isolated from blood cells. We analyzed the relation between BAR1 genotype and clinical characteristics and response to beta-blockade. Results—There were 156 patients with the CC, 110 with the GC, and 21 with the GG genotype. We compared survival was improved by metoprolol in all genotypes Conclusions—In this exploratory study patients with CHF, the G6 variant of the BAR1 may be of relevance in CHF and that patients homozygous for the hypofunctional Gly389 variant may particularly benefit from beta-blockade.
1101 Coronary Artery Disease in the Elderly: Clinical Aspects

Monday, March 19, 2001, 9:00 a.m.-11:00 a.m. Orange County Convention Center, Hall A4
Presentation Hour: 9:00 a.m.-10:00 a.m.

1101-54 Heterogeneity in Older Acute Myocardial Infarction Patients: The Importance of Age

Hajendra H. Minta, Stait S. Hallowe, Martha J. Hadford, Alan K. Berger, Yonglei Wang, Harlan Kmkmble. Yale University School of Medicine, New Haven, CT, Quadidigm, Middleton, CT

Background: Patients aged 65 years or older with acute myocardial infarction (AMI) have often been perceived as a homogenous group - "the elderly." However, the association of age with clinical characteristics among the traditionally labeled "elderly" is not well described. Methods: We evaluated 193,140 Medicare beneficiaries aged 65 years or older hospitalized with AMI at non-governmental acute care hospitals in 1994-95. Patients were assigned into age-based strata (see table) and evaluated for age trends in demographic characteristics, medical history and AMI presentation. Results: Significant differences by age were observed (p value of the Cochran-Armitage test for trend for all variables = 0.001 except prior AMI and hypertension for which p = ns).

<table>
<thead>
<tr>
<th>Age Group</th>
<th>% of Cohort</th>
<th>Male Sex(%)</th>
<th>Prior AMI(%)</th>
<th>Prior diabetes(%)</th>
<th>Prior hypertension(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>65-74 yrs</td>
<td>30.6</td>
<td>23.7</td>
<td>21.4</td>
<td>18.3</td>
<td>15.9</td>
</tr>
<tr>
<td>75-84 yrs</td>
<td>6.2 (S)</td>
<td>57.3 (S)</td>
<td>51.3 (S)</td>
<td>44.2</td>
<td>38.0</td>
</tr>
<tr>
<td>&gt;84 yrs</td>
<td>5.1 (S)</td>
<td>56.5 (S)</td>
<td>50.6 (S)</td>
<td>43.2</td>
<td>32.6</td>
</tr>
</tbody>
</table>

Conclusions: Traditionally defined "elderly" AMI patients are not a homogeneous population, but demonstrate significant differences by age. Future research should not treat this population as homogenous, but instead explore the therapeutic and prognostic implications of its heterogeneity.

1101-55 Depression Predicts 12-month Prognosis in Elderly Patients With Acute Myocardial Infarction

Iisaki Shintomi, Hisanori Sato, Hisayuki Sato, Etsu Hisnaka, Kunihoro Kingose, Daishuke Nakatani, Noritake Hoki, Tunsuho Kucuya, Masasagu Hori, Yozi Onishi. Osaka university Graduate school of medicine, department of internal medicine and therapeutics, suita, Japan.

Background: Several studies have found that depression is associated with an increased risk for cardiac events after the onset of acute myocardial infarction (AMI). However, few studies have examined this relationship in the elderly. Aim of the present study is to assess the impact of depression on prognosis of elderly patients hospitalised for AMI. Methods: Consecutive elderly patients with AMI admitted to the cardiology ward of our hospital from April 1998 through June 1999 and all patients who survived to be discharged were enrolled in this study (n=188:510 men; mean age 63±10 y). Depression was assessed using the 20-item self-report Zung Self-Rating Depression Scale (SDS). Patients with a score of 40 or higher was diagnosed as depression. The patients were followed for 12 months. Cardiac events (cardiac death, re-MI, revascularization, heart failure) were examined and compared between elderly (≥85 y, 283 patients) and young patients (<85 y, 335 patients). Results: The SDS score identified depression in 284 patients (42.7%). Prevalence of depression was not different between ≥85 y and <85 y patients (19.3% vs 13.5% respectively). The cardiac event rate at 1-year was significantly lower in elderly patients (26.0% vs 28.7%, p<0.05). Conclusions: Depression after higher incidence of cardiac events (odds ratio 1.54, 95% CI 1.04 to 2.29, p=0.032) after controlling for severity of myocardial infarction, risk factors, e.g., hypertension, diabetes mellitus, hypercholesterolemia, smoking and obesity. Depression was a significant risk factor for cardiac events (odds ratio 1.82, 95% CI 1.09 to 3.02, p<0.02) in the elderly patients. However, there was no association between depression and cardiac events in the young patients (odds ratio 1.31, 95% CI 0.80 to 2.15, p=0.275). Conclusion: Depression after AMI is a significant predictor of 1-year cardiac events for Japanese population, and its presence augments the risk especially in elderly patients.

1101-56 How is the Outcome of Coronary Stenting in the Elderly Compared to Younger Patients?

Daniela Talabotari, Piero Moncist, Alessandro Locci, Franco Fabioccino, Stefano Gaioll, Luca Granoni, Paola Ravagnani, Sergio Cozzizz, Antonio L. Bortis, Centro Cardiologico Monza RINCO, Institute of Cardiology, University of Milan, Milan, Italy.

Purpose: To assess clinical outcomes following coronary stenting in pts >75 yrs and to compare them to those obtained in younger pts. Methods: New-generation stents were implanted in 130 old (mean age=78±7 yrs; range 76-86) 200 middle-aged (M) pts (mean age=61±7 yrs; range 51-75) and 150 young (Y) pts (mean age=48±4 yrs; range 31-60). O pts were more hypertensive (p=0.061, M:59%, Y:41%; p=0.001), diabetics (p=0.14, M:11%, Y:4%; p<0.004) and presented more severe coronary artery disease (31 VD:51%,42% M, 34% Y; p=0.04). No significant difference in lesion length and morphology, reference vessel diameter and percent diameter stenosis was present. Stable angina (50% O, 64 M, 67% Y), unstable (31% O,22% M, 13% Y; p<0.001) and acute MI (13% O, 10% M, 12% Y; n=) were the indications for stenting. Gains in revascularization required coronary support devices in acute balloon pump in 3% of O and 0.5% of M and Y pts (ns). High and similar technical (O:95%,M:96%,Y:97%) and clinical success (O:91%, M:95%, Y:96%; ns) were achieved in all groups. MACCE were death (2.8% O,1.1%, 0% Y; ns), urgent CABG (0.7% O, 0%, M; 0% Y; ns), target lesion revascularization (0.5% O, 0.5% M, 0% Y; ns) and target vessel bleeding (0.5% O, 4.5% M, 1.2% Y; ns). Table shows six-month clinical and angiographic results. Conclusions:
Coronary stenting is safe and effective in a high-risk octogenarian patient cohort

Dmitri V. Baklanov, Constantin B. Marcu, Marçel C. Chawarski, Deanna F. Juhosz, Eugenio A. Carcsillo, Thomas J. Donohue, Hospital of St Raphael, New Haven, CT

Background: Despite the widespread use of coronary stenting, little is known about the acute and long-term results in octogenarians who represent an inherently high-risk population as well as an increasing percentage of treated patients with coronary heart disease. Methods: One hundred ninety-seven consecutive patients (67% females) older than 80 years old (84 +/- 3 years) who underwent 214 coronary stent procedures were studied. Each patient had post-procedural serial cardiac enzymes and ECGs collected, and was followed for a minimum of six months (range 6-24 months) after the procedure. Procedural success was defined as less than 25% residual stenosis, TIMI 3 flow, and absence of major complications (death, non-fatal myocardial infarction, coronary artery bypass graft surgery, major bleeding, and stroke). Sixty-five percent of patients presented with an acute MI or unstable angina, and 33% were functionally NYHA Class III or IV. Fifty-three percent of stenoses were classified as B2 or C. Hyperprotein labile receptor dichotomous variables were measured using T2 values, which are inversely proportional to tissue iron concentration. Results: Despite long-term iron-chelation in all patients, 58% were found to have excess myocardial iron deposition (T2 <20ms). In these patients, there was a progressive linear decline in left and right ventricular ejection fraction (LVEF and RVEF) (r=0.42, p=0.0001 for LVEF and r=0.53, p<0.0001 for RVEF) and a progressive rise in LV mass (r=0.41, p=0.001) and LV and cystolic volumes (r=0.36, p=0.0001) with increasing myocardial iron. LVEF correlated linearly with RVEF (r=0.69, p=0.0001). When the patients were grouped by 5-year age intervals, the highest mean myocardial iron and lowest mean EFs were found in the late fifties and early sixties, when compliance to chelation regimes is most difficult. This corresponds to the steepest fall in the survival curve in this age group. Mild myocardial iron deposition was detected as early as 7 years and severe deposition as early as 15 years of age. Conclusions: These data suggest a new mechanism, namely iron deposition for left and right ventricular failure in thalassemia major. Currently available iron-chelation regimes are ineffective in preventing myocardial iron deposition in the majority of these patients. Increased efforts need to be directed towards early detection in high-risk populations in order to prevent the unnecessary death of young patients from this treatable cardiomyopathy.

Conclusions: If IMI, RVI is associated with a lower long-term survival only in elderly patients. However, this difference in survival is a consequence of the increase in mortality produced in the early phase.

Conclusions: Baseline LVEF and LVEDV are significant predictors of survival, with LVEF being a major determinant of long-term survival. The absence of major complications (death, non-fatal myocardial infarction, coronary artery bypass graft surgery, major bleeding, and stroke) was an independent predictor of survival. Furthermore, separate AETs for left (LV) and right (RV) ventricular dysfunction have been proposed. Methods: We investigated this issue in 151 patients with thalassaemia major using cardiac magnetic resonance (mean age 27 years). Myocardial iron concentrations were measured using T2* values, which are inversely proportional to tissue iron concentration. Results: Despite long-term iron-chelation in all patients, 58% were found to have excess myocardial iron deposition (T2* <20ms). In these patients, there was a progressive linear decline in left and right ventricular ejection fraction (LVEF and RVEF) (r=0.42, p=0.0001 for LVEF and r=0.53, p<0.0001 for RVEF) and a progressive rise in LV mass (r=0.41, p=0.001) and LV and cystolic volumes (r=0.36, p=0.0001) with increasing myocardial iron. LVEF correlated linearly with RVEF (r=0.69, p=0.0001). When the patients were grouped by 5-year age intervals, the highest mean myocardial iron and lowest mean EFs were found in the late fifties and early sixties, when compliance to chelation regimes is most difficult. This corresponds to the steepest fall in the survival curve in this age group. Mild myocardial iron deposition was detected as early as 7 years and severe deposition as early as 15 years of age. Conclusions: These data suggest a new mechanism, namely iron deposition for left and right ventricular failure in thalassemia major. Currently available iron-chelation regimes are ineffective in preventing myocardial iron deposition in the majority of these patients. Increased efforts need to be directed towards early detection in high-risk populations in order to prevent the unnecessary death of young patients from this treatable cardiomyopathy.

Conclusions: In IMI, RVI is associated with a lower long-term survival only in elderly patients. However, this difference in survival is a consequence of the increase in mortality produced in the early phase.
1102-06 Systolic Myocardial Velocities by Pulsed Doppler Tissue Imaging Are Preserved Before the Onset of Heart Failure

Authors: Jun Koyama, Patricia A. Ray, Ravin Davidoff, Rodney H. Falk, Boston Medical Center, Boston, MA

Background: Pulsed Doppler tissue imaging (PDI) is a well-established method to estimate myocardial velocities, but there are few data concerning the clinical value of PDI in patients with advanced heart failure.

Methods: Fifty-seven consecutive consecutive patients with advanced heart failure were included in this study. The patients were divided into two groups: those with heart failure (HF) and those without HF. PDI was performed in the parasternal long-axis view, and the regional myocardial velocities were measured.

Results: The fractional shortening was within normal ranges, although it was significantly lower in the HF group compared to the non-HF group. The systolic and diastolic wall motion velocities (S-vel and D-vel) were also measured.

Conclusions: PDI is a reliable method for estimating myocardial velocities and can be used to monitor patients with heart failure.

1102-07 Analysis of Myocardial Sympathetic Innervation in Patients With Primary Cardiac Amyloidosis

Authors: Tadashige Fujii, K&hi Kubo. Shinshu University School of Medicine, Matsumoto, Japan

Background: Although a high incidence of myocardial adrenergic denervation has been reported in patients with cardiac amyloidosis, we also compared the findings with reported data in patients with familial amyloid polyneuropathy (FAP), assessment of cardiac amyloidosis and no autonomic symptoms. In 6 patients with congestive heart failure and myocardial washout (41.1 ± 4.7% vs 25.1 ± 3.7%, P < 0.01) were significantly lower than those of 16 patients with FAP.

Results: The heart/media activity ratios (1.66 ± 0.03) had significantly decreased H/M ratios (1.50 ± 0.03 vs 1.59 ± 0.04, P < 0.01 in the delayed images) and increased washout (44.2 ± 2.3% vs 37.4 ± 4.0%, P < 0.01) compared with the other 5 patients without heart failure. In patients with myocardial amyloidosis, the washout ratio was inversely correlated with the low frequency component of heart rate variability (\(r = -0.69, p < 0.05\)) among patients with AL amyloidosis and no autonomic dysfunction showed enhanced cardiac adrenergic neuronal activity with mild sympathetic dysfunction in the presence of the congestive heart failure. In contrast, patients with AL amyloidosis and no autonomic neuropathy and those with FAP. Of the 11 patients with AL amyloidosis and no autonomic dysfunction, 8 patients with congestive heart failure showed significantly decreased T/H ratios (1.50 ± 0.03 vs 1.54 ± 0.06; \(p = 0.01\) in the delayed images) and increased washout (44.2 ± 2.3% vs 37.4 ± 4.0%; \(p = 0.01\)) compared with the other 5 patients without heart failure. In patients with AL amyloidosis, the washout ratio was inversely correlated with the low frequency component of heart rate variability (\(r = -0.69, p < 0.05\)) among patients with AL amyloidosis and no autonomic dysfunction showed enhanced cardiac adrenergic neuronal activity with mild sympathetic dysfunction in the presence of the congestive heart failure. 

Conclusions: Patients with AL amyloidosis and no autonomic dysfunction showed enhanced cardiac adrenergic neuronal activity with mild sympathetic dysfunction in parallel with the presence of congestive heart failure. In contrast, patients with AL amyloidosis and no autonomic neuropathy and those with FAP exhibited prominent myocardial adrenergic denervation with normal sympathetic neural function. Thus, there was great differences in myocardial uptake and turnover of MIBG in patients with cardiac amyloidosis, which is dependent on the presence or absence of cardiac autonomic dysfunction.
Elevated Levels of Inflammatory Cytokines and Overexpression of iNOS in Skeletal Muscle of Patients With Chronic Heart Failure: Effects of Regular Aerobic Endurance Training

Vollmer Andreas, Auel-Leuk, Paul C, Cocksheim, Stephan Holzem, Dieter Moser, Wolfgang Wiesner, Gerhard Schuierer, Rainer Hackemeier. University Leipzig, Heart Center, Leipzig, Germany

Background: In patients (pts) with chronic heart failure (CHF) functional work capacity is inversely correlated with the expression of inducible nitric oxide synthase (iNOS) in skeletal muscle (SM). In vitro studies suggest that inflammatory cytokines regulate iNOS expression. The present study was designed to analyze the effect of exercise training (ET) on the amount of inflammatory cytokines in SM and its relation to iNOS expression in pts with stable CHF.

Methods: Twenty pts were prospectively randomized either to a training group (T) or an inactive control group (C). At baseline and after 6 months, pts underwent a needle biopsy of the vastus lateralis muscle. Expression of iNOS was quantified by immunohistochemistry (%iNOS positive stained tissue area) and confirmed by semiquantitative RT-PCR. To quantify the specific tissue concentration of IL-1β and TNF-α in SM quantitative immunomodulation histochemistry was performed.

Results: ET leads to a significant reduction of either IL-1β by 27% (from 1.01 ± 0.90 to 0.75 ± 0.86% positive stained tissue area; p=0.02 vs C) and TNF-α by 28% (1.20 ± 1.14 to 0.88 ± 0.91 % positive stained tissue area; p=0.05 vs C). Simultaneously iNOS expression decreased by 35% (2.20 ± 0.46 versus 1.45 ± 0.38 % positive stained tissue area; p=0.01 vs C) at a similar trend was to a decrease in iNOS expression in C (0.20 ± 0.59 versus 2.78 ± 0.83 % pos. tissue area). Changes in IL-1β and TNF-α were significantly changed in pts compared to controls (p<0.05, p<0.02).

Conclusion: These results suggest that in pts with impaired physical exercise training reduces the local concentration of inflammatory cytokines in the skeletal muscle. These beneficial training effects may contribute to reduced iNOS expression in SM of these patients.

872-3 The Endotoxin, Cytokine, and Metabolic Response to Acute Exercise in Patients With Chronic Heart Failure and Healthy Controls


Background: Acute exercise is a potent stimulus for the hypothalamo-pituitary-adrenal axis. It has been postulated that the increase in tumor necrosis factor-alpha (TNF) during histochemistry was performed.

Results: In patients (pts) with chronic heart failure (CHF) functional work capacity is inversely correlated with the expression of inducible nitric oxide synthase (iNOS) in skeletal muscle (SM). In vitro studies suggest that inflammatory cytokines regulate iNOS expression. The present study was designed to analyze the effect of exercise training (ET) on the amount of inflammatory cytokines in SM and its relation to iNOS expression in pts with stable CHF.

Methods: Twenty pts were prospectively randomized either to a training group (T) or an inactive control group (C). At baseline and after 6 months, pts underwent a needle biopsy of the vastus lateralis muscle. Expression of iNOS was quantified by immunohistochemistry (%iNOS positive stained tissue area) and confirmed by semiquantitative RT-PCR. To quantify the specific tissue concentration of IL-1β and TNF-α in SM quantitative immunomodulation histochemistry was performed.

Results: ET leads to a significant reduction of either IL-1β by 27% (from 1.01 ± 0.90 to 0.75 ± 0.86% positive stained tissue area; p=0.02 vs C) and TNF-α by 28% (1.20 ± 1.14 to 0.88 ± 0.91 % positive stained tissue area; p=0.05 vs C). Simultaneously iNOS expression decreased by 35% (2.20 ± 0.46 versus 1.45 ± 0.38 % positive stained tissue area; p=0.01 vs C) at a similar trend was to a decrease in iNOS expression in C (0.20 ± 0.59 versus 2.78 ± 0.83 % pos. tissue area). Changes in IL-1β and TNF-α were significantly changed in pts compared to controls (p<0.05, p<0.02).

Conclusion: These results suggest that in pts with impaired physical exercise training reduces the local concentration of inflammatory cytokines in the skeletal muscle. These beneficial training effects may contribute to reduced iNOS expression in SM of these patients.

872-4 Exercise Plasma Norepinephrine Levels as a Prognostic Marker for Cardiac Death in Patients With Mild Heart Failure

Toru Kikugawa, Kazuhide Ogino, Shuski Oshaki, Masahiro Kato, Akihito Enso, Osamu Igawa, Hiroshi Hasegawa, Manabu Nakajima, Yutaka Sato, Masahiro Aoyama, Japan. KyoTo University, KyoTo Japan

Background: High plasma norepinephrine levels are associated with a poor prognosis in patients with heart failure. Patients with heart failure have altered plasma norepinephrine response to exercise, but the value of exercise plasma norepinephrine for determining prognosis has not been well defined. This study determined whether exercise plasma norepinephrine levels could predict cardiac death in patients with mild heart failure. Methods: During 1987 - 1992, 148 patients with mild heart failure (mean age: 58±11 years) and 27 control subjects performed supramaximal treadmill exercise test with serial measurement of plasma norepinephrine levels. Cardiac, echocardiographic, exercise and catecholaminergic variables considered relevant to the cardiac death were examined by Cox regression model. Results: During a median follow-up of 9 years, 30 cardiac (117 heart failure deaths and 19 sudden deaths) occurred among patients. Significant predictors for cardiac death by univariate analysis was peak exercise plasma norepinephrine levels, resting plasma norepinephrine levels, left ventricular ejection fraction, peak exercise heart rate, peak exercise systolic blood pressure, age and cardiac rhythm. At multivariate analysis, the independent predictors for cardiac death were: 1) peak exercise heart rate (β=2.0; 2) left ventricular ejection fraction (β=0.07; 3) serum creatinine levels (β=0.72); and 4) plasma norepinephrine levels at rest (β=0.50). In addition, elevated exercise plasma norepinephrine level (1.3mp; 2.24; 60 pmp) was a prognostic predictor by Kaplan-Meier analysis (p<0.01). Conclusion: The present study showed that the exercise plasma norepinephrine levels can provide prognostic information in patients with mild heart failure, in addition to the degree of left ventricular systolic dysfunction, chronotropic incompetence, and resting levels of plasma norepinephrine. The determination of plasma norepinephrine levels during exercise is useful to predict cardiac death in patients with mild heart failure.
**11:15 a.m.**

**Effect of ACE Inhibitors and AT1 Blockers on Myocardial Expression of Matrix Metalloproteinases in Post MI Ventricular Remodeling.**

Sylvie Guiguet, Inveren A. Amann. VA Medical Center, Minneapolis, MN; University of Minnesota, Minneapolis, MN

Background: Matrix metalloproteinases (MMPs) have been demonstrated to play a significant role in post myocardial infarction (MI) ventricular remodeling. Methods: We studied the effects of the ACE inhibitor (ACE-i), Enalapril; AT1 blocker (AT1-i), Candesartan, and their combination on the tissue levels of MMP-2, MMP-9 and MMP-13 in the remote non-infarcted myocardium (NIMM) of 6 week post MI rats and corresponding areas of sham operated rats by RT-PCR. Infarcted rats were treated with ACE-i (1mg/kg) or AT1-i (10mg/kg) or combination in the drinking water. Treatment was started 24h after MI and continued for 6 weeks, when rats were sacrificed. Results: Hemodynamics and echocardiographic data showed that the MI hearts were significantly remodelled and dysfunction compared to sham (LV Developed Pressure (LVDP), 56±5 vs 11±6 mm Hg; LV Fractional Shortening (% (FS%)), 27±6 vs 35±6; p<0.05). As compared to sham, in water treated MI rats, there was a 92% increase in MMP-2, 53% increase in MMP-9 and 44% increase in MMP-13 mRNA in the NIMM. There was no effect of ACE-i on MMP. AT1-i treatment reduced the expression of MMP-2 (38%) and MMP-13 (20%). In contrast, the combination decreased the expression of all MMPs to normal levels (fs). Conclusion: These data suggest that whereas, AT1-i decrease MMP mRNA, ACE-i did not. However, in presence of AT1-i, ACE-i had a synergistic effect in reducing MMP expression.

**11:30 a.m.**

**Urotensin II Stimulates Collagen Synthesis by Cardiac Fibroblasts and Hypertrophic Signalling In Cardiomyocytes via G(alpha)q- and Ras-Dependent Pathways**

Alex Tzanidis, Ross D. Hannan, Walter G. Thomas, Done Onan, Fiona See, Henry Krum. Monash University Medical School, Alfred Hospital, Melbourne, Australia, Baker Medical Research Institute, Melbourne, Australia

Urotensin II (U-II) is a somatostatin-like peptide recently identified as the most potent vasoinhibitor known. In this study, we examined whether U-II promotes adverse cardiac remodeling through non-haemodynamic effects on the myocardium. In a rat model of heart failure post myocardial infarction, increased U-II peptide expression was observed in both infarct and non-infarct regions, particularly in areas of fibrosis. In isolated neonatal cardiac myocytes and fibroblasts, constitutive expression of both prepro-U-II and the U-II receptor, GPR14 (hereafter referred to as the urotensin receptor, UTR) resulted in significant U-II-dependent activation of hypertrophic signalling as demonstrated by increased activity of co-transfected reporter constructs for the hypertrophic phenotype, including atrial natriuretic peptide, myosin light chain-2 and a-skeletal actin. This effect was found to be mediated through G(alpha)q- and Ras-dependent pathways. These results indicate that, in addition to potent haemodynamic effects, U-II is implicated in myocardial fibrogenesis through increased collagen synthesis by cardiac fibroblasts, and may also be an important determinant of pathological cardiac hypertrophy in conditions characterized by U-II receptor upregulation.

**11:45 a.m.**

**Regional Variation and Dynamic Turnover of Cardiac Collagen Matrix in Canine Experimental Heart Failure**

Gordon W. Moe, Nafisah Nili, Effat Rozael, Andrea Korig, Marina Romanova, Bradley H. Strauss. St. Michael’s Hospital, Univ of Toronto, Toronto, ON, Canada

**Background:** Remodeling of the cardiac collagen matrix may be an important mechanism for the progression of heart failure (CHF). Although previous studies using models of cardiomyopathy often revealed little change in collagen content, detailed assessment of regional variations and the turnover of cardiac collagen as well as the impact of therapy on these parameters have not been conducted.

**Methods:** We measured collagen content (hydroxyproline), collagen synthesis (3H-hydroxyproline) and gelatinase (matrix metalloproteinase, MMP) activity (by zymography) from the LV endocardium, LA, RA, RV and interventricular septum (IVS) in 8 normal dogs (N), 8 dogs with CHF induced by RV pacing (CHF) and 5 dogs with CHF treated with a type 1 angiotensin (AT1) receptor blocker candesartan (CHF-AT1-B).

**Results:** Data (means±SEM) for collagen synthesis (cpm/mg) of various interstitial anatomic sites are shown in the table. *p<0.05 vs. N

<table>
<thead>
<tr>
<th>Site</th>
<th>N</th>
<th>RA</th>
<th>LV</th>
<th>IVS</th>
<th>CHF</th>
<th>CHF-AT1-B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyproline</td>
<td>0.42±0.05</td>
<td>0.5±0.06</td>
<td>0.14±0.07</td>
<td>1.7±0.16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMP-2</td>
<td>0.9±0.1</td>
<td>1.2±0.1</td>
<td>0.4±0.1</td>
<td>0.3±0.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMP-9</td>
<td>0.1±0.01</td>
<td>0.1±0.01</td>
<td>0.1±0.01</td>
<td>0.1±0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMP-13</td>
<td>1.2±0.1</td>
<td>2.1±0.1</td>
<td>0.8±0.1</td>
<td>0.3±0.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** Treatment with enalapril in early post MI appeared to have detrimental effects on cardiac remodeling, suggesting that ACE-i may play an important role in the reparative process in the acute phase post MI.
1132 Myocardial Remodeling

Monday, March 19, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: Noon-1:00 p.m.

Effects of Ramipril on Left Ventricular Mass and Function in Normotensive, High-Risk Patients With Normal Ejection Fraction. A Substudy of HOPE

Eva M. Lonn, Roya Shaih-Golestani, Qiong Yi, Jacqueline Bosch, Alison Magi, Salima Yazd, McMaster University, Hamilton, ON, Canada

Background: The effects of long-term ACE-inhibition on left ventricular (LV) mass and function in high-risk cardiovascular patients without overt hypertension and without heart failure are unknown. Methods: We compared echocardiographic changes in LV mass and function (LV mass index [LVM], thickness of the interventricular septum and posterior walls of the LV [IVS+PW], LV ejection fraction [LVEF], LV end-diastolic volume [LVEDV], LV end-systolic volume [LVESV] and wall motion score [WMS]) in 448 high-risk patients, randomized to Placebo, Ramipril 2.5 mg/day (Ram 2.5) or Ramipril 10 mg/day (Ram 10) and followed for 4 years. Patients enrolled in the study had cardiovascular disease or diabetes with additional risk factors, but no hypertension or well-controlled blood pressure, and no heart failure.

Results: Mean patients' age was 65 years and mean baseline blood pressure and ejection fraction were similar in all study groups. Changes in the echocardiographic measurements (baseline-end-study) were summarized in the table.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>LVM (g/m²)</th>
<th>IVS+PW (mm)</th>
<th>LVEF (%)</th>
<th>LVEDV (L)</th>
<th>LVESV (L)</th>
<th>WMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=151)</td>
<td>+0.3 ± 0.25</td>
<td>+0.2 ± 0.22</td>
<td>-2.0 ± 2.7</td>
<td>0.02</td>
<td></td>
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</tr>
<tr>
<td>Ram 2.5 (n=149)</td>
<td>+0.10 ± 0.3</td>
<td>-0.16 ± 0.3</td>
<td>-0.70 ± 0.3</td>
<td>0.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ram 10 (n=146)</td>
<td>+0.15 ± 0.4</td>
<td>-1.5 ± 0.9</td>
<td>0.1 ± 0.9</td>
<td>0.06</td>
<td></td>
<td></td>
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</tbody>
</table>

Adjustment for blood pressure changes during the study and multivariate adjustment did not alter the study results.

Conclusions: Ramipril significantly reduced LVM and LV volumes with trends towards improved LVEF and WMS. These effects were dose-dependent and could not be explained by blood pressure changes alone. Long-term ACE-inhibitor therapy has a beneficial, dose-dependent effect on LV remodeling and function in high-risk patients with cardiovascular disease without hypertension or with well-controlled blood pressure and no heart failure.

1132-45 Effect of Spiroloactone on Plasma Brain Natriuretic Peptide and Left Ventricular Remodeling in Patients With Congestive Heart Failure

Takayoshi Tsutamoto, Atsuyuki Wada, Keiko Maeda, Naoka Mabuchi, Masaru Hayashi, CHF with MR 136+44cc 96+37cc 67~23~~ lOt3.2

Sato-oh, Japan

Background: Aldosterone (ALD) promotes collagen synthesis and structural remodeling of the left ventricle (LV). ALD production is increased in patients with LV hypertrophy. Spironolactone (SP), a competitive ALD receptor antagonist, has been shown to decrease LV hypertrophy. In this study, we evaluated the effects of 4 months of treatment with SP on LV remodeling and function in patients with chronic severe MR.

Method. Thirty-seven patients with mid to moderate symptomatic left ventricular dysfunction who received standard therapy. were randomly divided into two groups: treatment with spironolactone (n=20) and placebo (n=17). To evaluate the effects of spironolactone or placebo. Results: The left ventricular end-diastolic volume index (LVEDVI) and LV mass index (LVMi) were significantly decreased (LVEDVI: 152±11 vs. 170±10 mL/m², p<0.001; LVMi: 107±6 vs. 140±7 g/m², p<0.002). The ejection fraction (EF) was significantly increased in the spironolactone group (32±2 vs. 35±1.9%, p=0.05), but did not change in the placebo group. Plasma levels of BNP and procollagen type III peptides (PiNPI) significantly increased after the treatment of spironolactone (BNP:202±90 vs. 927±29 ng/mL, p<0.01; PiNPI: 6.0±1.8 vs. 14.6±3.0 ng/mL, p<0.001), but did not change in the placebo group. There was a significant positive correlation between the changes of PiNPI and changes of the LVEDVI (r=0.43, p=0.045) as well as the LVMi (r=0.65, p<0.001) with spironolactone treatment.

Conclusion: These findings indicate that 4 months of treatment with spironolactone improves left ventricular volume, LVMi and EF and decreases plasma levels of BNP and PiNPI, suggesting that endogenous aldosterone has an important role in the left ventricular remodeling of patients with CHF.

1132-46 Effect of Spironolactone on Plasma Brain Natriuretic Peptide and Left Ventricular Remodeling in Patients With Congestive Heart Failure

Takayoshi Tsutamoto, Atsuyuki Wada, Keiko Maeda, Naoka Mabuchi, Masaru Hayashi, CHF with MR 136+44cc 96+37cc 67~23~~ lOt3.2

Sato-oh, Japan

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Conclusion: These findings indicate that 4 months of treatment with spironolactone improves left ventricular volume, LVMi and EF and decreases plasma levels of BNP and PiNPI, suggesting that endogenous aldosterone has an important role in the left ventricular remodeling of patients with CHF.

1132-49 Echocardiographic Predictors of Mortality in Nonischemic Cardiomyopathy: Report From the PRAISE-2 Echocardiographic Substudy

Christopher H. Cabell, Eric J. Velazquez, Jean G. Dumesnil, Douglas A. Criger, Robert N. Linton, Allen B. Miller, Anne S. Cropp, James G. Jollis, Thomas Ryan, Duke Clinical Research Institute, Durham, NC, Pfizer Central Research, Groton, CT

Background: Prognostic serum markers with congestive heart failure in patients with nonischemic cardiomyopathy. Methods: Recruited patients with NYHA class > I and severe LV dysfunction were randomized to amlodipine or placebo. The primary outcome was all cause mortality.

Results: There were no significant differences between treatment arms in clinical characteristics, echo parameters or mortality. In multivariate analyses, only mitral regurgitation was independently predictive of mortality. With each increased grade of mitral regurgitation the adjusted odds of death was 2.07 (95% CI 1.20, 3.55). Conclusion: In this study, echocardiographic findings were strongly predictive of mortality. Both syst-
Sensitivity, Specificity, and Predictive Value of Serum markers of Cardiac Extra-Cellular Matrix Turnover in Heart Failure

Takaroshi Yamazaki, Jong-Dae Lee, Hiromasa Shimizu, Hiroyasu Uzui, Yasuhiko Yamamoto, Kazuhisa Kodama. Osaka Police Hospital, Osaka, Japan

Background: Plasma levels of endogenous atrial (ANP) and brain (BNP) natriuretic peptides increase with the severity of chronic heart failure. The biological receptors of both peptides also increased in patients with left ventricular (LV) remodeling after myocardial infarction (MI), the compensatory activity may attenuated. To elucidate the hypothesis, the roles of ANP and BNP in LV remodeling were studied in patients with or without LV remodeling.

Methods: Plasma ANP, BNP and cGMP level were measured by the radioimmunoassay method in patients with MI and post-MI dilated cardiomyopathy (DM) with or without LV remodeling. LV remodeling was defined on echocardiogram as a decrease of LV ejection fraction (LV EF) of 10% or more from the pre-MI value. LV EF was calculated with the area-length method using LV grams at 1 M and 6 M. Significant dilatation or thickening were defined as a decrease in LV cavity or wall thickness by >15%.

Results: Tested markers were not affected by age nor gender. Mean PIIINP was higher in patients with CHF than in controls (4.0±2.4 vs. 3.5±1.2 μg/L, p<0.01). Values of PIIINP and PINP were not different between the two sample populations. In CHF patients, PIIINP levels were positively associated to isometric (5.3 vs. 4.7 μg/L, p<0.02) and negatively to UMC gradient (4.7 vs. 5.4 μg/L, p<0.01), and were correlated to serum ANP (r=0.177, p<0.005) but not to NYHA class nor to LVEF. Sensitivity and specificity for the diagnosis of heart failure were respectively 93% with 55% and 93% with 55%, PIIINP level was a cut point 50% and 90% and 83% with 4.1 μg/L as a cut point. In CHF patients, baseline PIIINP >3.85 μg/L was associated with an increased risk of death (9.2±3.9 vs. 1.3±4.1, p<0.003) and death or hospitalization (9.1±3.8 vs. 1.3±5.3, p<0.001). PIIINP and PINP were well associated with each other. As opposed to precociously type I, serum procollagen type III mRNA discriminates heart failure patients from healthy subjects and was associated with poor outcome in CHF. It should be further investigated as a tool for diagnosis and risk stratification of CHF patients.

Conclusion: These results demonstrate that TGFβ1 may be an important mediator of this process.
METHODS: We prospectively studied 134 asymptomatic patients after MI. LV volume was measured by gated single photon emission computed tomography (99mTc-diatocil volume index, EDV, ml/m2, diaction/EDVI = two standard deviations of mean), remodernization by Devereux-based formulas (stroke volume index, SVI, ml/m2). Duration and QT interval (difference of longest and shortest QT intervals, 12-lead electrocardiogram), severity of ventricular arrhythmias (LOW grade) and heart rate variability (EDDI, ny, standard deviation of intervals of electrocardiogram, 24 hour Holter) were analyzed.

RESULTS: Of 134 patients 37 (28%) showed LV dilatation. During Follow-Up (mean 87 months, visits: 4 days, 4 weeks, 0.5, 1.5, 3 and 5 years) 16 (12%) of 134 patients died. Initially low SVI in non-survivors normalized after 4 weeks but fell again thereafter. LVSC in non-survivors increased (beginning 2 years after MI). EDVI and LOWN-score formed at baseline (prior to beta-blocker) and at 6 months and 1 year of beta-blocker therapy. The activity of plasma MMP-3 (stromelysin) and TIMP-1 in patients with congestive heart failure was significantly higher and the ratio of MMP-3/TIMP-1 higher than in patients without heart failure.

CONCLUSION: Patients on a single immunosuppressant showed a low incidence of rejection and transplant arteriopathy, with excellent intermediate-term survival. Long-term follow-up is awaited to confirm these promising initial results.
Cardiomyopathy: Predicting Prognosis

Monday, March 19, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: Noon-1:00 p.m.

1134-02 T-Wave Alternans is Prevalent and Correlates With NYHA Functional Class, LV Function, and Size in Patients With Kittlén-Patented Dilated Cardiomyopathy

Yee Guan Yap, Kadret Aytemir, Nol Mohn, Mark Gallagher, William McGinnis, A. John Camm. St. George’s Hospital Medical School, London, United Kingdom

Background: Using T-wave alternans (TWA) is a measure of transmural dispersion & marker of ventricular tachycardia. We hypothesized that TWA is influenced by LV function & size in DCM patients. Methods: We performed TWA on 99 DCM patients (41 M, age: 47.9 ± 14.5) & 54 controls (28M, 42.1 ± 16.1) using controlled bicycle exercise (CDH2000, Cambridge Heart). Electrocardiogram, VQmax, Holter recording & late potential were also assessed. Negative TWA & T-wave alternans were used. Results: TWA patients had worse NYHA class, LV function & size. No association between TWA & history of VT/sustained VT, NSVT, VPBs frequency, GT dispersion & late potential (p=NS). Conclusions: In DCM patients, TWA is prevalent & associated with worse NYHA class, LV size & function, suggesting a marked degree of transmural dispersion in those patients & carries a prognostic significance. 

1134-03 Quantitative Assessment of Global and Regional Myocardial Function in Patient With Thalassemia Major With and Without Myocardial Iron Overload

Michael F. Vogel, Lisa Anderson, Sally Holden, John E. Deanfield, Malcolm Walker. Middlesex Hospital, London, United Kingdom; Royal Brompton Hospital, London, United Kingdom

Background: Development of congestive heart failure is a late complication of myocardial iron overload in patients with thalassemia major. As myocardial function and exercise capacity may remain normal until late in the disease process, early recognition of myocardial dysfunction due to iron loading is desirable to guide interventions such as chelation therapy. Methods: Iron load of the myocardium was studied with magnetic resonance imaging (MRI) by measuring T2*, which is inversely proportional to tissue iron. Within 30 days of MRI tissue Doppler imaging (TDI) of the RV and LV free wall and the septum was performed in an apical four-chamber view. 46 patients with thalassaemia were examined at age 29.2 (17.5-35.8) years and compared to 114 controls with normal hearts.40/48 patients were asymptomatic, and 44/46 had normal LV fractional shortening on m-mode electrocardiogram. Results: Compared to normals all the thalassaemia patients had reduced global LV and RV longitudinal function and impaired diastolic function with a prolonged isovolumic relaxation time. 36/46 had excess myocardial iron deposition (T2*<20ms).Of these, 30 had regional wall motion abnormalities in the septum (n=13), LV (n=5), IV (n=1) and septum and LV (n=1) detected by TDI. By contrast only 31/2 patients with normal T2* and normal myocardial iron concentration had regional wall motion abnormalities, located in the septum in 9 (p<0.001). Conclusions: Asymptomatic thalassemia patients with abnormal myocardial iron load and normal LV fractional shortening have impaired longitudinal function, and a high incidence of regional wall motion abnormalities, which may both be early signs of myocardial dysfunction not detectable by conventional indices of functional assessment.
Severely Decreased Cardiac 123-I Metyldobenzylguanidine Uptake Predicts Future Deterioration of Heart Failure in Patients with Idiopathic Dilated Cardiomyopathy


Background: Cardiac sympathetic nerve dysfunction plays an important role in the pathogenesis and development of heart failure. The purposes of this study is to evaluate the prognostic significance of Tc99m-metidobenzylguanidine imaging (MIBG) in patients with idiopathic dilated cardiomyopathy (DCM).

Methods: Diagnostic catheterization, echocardiography and MIBG were performed at initial diagnosis of DCM in 116 patients, 116 men, 51.5±12.4 years. For MIBG imaging, heart to mediastinum uptake ratio at initial diagnosis and during follow-up period, NYHA classification and development of heart failure were measured. Multiple logistic regression analysis showed that HiMd was a predictor for deterioration from analysis. During the follow-up period, 37 patients developed heart failure resulted in more than 100 bpm and more than 100 bpm. TWA was negative in 37 pts (36% Group C) and deteriorate in 21 patients (20%).

Conclusion: This study demonstrates that MIBG Imaging is a good predictor for deterioration of heart failure group. Multiple logistic regression analysis showed that HiMd was a stronger predictor of the deterioration of heart failure (chi square=12.6, p<0.004).

Has the Prognostic Value of Idiopathic Dilated Cardiomyopathy Improved in the Community? The Heart Muscle Disease Registry of Trieste

Andrea Di Lenarda, Giustino Baddabini, Roberto Gortan, Elena Carri, Meuro Diurisi, Cristian Zoffoli, Corrado Del Giudice, Matteo Taverone, Fabrizio Tarchi, Giandomenico Department of Cardiology, Trieste, Italy.

Objectives: Although large clinical trials have demonstrated that new treatments for heart failure (HF) can reduce patient morbidity and mortality, there is no clear evidence that these results have been translated into an improved prognosis of the disease in the community.

Methods: From 1991 to 1994, 260 patients affected by idiopathic dilated cardiomyopathy (IDC) were consecutively studied in the Department of Cardiology of Trieste and prospectively enrolled in our Heart Muscle Disease Registry. Ninety-five patients (group 1) were recruited between June 1991 and January 1993, whereas 165 (group 2) between January and September 1992. Baseline clinical profile was similar in the 2 groups. Compared to patients of group 1, those of group 2 were: a) systematically followed up in our HF Clinic; b) more frequently treated with ACE-inhibitors (p<0.01, p=0.001), beta-blockers (p<0.04, p=0.001), statins (p<0.01, p=0.001), and less frequently treated with diuretic agents (p<0.01, p=0.001). Autonomic derangement was identified in 9 patients of group 2 (p<0.001).

Results: Two, 5 and 10 year hospitalization-free survival was respectively 75, 55 and 35% in group 2 vs 67, 53 and 38% in group 1; p=0.002 after stratification for HF severity. Two, 5 and 10 years risk of major adverse events (death, heart transplant, hospitalization) were respectively 38, 52 and 70% in group 2 vs 33, 45 and 60% in group 1; p=0.001. Rehospitalization for worsening HF was respectively 11, 22 and 30% in group 2 vs 3, 12 and 21% in group 1 (p<0.001), while the risk of arrhythmias-related events was respectively 6, 20 and 50% in group 2 vs 2, 16 and 25% in group 1 (p=0.01). Rehospitalization for worsening HF were respectively 8, 10 and 12% in group 2 vs 3, 6 and 10% in group 1 (p=0.001), while hospitalization for arrhythmias were respectively 8, 10 and 10% in group 2 vs 4, 9 and 6% in group 1 (p=0.001).

Conclusions: The analysis of our Registry shows that the use of new treatments and the planning of a close clinical follow up are associated with a significant benefit on morbidity and mortality in IDC patients, mainly due to a reduction in in-patient failure-related events.

Onset Heart Rate Criteria of Microvolt-Level T-Wave Alternans Provides An Additional Prognostic Value in Nonischemic Dilated Cardiomyopathy

Ichiroko Nakamura, Yoshio Ohinma, Masayuki Adachi, Kazutoshi Nakajima, Akito Ishida, Erdaljo Galano, Kihito Yoshida, Mitsuhiko Yosokawa. Kobe University School of Medicine, First Department of Internal Medicine, Kobe, Japan.

To prevent sudden cardiac death (SCD) is one of the most current issues in non-ischemic dilated cardiomyopathy (DCM). Recently, the analysis of microvolt-level T-wave alternans (TWA) has been proposed as a powerful non-invasive tool to identify the high risk patients. The importance of onset heart rate (OHR) in TWA has been well recognized in previous study by Smith et al. The goal of the present study is to clarify whether the OHR in TWA provides an additional prognostic value or not in pts with DCM. Methods and Results: We prospectively investigated 104 patients (41 men, 63±15 years) with DCM undergoing TWA during exercise testing using a CH2000 system (Cambridge Heart, Inc.), as well as determination of left ventricular en diastolic diameter, left ventricular ejection fraction (EF), signal averaged ECG, the presence of non-sustained ventricular tachyarrhythmia and NYHA classification. The end point of this study was defined as cardiac death (CD), sustained ventricular tachycardia/ventricular fibrillation (SVT/VF), or congestive heart failure (CHF). Forty-six patients showed TWA positive and were divided into the following two groups according to the median value of OHR: Group A (n=22; 62%); OHR less than 100 bpm and Group B (n=22; 38%); with OHR less than 100 bpm and more than 100 bpm. TWA was negative in 37 pts (36% Group C) and deteriorate in 21 patients (20%). During a follow-up duration of 21±14 months, there were 14 total cardiac events (4CD, 10SVT/VF, 10.1CHF), 11 cardiac events (4CD, 7SVT/VF, 10.1CHF) including SCD in Group A, 2(SVT/VF) in Group B, 1(SVT/VF) in Group C. Univariate analysis showed that TWA with OHR less than 100 bpm (TWA-OHR), TWA, EF, and NYHA were identified as univariate predictors of cardiac events. Multivariate Cox hazard analysis revealed that TWA-OHR was the only independent predictor in stratifying the high risk patients in DCM. (chi-square, 7.5; % Risk Reduction, 90%; p=0.008).

Hypertensive End Organ Damage and Premature Mortality Are p38 MAPK Dependent in a Rat Model of Cardiac Hypertrophy and Failure


Background: Isoforms of p38-Mitogen Activated Protein Kinase (MAPK) in perfused hearts and/or cultured cardiac myocytes are activated by neurohormones, cytokines, and stress, ischemia and reperfusion. The aim of the present study was to investigate (1) activation of cardiac p38 during the development of HF and (2) the chronic effects of a specific p38 inhibitor SB203580 in a model of cardiac hypertrophy and failure (pseudonormalization of restraint-stroke-prone strain (SHR-SP)).

Methods: In the time course study (1), SHR-SP were divided into two groups and fed either standard (SRC-SP) (n=15) or a high salt/fat diet (SFD-SP) (n=35) to accelerate HF. Animals were sacrificed at regular intervals for p38 analysis (phospho-specific antibody). A time-course of SB203580 (10 mg/kg) was also assessed as control. In the treatment study (2), SHR-SP were divided into four groups (n=20 each) and fed either SRC, SFD or SFD plus SB203580 (1200 or 2000ppm).

ABSTRACTS - Cardiac Function and Heart Failure 169A

POSTER SESSION

1135 Signal Transduction Pathways Associated With Development and Progression of Heart Failure

Monday, March 19, 2001, Noon-2:00 p.m.,
Orange County Convention Center, Hall A4
Preseession Hour: Noon-1:00 p.m.

1135-68 Increased Expression of Mitochondrial Cytochrome c and Caspases 2, 3 and 7 in Myocardium of Dogs With Chronic Heart Failure

Qualleda Mendi, Filamant C. Ound, Yuska G. Shiga, Takayuki Mikiura, Akihito Yoshida, Todor, George Suzuki, Sidney Goldstein, Harri N. Babbath. Henry Ford Health System, Detroit, MI.

Background: Cardiomyopathy apoptosis or programmed cell death occurs in heart failure (HF) and may play an important role in the progression of the disease. One signal transduction pathway considered important in mediating this process is cell death is increased cytosolic levels of mitochondrial cytochrome c. Cytochrome c can activate a series of caspases, members of a family of cystein proteases, that trigger apoptosis. Caspases 2, 3, 6, 9, and 11 initiate the apoptotic process while caspases 3, 6, and 7 execute apoptosis.

Methods: To explore whether this signaling pathway is activated in the failing heart, we examined the expression of cytochrome c and tissue levels of caspase 2, 3, and 7 in LV myocardium of 6 dogs with chronic HF (LV ejection fraction 21±1%) produced by Intracoronary microembolizations. LV tissue from 6 normal (NL) dogs was used for comparison. Expression of cytochrome c was determined from Western blots and tissue levels of caspases 2, 3, and 7 were significantly higher in HF dogs compared to NL (Table).
Discordant Regulation of Apoptosis Associated Proteins in Cardiomyocytes Isolated From Patients With Ischemic Versus Idiopathic Dilated Cardiomyopathy

Anastasia Todor, Victor G. Shorrov, Norman Silverman, Dinmay Goldstein, Hanii N. Sabhni. Henry Ford Health System, Detroit, MI

Background: Cardiomyocytes (CM) apoptosis has been shown to occur in myocardium of patients with ischemic (ICM) and dilated cardiomyopathy (IDC). The mechanisms responsible for activation of this cell suicide gene program are not fully understood.

Fas is a member of the tumor necrosis factor receptor family. Activation of Fas by its ligand can cause apoptosis of Fas-bearing cells by activating members of the caspase family. The stress-activated protein kinase (SAPK) cascade and p38 mitogen activated protein kinase (~38 MAPK) have also been implicated in the activation of CM apoptosis.

Methods: Fas, Fas-L, c-Jun and ~38 MAPK were determined in myocardium of 10 normal (NL), 10 IDC and 10 ICM patients. At least 1000 cells were counted in each case. The protein levels were normalized to actin expression.

Results: The results are shown in the table. Compared to NL, Fas was significantly downregulated in IDC but unchanged in ICM. Fas-L, in the other hand, was downregulated in IDC but significantly upregulated in ICM. c-Jun, a protein downstream of the FAS cascade, was upregulated in ICD and downregulated in IDC while ~38 MAPK was downregulated in IDC and upregulated in ICM.

Conclusion: The downregulation of Fas-L in the face of unchanged Fas in ICD makes Fas-mediated apoptosis not likely to be involved in this disease entity. On the other hand, the marked upregulation of Fas-L in IDC, while does not ensure Fas-mediated CM apoptosis, it makes such a possibility more likely. The FAS pathway appears to be more active in IDC while the ~38 MAPK cascade prevails in ICM. These differences may be important determinants in the future development of toxicity/specific treatments for heart failure.

Mortality at 28 weeks

<table>
<thead>
<tr>
<th>Group</th>
<th>NL</th>
<th>IDC</th>
<th>ICM</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>0%</td>
<td>90%</td>
<td>0%</td>
</tr>
</tbody>
</table>

MCP-1 mRNA (copies of mRNA/ng tissue)

<table>
<thead>
<tr>
<th>Group</th>
<th>NL</th>
<th>IDC</th>
<th>ICM</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNA</td>
<td>394+140</td>
<td>416+793</td>
<td>2699+511</td>
</tr>
</tbody>
</table>

Macrophage no/mm² (efield)

<table>
<thead>
<tr>
<th>Group</th>
<th>NL</th>
<th>IDC</th>
<th>ICM</th>
</tr>
</thead>
<tbody>
<tr>
<td>6237±243</td>
<td>5875±700</td>
<td>1036±331</td>
<td></td>
</tr>
</tbody>
</table>

Macrophage no

<table>
<thead>
<tr>
<th>Group</th>
<th>NL</th>
<th>IDC</th>
<th>ICM</th>
</tr>
</thead>
<tbody>
<tr>
<td>44±2</td>
<td>16±2</td>
<td>23±6</td>
<td></td>
</tr>
</tbody>
</table>

Cardiac output (ml/min)

<table>
<thead>
<tr>
<th>Group</th>
<th>NL</th>
<th>IDC</th>
<th>ICM</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRC</td>
<td>100±3</td>
<td>128±9.9</td>
<td>162±5.6</td>
</tr>
</tbody>
</table>

For new members, 89,071 (10.7%) joined in January. The latter swipes were verified and tabulated using a computerized card swipe tracking system.

Conclusion: These findings, from the largest database reported to date, are the first to demonstrate higher average card swipes in February and March than those joining in December. The study also demonstrated that new members were more likely to use the clubs on average 5±1/month.

POSTER SESSION

1136 Cardiac Rehabilitation

Monday, March 19, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: Noon-1:00 p.m.

1136-43 The Challenge of Enhancing Exercise Compliance

Barry A. Formes, James M. Crouse, Rich Stewart, Karen J.arch, Geoffrey C. Timmins, William Beaumont Hospital, Royal Oak, MI

Background: Recent public health recommendations have emphasized the importance of moderate-intensity exercise on most, and preferably all days of the week. Although health club memberships have escalated in recent years, there has been a paradoxical increase in the number of people with inactive lifestyles. Exercise noncompliance is a major public health concern, and the need for effective intervention strategies is critical.

Methods: We conducted a retrospective review of member utilization records in one of the largest commercial fitness/health clubs (n=325) in the U.S. We identified new members (n=130) who joined in one of the four fiscal quarters of 1999. Exercise compliance was assessed using computerized card swipe tracking system with specific reference to January joiners (n=35) in the U.S. Physical activity level was quantified for each new member using a questionnaire. New members were classified as active if they met the physical activity criteria of the American College of Sports Medicine. The primary outcome measure was the proportion of new members who remained active at 6 months. The secondary outcomes were the proportion of new members who met the physical activity criteria at 6 months.

Results: Of the 130 new members, 102 (78%) were active at 6 months. The proportion of new members who met the physical activity criteria at 6 months was 78%.

Conclusion: Our study demonstrates that although exercise noncompliance is a major public health concern, the majority of new members are able to achieve the recommended level of physical activity with proper intervention strategies.
1138-73 Physical Activity Promotes a Healthy Cardiovascular Risk Factor Profile But Is Unrelated to the Presence or Extent of Subclinical Atherosclerosis

Allen J. Taylor, Tammy Watkins, Debbie Bell, Jon Carrow, Jody Bindeman, Irwin M. Reesman, Honey Wong, Sanj Bhatnagar, Patrick O. Maloney. Walter Reed Army Medical Center, Washington, DC

Background: Regular physical activity leads to a more favorable cardiovascular risk factor profile and the presence and extent of subclinical atherosclerosis. The degree of physical activity was compared to the cardiovascular risk factor profile and the presence and extent of subclinical atherosclerosis.

Results: Sports-related physical activity was associated with lower body mass index (r = -0.11; P = .001), higher HDL cholesterol (r = 0.13; P = .003) and less glucose resistance (r = -0.11; P = .001) compared to those who were sedentary. In a multivariate regression analysis, sports-related physical activity was a strong predictor of HDL cholesterol (β = 0.16; P = .001) and glucose resistance (β = -0.16; P = .001). In contrast, the cardiovascular risk factor profile did not correlate with the presence or extent of subclinical atherosclerosis.

Conclusion: Physical activity, particularly sports-related activity, is associated with a more favorable cardiovascular risk factor profile and decreased glucose resistance. However, it does not appear to be related to the presence or extent of subclinical atherosclerosis.
Improved cGMP Generation Correlates to Hemodynamic Improvement in Heart Failure Patients After 21 Days Treatment With the ET-A Receptor Antagonist LU135252

Jan Mondi, Sebastian Philipp, Michaela Schweinermann-Freitoebe, Thomas Langenkeidel, Thomas Notte, Rainer Oester, Thomas Luxecker, Roland Willenbrock, Reiner Vollhaber-Clinik, Charité, Humboldt-University, Berlin, Berlin, Germany; Knoll-BASF Pharma, Germany.

Background: The ratio of the second messenger cGMP to plasma concentrations of ANP or BNP correlates to the effectiveness of the natriuretic peptides. The present study was designed to analyze whether a 3 week treatment of heart failure patients with the specific ET-A receptor antagonist LU135252 influences the cGMP/BNP ratio and whether this ratio correlates to hemodynamic changes. Methods: Patients with an ejection fraction <55% (n=157, mean age 57 years) received LU135252 (double-blind, either 100, 300 mg or placebo) over a period of 21 days. Plasma concentrations of ANP, BNP and cGMP were determined before randomisation and after 21 days of treatment. Invasive hemodynamic evaluation was performed before and after the first application of LU135252 and after 21 days of continuous treatment and measured significant changes to cardiac index and pulmonary vascular resistance. Results: Plasma BNP concentrations increased with 100 mg (56-10 at baseline to 34+5 pmol/l, p<0.001) and 300 mg (46-8 to 33+3, p<0.001). The cGMP/BNP ratio increased in all treatment groups to 0.30+0.03 (30 mg), 0.26+0.03 (100 mg) and 0.26+0.04 (300 mg), indicating improved second messenger activity by the end of 21 treatment days. The cGMP/BNP ratio was significantly correlated (p<0.001) to the decrease in pulmonary vascular resistance, while no such correlation existed between cGMP/BNP ratio and systemic vascular resistance. Conclusions: These data indicate that the increased cGMP/BNP ratio specifically reflects the decrease in pulmonary vascular resistance. The improved cGMP/BNP ratio might either be a direct effect of chronic ETA-receptor blockade on the efficacy of specific natriuretic peptides or might be a marker of improvement of heart failure.

2:30 p.m.

BG9719 (CVT-124), an AI-Adenosine Receptor Antagonist, Protects Against the Decline in Renal Function Observed with Standard Congestive Heart Failure Therapy


Background: Increases in renal function are common and associated with adverse clinical outcomes in congestive heart failure (CHF) patients. Antagonism of AI-Adenosine receptors may improve renal function due to selective renal afferent arteriolar vasodilation and increase sodium excretion via effects on the proximal and distal tubules. Methods: BG9719, a selective AI-Adenosine receptor antagonist, was given to 79 stable NYHA Class II or III CHF patients with edema despite treatment with ACE inhibitors and diuretics. Patients were randomized on a 1:1 ratio to BG 9719 (0.75 ug/mL) or placebo, on AEC inhibitors and diuretics, but diuretics were discontinued. On 2 separate dosing days, single infusions of IG9719 were administered to a furosemide (80 mg) in a randomized, double-blind, placebo-controlled crossover study to assess renal function and output. Results: A statistically significant dose response for renal output (urine volume, sodium excretion) was observed across three dose levels of BG9719. No significant increase in potassium excretion was observed. Urinary function (% change from baseline to creatinine clearance) improved after BG9719 compared to placebo (+13.5% ± 3.1%). In contrast, the increased renal output seen with furosemide was associated with a significant decline in renal function. BG9719, when given in association with furosemide, produced an additive effect on renal output and protected renal function when compared to furosemide alone (+17% ± 17%).

Change From Baseline in Creatinine (0-6 hrs)

<table>
<thead>
<tr>
<th>Excretion</th>
<th>Placebo</th>
<th>BG 9719 (0.75 mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na* (mEq/L)</td>
<td>8.7</td>
<td>43.9</td>
</tr>
<tr>
<td>K* (mEq/L)</td>
<td>9.3</td>
<td>14.2</td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>180.9</td>
<td>666.8</td>
</tr>
<tr>
<td>Glomerular Filtrate (mL)</td>
<td>187.8</td>
<td>270.0</td>
</tr>
</tbody>
</table>

3Statistically significant change (p<0.05) or ± disc response.

Conclusions: On a background of ACE inhibition, single dose treatment with BG9719 alone induced a potassium neutral neturul trend associated with improved creatinine clearance, in contrast, creatinine clearance declined with furosemide. The addition of BG9719 to standard therapy further improved renal output while protecting renal function. Treatment with an AI-Adenosine receptor antagonist may be useful in the therapy of CHF.
ABSTRACTS - Cardiac Function and Heart Failure 173A

**830-6** 
Ranolazine Improves Left Ventricular Mechanical Efficiency in Dogs With Heart Failure: Comparison with Dobutamine

Hani N. Sabbah, Margaret P. Chandler, George Suzuki, Hideaki Morita, Omar Nass, Brent Blackwood, Andrew Wolff, William C. Stanley, Henry Ford Health System, Detroit, MI, Case Western Reserve University, Cleveland, OH

Background: Ranolazine, a partial fatty acid oxidation (pFOX) inhibitor was shown to acutely improve LV function in dogs with chronic heart failure (HF). In the present study, we tested the hypothesis that partial switching of the substrate use of the heart away from fatty acids towards carbohydrates with ranolazine improves LV function by improving mechanical efficiency without the need for an increase in myocardial oxygen consumption (MVO2) and coronary blood flow.

Methods: Chronic LV dysfunction and failure was produced in 6 dogs by multiple sequential intracoronary micromobilizations. LV ejection fraction (EF), stroke volume (SV), total LV coronary blood flow (CBF), MVO2 and myocardial efficiency were measured before (PRE) and after (POST) intravenous administration of dobutamine (2 to 4 μg/kg/min for 30 min) or ranolazine (0.5 μg/kg bolus + 1.0 μg/kg/min for 30 min). LV mechanical efficiency was determined as the rate of LV power to LV energy expenditure, calculated from the LV systolic pressure, cardiac output, and the MVO2.

Results: The results are shown in the table. Both dobutamine and ranolazine significantly increased EF and SV to the same extent and without having any effects on heart rate or systemic pressure. The improvements in LV function with dobutamine were associated with increased CBF and MVO2 and no change in LV efficiency. In contrast, ranolazine improved LV function without increasing CBF or MVO2 along with a significant improvement in LV efficiency from 24 ± 3% to 35 ± 4% (P<0.05).

<table>
<thead>
<tr>
<th></th>
<th>Dobutamine</th>
<th>Ranolazine</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRE</td>
<td>POST</td>
<td>POST</td>
</tr>
<tr>
<td>EF (%)</td>
<td>29 ± 4</td>
<td>39 ± 5</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>20 ± 3</td>
<td>28 ± 4.4</td>
</tr>
<tr>
<td>CBF (ml/min)</td>
<td>69 ± 13</td>
<td>95 ± 19</td>
</tr>
<tr>
<td>MVO2 (μmol/g/min)</td>
<td>218 ± 111</td>
<td>106 ± 69</td>
</tr>
</tbody>
</table>

Conclusion: Unlike dobutamine, acute intravenous infusion of the pFOX inhibitor ranolazine significantly improved LV function through a marked increase in LV mechanical efficiency. This points to a novel approach for the treatment of HF based on a class of drugs that optimize myocardial efficiency. Additional studies, however, are needed to determine whether the benefits of ranolazine in HF can be maintained with chronic therapy.

ORAL CONTRIBUTIONS

**832** 
Cardiomyopathy: The Genetic Puzzle

Monday, March 19, 2001, 2:00 p.m. - 3:30 p.m.
Orange County Convention Center, Room 231A

**832-1** 
Mutations in the Gene for Troponin I (TNNI3) in Familial Hypertrophic Cardiomyopathy

Jens Mogensen, Penny M. Elliott, Bo C. Klausen, Ole Hønsvig, Henrik Egelund, Ulrik Baandrup, Poul S. Andersen, Michael Christiansen, Henrik Budsgaard, William J. McKenna, Anders D. Borglum. Søborg Hospital, Department of Cardiology, Aarhus, Denmark

Background: Familial hypertrophic cardiomyopathy (FHC) is a prevalent hereditary heart disease. Disease associated mutations have been identified in 9 different sarcomeric genes. Aim: To investigate the frequency of TNNI3 mutations and the associated phenotype in a more general population of HF patients, not just those with severe HF and hyponatremia.

Methods: In the current study, we have examined all exons of the TNNI3 gene in 96 individuals with a clinical diagnosis of FHC. 80 individuals were referred to our department due to systolic LV dysfunction and 16 individuals were neither referred to our department nor had myocardial hypertrophy. Mutation detection was carried out by direct sequencing.

Results: Two novel and 2 previously reported missense mutations were identified in 6 unrelated families (frequency: 5%). Mutations were absent in 140 control chromosome.

Conclusion: TNNI3 mutations appear to be associated with a heterogeneous phenotype and often a severe prognosis.

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Number of positive individuals</th>
<th>Number of symptomatic individuals</th>
<th>Number of sudden death cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arg162His</td>
<td>7</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Arg162Gln</td>
<td>7</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Ser196Leu</td>
<td>5</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Ser196Pro</td>
<td>5</td>
<td>1</td>
<td>-</td>
</tr>
</tbody>
</table>

Table: Genotype and allele frequency of the calcineurin gene polymorphism (II; (Frequency))

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Allele</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC</td>
<td>CT</td>
</tr>
<tr>
<td>Patients (n=148)</td>
<td>28 (0.19)</td>
</tr>
<tr>
<td>Controls (n=60)</td>
<td>7 (0.07)</td>
</tr>
</tbody>
</table>

The prognosis of familial hypertrophic cardiomyopathy caused by Myosin Binding Protein-C Glu451Gln Mutation is More Unfavorable Than That of Ins791 Mutation

Hideshi Niinuma, Ryuichiro Anan, Linda L. Bachinski, Barry J. Maron, Shinichi Aihara, Robert Roberts, J. G. Seidman, Christine E. Seidman, Chuiwa Tei, Kagoshima University, Kagoshima, Japan, Harvard Medical School, Boston, MA

Background: We have reported that the mutation in the cardiac myosin binding protein-C gene cause a familial hypertrophic cardiomyopathy with a notable feature: later onset and better prognosis than familial hypertrophic cardiomyopathy caused by the mutations in beta cardiac myosin heavy chain gene and cardiac troponin T gene. In these two genes, it has been reported that each mutation cause different clinical features such as age at onset, left ventricular wall thickness and prognosis. But in the cardiac myosin binding protein-C gene, clinical features in each mutation have not been analyzed sufficiently.

Methods: We have analyzed and compared the prognosis of eight familial hypertrophic cardiomyopathy families who have three different mutations; 20 individuals in one family have cardiac myosin binding protein-C gene Ins791 mutation (one base insertion mutation, predicted to produce a truncated protein and full length one amino acid substituted protein), 10 individuals in three families have cardiac myosin binding protein-C gene Glu451Gln mutation (missense mutation, predicted to produce a truncated protein and full length one amino acid substituted protein). Eight disease-related deaths of 20 affected individuals were observed in cardiac myosin binding protein-C gene Glu451Gln (missense) mutation, eight disease-related deaths of 108 were observed in cardiac myosin binding protein-C gene Ins791 mutation and 36 disease-related deaths of 60 were observed in beta cardiac myosin heavy chain gene Arg719Trp mutation. The prognosis of cardiac myosin binding protein-C gene Glu451Gln mutation is significantly better than that of beta cardiac myosin heavy chain gene Arg719Trp mutation (p<0.05), but is more unfavorable.
Cardiac Function and Heart Failure

174A ABSTRACTS - Cardiac Function and Heart Failure

Sudden Death Among Patients with a Hereditary Cardiomyopathy Due to a Missense Mutation in the Rod Domain of the Lamin A/C Gene

Sanjana Bhardwaj, Takeshi Sasaki, Christine Siedman, Himberno Virdiallet. Hope Children's Hospital, Oak Lawn, IL, Marshfield Clinic, Marshfield, WI.

Background: Missense mutations in the rod domain of the lamin A/C (LMNA) gene are a genetic cause for adult-onset dilated cardiomyopathy (DCM). Although the variant of LMNA is associated with progression or conduction system (SCD) disease and heart failure (HF), thus far there is no clinical, pathological and genetic correlate for sudden death (SD) that occurs frequently in this entity.

Methods: We undertook a prospective study of a kindred with the variant of DCM and SD. Subjects were considered to be genetically predisposed if they were heterozygous for LMNA or obligate carriers. Clinical work up included an entire cardiovascular evaluation.

Results: We evaluated 4 patients with a family history of DCM or SD. One had PM. Pathological evaluation in SD cases demonstrated distinct degenerative changes and marked fatty infiltration throughout the CS, the atria and ventricles. Conclusions: 1) Patients with the variant of familial DCM exhibit a pattern of disease progression far more predictable than the observed in individuals with “idiopathic” DCM. 2) The clinical stages of the disease will be useful in counseling the unaffected relatives and in deciding the optimal timing of anticoagulation and/or ICD placement. 3) Finally, the significant lack of myocardium in the atria may explain the patients’ excessive risk for SSS, stroke and SD.

832-4 Differentially Expressed Genes in Human Hearts with Hypertrophic Cardiomyopathy

De-Sun Lim, Valeria Rubinca, Robert Roberts, Ali J. Marwan, Baylor College of Medicine, Houston, TX.

Hypertrophic cardiomyopathy (HCM), a single gene disorder, is caused by mutations in sarcomeric proteins. Patients with LMNA, a paradigm of cardiac hypertrophic responses, exhibit diverse clinical and pathological phenotypes. While the molecular genetic basis of HCM is well defined, the pathogenesis of its diverse forms is unknown, but is expected to involve activation of diverse pathways. To identify molecules involved in the pathogenesis of cardiac phenotypes in HCM, we performed mRNA subtraction between normal and HCM human hearts. We screened 268 independent clones and found that 66 were differentially expressed. Sequence analyses identified an array of 20 functionally known genes, of which 14 were analyzed by Northern blottings. Expression of 12/14 genes was increased by >2 fold in the HCM heart. To determine whether differentially expressed genes were also upregulated in other HCM hearts, Northern blotting was repeated for 6 genes in 5 additional hearts. Expression of myosin light chain 2 (MLC2) was increased in 3, skeletal muscle LIM protein in 4, voltage-dependent anion channel 1 in 1, a subunit of G protein in 3, heart-healthy protein 70 in 2, and MSHD dehydrogenases in 2 hearts, at least by 2 fold. These findings suggest that an array of genes with diverse functions is upregulated in the myocardium of human patients with HCM to a variable degree. The diversity of the differentially expressed genes and differences in this pattern of myocardial gene expression between different HCM hearts may contribute to the diversity of clinical and pathological phenotypes of HCM. Identification and characterization of differentially expressed genes may provide new therapeutic and prevention approaches in HCM.

List of Differentially Expressed Genes

- Ventricular tachycardia
- Genomic DNA
- Skelelae demylinated
- Healthy heart
- Mitochondria
- Genes

832-5 Genetic Screening in Hypertrophic Cardiomyopathy: Most Beta-Mysins Mutations That Are Identified Are Novel With Undetermined Clinical Outcomes


Background: Hypertrophic cardiomyopathy (HCM) may be caused by one of several mutations in 9 sarcomeric genes, commonly, by mutations in the beta-myosin heavy chain gene (MYH7) - with mutations, mostly comprise in the heart in heart versus function of beta-myosins heavy chain. However, some of these mutations have been associated with marked cardiac hypertrophy and a high incidence of sudden death, and others with mild phenotype. Some of these mutations have been associated with marked cardiac hypertrophy and a high incidence of sudden death, and others with mild phenotype. Some of these mutations have been associated with marked cardiac hypertrophy and a high incidence of sudden death, and others with mild phenotype.

Methods: Genomic DNA from 100 consecutive unrelated HCM patients was screened with SSCP for mutations in the first 23 exons of MYH7 (coding head and head-end region of beta-myosin). Anatomical changes were sequenced. Whenever possible, restriction fragments confirmed abnormal sequence.

Results: 17 distinct MYH7 mutations resulting in single amino acid substitutions in conserved regions of beta-myosin were found in 19 of the 100 patients: 13 of the mutations or 28% have not been reported previously. All novel mutations were in or near important functional domains of beta-myosin, and 2 resulted in novel amino acid substitutions. 2 mutations are known in patients with the variant of DCM or SD. 3 occurred in proximal function in most patients renders genotype-phenotype correlations even more challenging; and (4) any methods selected for genetic analy-

Conclusions: (1) MYH7 mutations are more common than we have previously reported; (2) most MYH7 mutations are novel with as yet undefined natural histories. Further studies are necessary to define clinical outcomes of the novel molecular causes of HCM. It should also now be possible to determine whether mutations in the same functional domain of beta-myosin have similar natural histories.

832-6 Predictors of Recurrent Stroke Among Patients With Acute Ischemic Stroke: The VA Experience

Gilbert J. L'ltalien, Linda S. Williams, Morris Weinberger. Roudebush Veterans Affairs Medical Center, Indianapolis, IN, Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT.

Background: We sought to determine whether clinical, demographic factors or both predict recurrent stroke among VA patients admitted to VA hospitals for acute ischemic stroke.

Methods: All VA patients were identified with a first-listed discharge diagnosis of ischemic stroke.
The benefits of radiofrequency treatment of paroxysmal supraventricular tachycardia in discharge diagnoses, hospital length of stay, & charge destination, and Charlson index. JACC February 2001

Changes in autonomic function during tilting in young and elderly patients with vasovagal syncope. The mechanism of the tachycardia or other electrophysiologic data. Atrioventricular nodal reentrant tachycardia is the most frequent cause for paroxysmal tachycardias in patients older than 70 years. The ratio male/female was not different in each group. The incidence of atrioventricular nodal reentrant tachycardia and normal sinus rhythm ECG from childhood to old age.

The ratio of recurrent stroke was 0.23. Clinical variables such as diabetes (HR=1.3, p<0.0001) and atrial fibrillation (AF) (HR=1.5, p<0.01), were the strongest predictors of recurrent stroke followed by the Charlson Index (HR=1.1, p=0.01), atrial fibrillation (HR=1.1, p<0.01), age (HR=1.0, p<0.05), number of discharge diagnoses (HR=0.97, p=0.06), and US region (HR=0.85, p<0.05) Conclusion: Cardiovascular risk factors such as diabetes and AF tend to dominate in the multivariate factors contributing to recurrent stroke. The VA registry. Prophylactic therapies should be more aggressively targeted to treat these factors.

Interests of Radiofrequency Ablation of Paroxysmal Supraventricular Tachycardia in Elderly Patients

Background: Paroxysmal supraventricular tachycardia are not often tolerated in old patients. The purpose of the study was to evaluate the risk factors and methods of radiofrequency catheter ablation of paroxysmal supraventricular tachycardia in patients older than 70 years old compared to those obtained in patients younger than 70 years. The study population consisted of 209 patients, 18 to 80 years old (mean 56±19) mix referral paroxysmal supraventricular tachycardia and normal sinus rhythm ECG: 157 are younger than 70 years (group 1), and 52 older than 70 years (group 2). Clinical presentation was similar in both groups. Fasted was the mean frequency (72, 60%), group classified by a higher incidence of dilated cardiomyopathy in group 2 (21%) than in group 1 (4%). 0.01). Electrocardiographic data were similar in groups 1 and 2: atrioventricular nodal reentrant tachycardia was more frequent (82, 60%) than accessory pathway ventricular tachycardia (18, 15%). Incidence of immediate complications related to the procedure were similar, 11% in group 1 (1 definitive complete AV block) and 12% in group 2 (1 death). The follow-up (0.1 years) indicated a similar incidence of late recurrences of tachycardia (7, 11.5%), a regression of cardiomyopathy in all patients but one, the occurrence of 2 deaths unrelated to a cardiac cause in group 2 (NS), and the development of coronary artery stenosis in 0.5% in group 1, 0% in group 2 (NS). Conclusion: The benefit of radiofrequency treatment of paroxysmal supraventricular tachycardia in elderly patients is higher than in younger patients in term of regression of dilated cardiomyopathy which is frequent in this range of age. The incidence of complications is not increased, but is often more severe.

Is the Electrophysiologic Mechanism of Paroxysmal Supraventricular Tachycardias Modified by the Age of the Patient?

Background: The purpose of the study was to evaluate the influence of age on the mechanism of paroxysmal supraventricular tachycardia in patients without Wolff-Parkinson-White Syndrome. Methods: 494 patients aged 9 to 86 years, with paroxysmal supraventricular tachycardia and normal sinus rhythm ECG were studied. Electrophysiological mapping was performed in 416 patients (84%). The low frequency (0.06-0.10 Hz) and high frequency (0.15-0.40 Hz) frequency bands (indexes of sympathetic and parasympathetic tone. The incidence of vasodepressor syncope in these patients. Frequency domain measurements (expressed as In(ms²/Hz) of the low (0.06-0.10 Hz) and high (0.15-0.40 Hz) frequency bands (indexes of sympathetic and parasympathetic tone respectively) and the ratio low / high frequency were computed from Holter recordings for 4 minute intervals before and after tilting in both groups. Results: The mean values of low and high frequency were significantly higher in the young than in the elderly patients before tilt (low frequency: 5.30±0.84 and high frequency: 5.32±0.49, p<0.01), while the low / high frequency ratio did not differ (1.02±0.16). In response to tilt, low frequency decreased in both groups, but in the elderly patients the decrease was greater (A low frequency: 0.64±0.47 versus 0.30±0.22, p<0.01). High frequency decreased to the same extent in both groups (A high frequency: 0.31±0.20 in young, 0.29±0.34 in elderly patients). The low / high frequency ratio remained constant in the young patients but decreased significantly in the elderly (from 1.65 to 0.83 in the young, 0.70 to 0.57, p<0.002). Of the 21 young patients, 10 had a cardioinhibitory response to tilt, 4 had a vasodepressor and 7 a mixed type response. Of the 16 elderly patients, 1 had a cardioinhibitory, 9 a vasodepressor and 5 a mixed type response.

Conclusions: Elderly patients have a more marked withdrawal of sympathetic tone in response to tilt than do young patients. This greater degree of sympathetic inhibition could explain the higher incidence of vasodepressor syncope in these patients.

Poster Session

POSTER SESSION

Monday, March 19, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4

Presentation Hour: 3:00 p.m.-4:00 p.m.

A New Method to Assess Left Ventricular Recovery on Chronic Circulatory Support Using Automated Echocardiography

John Quinlan, III, Donald Devenny, Darby T. Griffith, Robert L. Normand. University of Pittsburgh, Pittsburgh, PA

Background: Identification of patients who may have recovery of left ventricular function on chronic mechanical assist devices for severe heart failure is difficult.

Methods: To test the hypothesis that automated quantitative echocardiography can assess cardiac recovery, 13 patients aged 45 ± 15 yrs on 267 ± 192 days of left ventricular assist device support for severe heart failure were studied. Devices were Thoratec in 28, and Novacor in 6.

Echo automated border detection and noninvasive arterial pressure were used to measure stroke area, fractional area change, and estimate preload-adjusted maximal power, a load-independent index of ventricular function. On-line data were collected during full mechanical support at 6.0 ± 1.3 L/min and during a transient decrease to partial support at 3.0 ± 0.6 L/min.

Results: With partial mechanical support, 9 patients demonstrated a failing left ventricular pattern: stroke area decreased from 5.6±1.4 to 4.4±1.3 cm², fractional area change decreased from 39±22 to 21±17%, and preload adjusted maximal power was 1.6±1.4 mW/cm². All 9 of these patients remained device dependent, 7 were transplanted, 1 died on the device and one is awaiting transplant.

In contrast, 4 patients demonstrated a recovered left ventricular pattern with partial mechanical support: stroke area increased from 5.0±1.3 to 9.4±1.7 cm², fractional area change was > 30%, and preload-adjusted maximal power (figure) was 5.5±1.8 mW/cm², (p<0.05 versus device-dependent patients).

All 4 of these patients with this pattern were weaned to successful device removal and survived to discharge.

Conclusion: Noninvasive assessment using echo automated border detection during partial mechanical support has potential to determine ventricular recovery and predict successful device removal in patients on chronic left ventricular assist devices.

Does Standby Cardiopulmonary Bypass Support Improve Survival in Patients Who Sustain a Cardiac Arrest During Elective Percutaneous Coronary Interventions?

Fayaz Shahel, Syed Mahmood, John Hakim, Cathy Pollock, Elizabeth Humphreys. Washington Adventist Hospital, Tacoma, MD

Background: Since 1988, a policy of "standby Cardiopulmonary Bypass Support (CPS)" has been used for all elective coronary interventions. CPS is defined as a perfusionist physically present along with the CPS system at and dedicated to the catheterization laboratory. Method/Results: A total of 23,472 Cl were undertaken using this policy and 90 (0.3%) required emergent institution of CPS due to refractory cardiac arrest. Cardiac arrest occurred following abrupt vessel closure in 28 patients, left main dissection in 5 patients, vessel perforation/embolus in 5 patients, and refractory pulmonary oligaemia in 1 patient. All patients were intubated receiving CPR while CPS was instituted. Mean time to CPS was 18 ± 9 minutes. Ten patients were sustained on CPS for 134 ± 22 minutes until a surgical suite became available. Four of 38
In-hospital mortality (36.7%) remained in refractory ventricular tachyarrhythmia until revascularization was completed. Two patients required percutaneous LV venting. Twenty-nine patients (74%) went on to complete their CI and 24 survived to be discharged from the hospital. Those who had CI had less CPS survival removed percutaneously. Two of these developed femoral artery pseudoaneurysm. Of the 10 patients who went to surgery, 7 survived. Conclusions: “In-hospital mortality” along with “first available operating room” appears to decrease mortality in patients who maintain a cardiac arrest during elective CI. Also, this policy may make CI safer in hospitals without immediate surgical back-up.

Methods: We sought to describe the clinical predictors of in-hospital mortality and complications in 1,009 patients treated with intra-aortic balloon pumping at the Texas Heart Institute. All patients treated with IABP at the Texas Heart Institute were included and examined with a stepwise linear logistic regression model for each of the independent variables.

Outcome Variable Odds Ratio Significance

<table>
<thead>
<tr>
<th>Category</th>
<th>Odds Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IABP-Related bleed</td>
<td>1.47</td>
<td>0.0021</td>
</tr>
<tr>
<td>Transmyocardial laser revascularization procedure</td>
<td>0.65</td>
<td>0.0001</td>
</tr>
<tr>
<td>Low molecular weight dextran</td>
<td>0.59</td>
<td>0.004</td>
</tr>
<tr>
<td>Coronary bypass surgery</td>
<td>0.52</td>
<td>0.0001</td>
</tr>
<tr>
<td>Lower Extremity ischemia (4 ± 2)</td>
<td>0.44</td>
<td>0.002</td>
</tr>
<tr>
<td>IABP-Related bleeding (10 %)</td>
<td>2.18</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Conclusions: Specific variables can be identified that independently predict in-hospital mortality and complications. Female gender continues to be associated with both increased in-hospital mortality and a greater risk of lower extremity ischemia.
trophy (LVH) necessary to hyperplasmin or an isolated cardiomyopathy (DCM) still abating alone may be misleading. We aimed at determining unambiguous echocardiographic criteria allowing a differentiation of these disorders. Methods: In seven out of a series of 270 patients referred for evaluation of echocardiographic patterns characteristic for VNC by validation against the anatomic examination due to death (n=4) and heart transplantation (n=3). These criteria when then applied to LVH (n=9) and DCM (n=10) patients to test thorough discriminative validity. Results: After excluding any accompanying cardiac abnormality (by definition) the following criteria were found to allow the diagnosis of VNC: (1) two-layer structure of thickened wall consisting of a compacted (C) thick endo-epicardial interface tissue a b thicker non-compacted (NC) myocardial layer (endo-epicardial ratio >1.5) was found in early stages of VNC. The endo-epicardial ratio of NC was 1.50±0.8 in VNC and DCM and 1.5±0.6 in LVH. (2) Intramyocardial trabeculated spaces were mostly absent in VNC and DCM. The trabeculation ratio of trabeculated myocardium for VNC vs. DCM was 1.9±1.0 vs. 1.1±0.5 and 0.8±0.4 (both p<0.01 vs. VNC) and trabeculated (tv) and endomyocardial spaces (Ev). The trabeculation criteria including a ratio of tv/2 were diagnostic for VNC allowing unambiguous differentiation from LVH and DCM. 1167-65 Consistent Effects of Growth Hormone on LV Function in Early and Advanced Stage of Heart Failure in Cardiomyopathic Hamsters Takao Nishizawa, Mitsuhiro Iwase, Hiroaki Kanazawa, Tetsuro Nagasaka, Takaaki Kato, Takao Sakuma, Subrina Jesmin, Satoshi Fujii, Akira Kitabatake. Hokkaido University Graduate School of Medicine, Sapporo, Japan Background: TO-2 cardiomyopathic hamsters progressively developed LV dysfunction, resulting in congestive cardiac failure. We describe consistent echocardiographic findings in TO-2 cardiomyopathic hamsters, which were treated with human recombinant GH (2 IU/kg, s.c., daily, Y: n=8, A: n=9) or saline (V: n=8, A: n=9) for 4 weeks. Plasma GH levels in young TO-2 hamsters were significantly lower than those of age-matched control YTO-2 hamsters (1.2±0.3 vs. 3.0±0.5 ng/ml). In adult hamsters, plasma GH levels were not significantly different between groups (TO-2: 1.3±0.9 vs. YTO-2: 1.4±0.7 ng/ml). Body weight gain in young GH-treated group was greater than in adult untreated group (+22.0±0.8 vs. +19.5±0.7 g). Body weight gain and LVH was greater in adult treated group (+37.7±1.2 vs. +19.5±1.4 g). Body weight gain in adult GH- treated group was also greater than in adult untreated group (+22.0±0.8 vs. +19.5±0.7 g). LVH function was progressively depressed in young untreated TO-2 hamsters, i.e. LV fractional shortening (%FS) decreased from 54.6±2.2 to 49.3±1.4% and LV end-systolic dimension (DD) increased from 40.0±1.1 to 50.3±1.7 mm. In young GH-treated group, LVFS (40.3±1.2) at 12 weeks was significantly higher than in untreated group (p<0.01). LVDD (5.3±0.7 mm) in untreated group was also significantly lower than in treated group (p<0.01). LV function was gradually depressed in adult untreated hamsters, i.e. LVFS decreased from 21.5±2.5 to 12.6±3.0% and LVDD increased from 6.0±2.2 mm to 7.8±0.3 mm. In adult GH treated hamsters, LVFS (19.0±1.3%) at 22 weeks was significantly decreased (p<0.001) greater than in untreated group, however, LVDD (5.3±0.7 mm) was similar to that in the untreated group. Furthermore, LV function was gradually depressed in adult untreated hamsters, i.e. LVFS decreased from 21.5±2.5 to 12.6±3.0% and LVDD increased from 6.0±2.2 mm to 7.8±0.3 mm. In young GH treated hamsters, LVFS (19.0±1.3%) at 22 weeks was significantly decreased (p<0.001). LV function was also gradually depressed in adult untreated groups, however LVDD (5.3±0.7 mm) in untreated group was also significantly lower than in treated group (p<0.01). Furthermore, LV function was gradually depressed in adult untreated hamsters, i.e. LVFS decreased from 21.5±2.5 to 12.6±3.0% and LVDD increased from 6.0±2.2 mm to 7.8±0.3 mm. In young GH treated hamsters, LVFS (19.0±1.3%) at 22 weeks was significantly decreased (p<0.001). LV function was also gradually depressed in adult untreated groups, however LVDD (5.3±0.7 mm) in untreated group was also significantly lower than in treated group (p<0.01). Consequently, GH can be used to treat LVH in these hamsters. Conclusion: GH is useful to treat LVH in these hamsters. 1167-66 Predictors of Sudden Death and Death Due to Progressive Cardiomyopathic Heart Failure in Patients in MERIT-HF Sidney Goldstein, Hans Wiedel, Henry Ford Health System, Detroit, MI, MERIT-HF Study Group, DeGraaffs Hospital, Gothenburg, Sweden Background: Predictors of the mode of death are important in making decisions with regard to the appropriate drug or device therapy for heart failure. Methods: We had observed that, in Otsuka Long-Evans Tokushima Fatty (OLETF) rats, a model of type II diabetes mellitus (IDDM), nuclear capillary angiogenesis and concomitant fibrosis are diminished, which may result in myocardial compliance and function. Thus, we studied whether benzamil (BN) reverses the cardiac remodeling methods. Male OLETF rats (8 weeks) were treated for 12 weeks with BN (3 mg/kg/day) (DMT), no treatment (DN), or vehicle (DM, n=10). The results were as follows: DMT showed a significant improvement in LV function compared with DN. Conclusion: BN is a novel drug that can be used in the treatment of type II diabetes mellitus.
178A ABSTRACTS - Cardiac Function and Heart Failure

Methods: The study included 311 patients in the MERIT-HF trial with NYHA Class II-IV heart failure and EF<40% were studied.

Results: The median EF at baseline was 28.5% (IQR 20-31) and 51.7% (IQR 43-60) at follow up. The median duration of follow up was 28.5 months (IQR 12-56). The median time to occurrence of the primary composite outcome at follow up was 36 months (IQR 12-60).

Conclusions: Advanced age, low systolic blood pressure and NYHA Class tend to predict death in patients with non-ischemic heart failure, occurring almost twice as frequently as in patients with ischemic heart failure, occurring almost twice as frequently as in patients with ischemic heart failure.
6168 Myocardial Viability by Dobutamine Stress
Electrocardiography Predicts Improvement in Ejection Fraction with B-Blockade in Patients with Heart Failure: The BEST Trial.
Erik E. Eildrum, Paul A. Osepchuk, Susan Mayer, Marilyn St. John Dohler, Christopher Appleton, Jonathan Flehn, Joo Ch, Brian Greenberg, Anthony Delmonico, Heidi Krassel Steinmaur. For The BEST Investigators. UTH Southwestern Medical Center, Dallas, TX.
Background: B-blockers (BB) improve survival and reduce hospitalization in chronic heart failure (CHF) by biologically improving left ventricular (LV) ejection fraction (EF) over 2-3 months of therapy. However, BB acutely reduce EF by pharmacologic withdrawal of adrenergic support to the failing heart. A goal proctor of these individual who will improve with this therapy has not been identified. This substudy of the Beta-Blocker Evaluation of Survival Trial (BEST) examines whether myocardial viability, as determined by dobutamine stress electrocardiography (DSE) will predict EF improvement.
Methods: 79 patients with Class III/IV CHF studied with DSE prior to receiving treatment with bucindolol (n=41) or placebo (n=38). Regional wall motion was assessed by a blinded central reader using the 16 segment model and a regional wall motion score index (WMSI) was calculated as the sum of the scores in each segment divided by the total number of segments visualized. Contractile reserve was defined as a change in WMSI < -0.2. WMSI was changed to compare in LVEF by MUGA after 3 months of therapy. Death or CHF hospitalization (events) in the bucindolol patients with and without reserve were compared to placebo patients using the log-rank test to compare time-to-event data. The average duration of follow-up was 24 months.
Results: Change in WMSI correlated inversely with change in LVEF at 3 months in the bucindolol patients (r=-0.72, p<0.0001). While this subtest was not powered for events, bucindolol patients reserve had a lower trend fewer events (p=0.146) and those without reserve had no benefit of therapy (p=0.8).
Conclusions: Presence of contractile reserve predicts improvement in EF with BB therapy in patients with CHF and suggests that reverse remodeling is related to myocardial viability.

6168-69 Echo-Doppler Mitral Flow Monitoring: an Operative Tool to Evaluate Day-to-Day Tolerance and Effectiveness of Beta Blockers Therapy in Patients With Chronic Heart Failure.
Soccorso Capronnoli, Oreste Fiebo, Giampaolo Guzzonli, Angelo Capronnoli, Maria Teresa La Rovere, Marco Giennini, Andrea Mortara, Gianantonio Frins, Margherita Venti, Franco Cudobi. Fondazione S. Maugeri, Clinica delle Ematologie e Cardiologia O.R.C.S. Int.J. Scienze, Mesio di Montecarlo, Pavia(Pavia), Italy
Background: prediction of effectiveness and tolerance of treatment with beta-blockers in patients with chronic heart failure (CHF) have not been still identified. Recent data shown that baseline mitral flow and its variations after loading manipulations are a powerful prognostic marker in this population: Aims: to evaluate if mitral flow variables can predict the tolerance and the effectiveness of a chronic treatment with metoprolol in patients with CHF.
Methods: the mitral flow pattern (MFP) has been recorded by methodic echo-Doppler at baseline after intubation of intravenous of nitrate (1.5 mg intravenous/kg) and after passive leg lifting in 116 consecutive patients (82.9% male) with CHF (EF<50%). The clinical management of filtration dosage, therapeutic variations, interruption treatment, additional examinations and the hard cardiac events (sudden death and transplantation) in this population have been considered. According to the deceleration time (DT) of early diastolic filling of mitral flow after loading manipulations we identified the following MFP: G1 restrictive irreversible (DT>130 msec); G2 restrictive reversible(DT=130 msec); G3 non-restrictive stable (DT<130 msec). Results: G1 < G2 < G3 (p<0.05) & tab, MFP and NYHA functional class were significantly correlated to the complexity of the clinical management (r=0.04, p<0.00). The patients that had, or acquired a restrictive MFP after loading manipulations suffered a better number of cardiac events than those that had or acquired a non-restrictive MFP (18/2088% vs. 9/89 6%, p<0.001). Conclusions: In patients with CHF similar degree of sestol dysfunction, investigation a restrictive diastolic reserve are more frequently intolerant to treatment and manifest a small clinical benefit after beta-blockers therapy.

6168-70 Efficacy and Safety of Carvedilol in Severe Heart Failure Patients Accepted for Heart Transplantation
Christiane E. Angermann, Angelika Costerd-Jaekla, Mario C. Deng, for the EFICAT-Trial study group. Medical Clinic I (Heart) of the University, Munich, Germany.
Cardiothoracic Clinic of the Universitas Kiel, Muenster, Germany.
Background: Carvedilol has shown beneficial effects on mortality in NYHA class III-IV patients with congestive heart failure (CHF). This study was performed to determine effects of carvedilol in patients with end stage CHF accepted for transplantation (TX).
Methods: The study was designed as a double-blind, randomized, placebo-controlled trial and conducted in 3 German transplant centers. Study duration was 12 months. Patients accepted for TX with advanced left ventricular (LV) systolic dysfunction categorized as NYHA IV at least once since onset of CHF were eligible. The primary endpoint was the absolute change from baseline to last available LV ejection fraction (EF) measurement determined by radionucleotide ventriculography between Carvedilol and placebo. Results: The trial prospectively randomized 110 patients with GEF of ischemic (n=44) or non-ischemic (n=76) etiology, a mean ISMD (median) age of 53.9 (39.8) years, and a mean LVEF at baseline of 19.8 (6.8) [20.1]. Mean ISMD (median) absolute change of LVEF from baseline was +0.0 (+0.0) [0.0 to -0.0] in the Carvedilol group versus +0.7 (1.1) [0.0 to 4.0] in the placebo treated patients (p=0.088 [0.006, Wilcoxon, 2-sided) in the intention-to-treat population (n=74) and +8.2 (10.3) [+6.0% in Carvedilol versus +1.4 (7.9) [0.0% on placebo (p=0.01 [0.019, Wilcoxon, 3 sided) in the per protocol population (n=65). Serious adverse events were experienced by 33/60 patients (13 death) on placebo and 29/58 patients (9 deaths) on Carvedilol. Conclusions: Given in patients with end stage CHF accepted for TX pharmacological therapy may significantly improve cardiac function over a prolonged period of time. Carvedilol appears to be an appropriate and safe drug also in this severely ill population.

6168-71 The Prognostic Value of Peak Exercise Oxygen Consumption (VO2) Testing in Heart Failure Patients on Beta-Blockers
Background: in the early 1980s, studies showed that testing of peak oxygen consumption (VO2) in patients with heart failure (CHF) predicted outcome and aided in the timing of cardiac transplantation. However, these studies were performed before beta-adienergic blockers were shown to decrease mortality in the CHF patients and, hence, these drugs became widely used in this population. Moreover, since beta-blockers are known to affect heart rate and blood pressure and may cause fatigue, their effect on VO2 peak measurements and their prognostic value is not clear. Thus, the purpose of this study was to define the prognostic role of VO2 peak in predicting mortality in patients with CHF.
Methods: Patients from the heart failure/transplant clinic (N=279) who underwent VO2 peak testing from 5/1/93 to 9/1/90 were studied. A patient’s VO2 peak test date was either his/her first test ever (if never on beta-blockers) or the first test date after being started on beta-blockers. Patients were excluded if actual VO2 survival was unknown or if patients were taking a beta-blocker other than carvedilol or metoprolol.
Results: Of the 279 patients studied (age range 19-73 yrs), 59 died and 36 were transplanted. For sixty-three percent (N=120) were on beta-blockers at the time of their VO2 test. The mean VO2 peak of the patients who were still alive at the end of the follow-up period was significantly higher than in those who were not (p=0.001).

6168-72 Is There a Difference in Patient Comprehension of Acute and Chronic Clinical Cardiovascular Trials?
Rita Yavu, Kian Uzbil, Nomi Gordon, Ammon Merendorfer, Nadir Kacber, Bethark Barka, David A. Halon, Basil S. Lewis. Lady Davis Carmel Medical Center, Haifa, Israel.
Background: Despite attention to SCIP guidelines and concern for patient rights, little attention has been paid to pts role in viewing participation in randomized clinical trials. Pr comprehension may be different if recruited in an acute vs chronic medical situation.
Methods: We studied 70 consecutive pts participating in 8 clinical heart failure (CHF) trials. After (and 3-6mth later) of follow-up period, anonymous self-completed questionnaire was administered and analyzed. Findings were compared with those of 150 acute intervention (MI) pts who answered similar questionnaire after participation in the ISIS-4 study.
Results: Twelve (18%) of CHF trial pts reported little or no comprehension of the trial, while 38 (56%) believed they had partial and 18 (27%) full understanding of the trial. Findings were almost identical in MI trial pts (18%, 52%, 29%, H). In both CHF and MI pts, perceived comprehension was greater in those with a longer recollected duration of explanation (p=0.003, MI p<0.001). In CHF pts comprehension was greater in pts who had participated in a positive study (p=0.003). In neither group was comprehension related to recollected type of explanation (oral, written, both) or by whom explanation given (physician, nurse, both).
Relation between recollected duration of explanation and perceived comprehension

Abstracts - Cardiac Function and Heart Failure 179A
Background: Traditional risk factors fail to fully predict acute myocardial infarction (AMI). During exercise, in contrast to subjects without heart failure, some moderate heart failure patients showed a slight cTnl-release after symptom-limited exercise. Bicycle training at submaximal heart rate appears to be safe in terms of a cTnl-release.

Results: Comparison of % Increase with Exercise.

<table>
<thead>
<tr>
<th></th>
<th>Ischemia</th>
<th>No Ischemia</th>
<th>Unadj p-value</th>
<th>Adj age gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>cTnl (pg/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline max after E</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No HF (n=15)</td>
<td>10.9±10</td>
<td>40.0±14</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Moderate HF (n=10)</td>
<td>4.2±3.6</td>
<td>77.0±17</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Severe HF (n=5)</td>
<td>11.8±11</td>
<td>50.0±26</td>
<td>0.03</td>
<td></td>
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</tbody>
</table>

In moderate HF, cTnl exceeded 100 pg/ml at rest in 2, after E in 6 patients. After T, cTnl was increased only in this 2 patients who showed elevated cTnl already at rest. Conclusion: Exercise produced significant increase in cTnl. T and fibronogen both in subjects who did and did not develop ischaemia. These thrombomodulin(ADP)-induced and profibrinolytic (TPA) changes may provide a balance and explain why exercise rarely leads to thrombosis. However, the percent increase for TPA versus VWF was greater among subjects without ischaemia than those with ischaemia. Further prospective study is needed to determine whether an imbalance in the hemostatic response to exercise stress is predictive of AMI.
Methods: Randomly selected subjects (385 women & 298 men) in 4 age groups (50-59 (n=177); 60-69 (n=207); 70-79 (n=177); >80 years (n=122)) filled in a heart failure questionnaire, were examined clinically, had an electrocardiogram (ECG) and an echocardiogram (2-D and M mode echocardiography and plasma BNP measured with radioimmunoassay) for LVD were evaluated in a multiple regression analyses, where NT-proBNP, sex, systolic blood pressure, CREA and NECG came out as independent predictors of LVD. A high NT-proBNP concentration (95.6%) BNP 97.8%. A group of 301 individuals with evidence of left ventricular systolic dysfunction (LVEF) in a large age-controlled sample of the general population.

Results: Left ventricular dysfunction (LVD) was present in 11% of the subjects, defined as the single most powerful marker for LVD as well as for the clinical diagnosis of heart failure, and may reduce the need for echocardiography in some individuals.

Conclusion: The role of NT-proBNP in screening is likely to be to exclude L.V.S.D., so avoiding the need for echocardiography in some individuals.

N-Terminal Pro Brain Natriuretic Peptide Reduces the Need for Echocardiography in the Diagnosis of Heart Failure in the General Population

Roen A. Grooming, Ian Raymond, Frants Pedersen, Jens C. Nilsson, Matthais Boumann, Jurgen Trautwein, Per R. Hildebrandt, Department of Cardiology and Endocrinology, H:S Frederiksberg Hospital, University of Copenhagen, Copenhagen, Denmark, Integrared Health Care Solutions. F Hoffmann-La Roche Ltd., Basel, Switzerland

Background: The purpose of the study was to evaluate N-terminal pro brain natriuretic peptide (NT-proBNP) as a marker for heart failure and/or impaired left ventricular ejection fraction (LVEF) in a large age-controlled sample of the general population.

Methods: Randomly selected subjects (385 women & 298 men) in 4 age groups (50-59 (n=177); 60-69 (n=207); 70-79 (n=177); >80 years (n=122)) filled in a heart failure questionnaire, were examined clinically, had an electrocardiogram (ECG) and an echocardiogram (2-D and M mode echocardiography) and plasma levels of NT-proBNP and creatinine (CREA) were measured.

Results: Left ventricular dysfuntion (LVD) was present in 11% of the subjects, defined as LVEF 50% NT-proBNP and creatinine (CREA) came out as independent predictors of LVD.

Conclusion: The role of NT-proBNP in screening is likely to be to exclude L.V.S.D., so avoiding the need for echocardiography in some individuals.

A Type Natriuretic Peptide (BPN) Predicts Future Cardiovascular Events in Patients Presenting to the Emergency Department With Dyspnea

Alex T. Harrison, Padma Krishnasamy, Redzma Kazanegra, Quyen Dao, Alan Matsell, San Diego VA Health Care System. San Diego, CA, University of California San Diego (UCSD). San Diego, CA

Background: BNP is a natriuretic peptide secreted from the cardiac ventricle in response to volume expansion and pressure overload. We have recently demonstrated that these parameters are associated with left ventricular dysfunction (LVD), which is defined as a left ventricular ejection fraction (LVEF) of less than 50%.

Methods: In 325 patients presenting to the ED with dyspnea, BNP levels were determined. Patients were then followed for 6 months looking for the following endpoints: death, hospitalization, and readmission. The results of this study were compared to the previously published findings.

Results: The median L.V.E.F. was 50.7%. Based on a subgroup considered free from evidence of cardiovascular disease, L.V.E.F. was defined as an L.V.E.F. of 50% or less. This was found in 50 individuals (6.7%). Peptide concentrations were higher in individuals with L.V. systolic dysfunction than in individuals with normal L.V. function: N-ANP: 50.0 + 13.30 pg/ml. BNP: 15.0 + 13.30 pg/ml (p < 0.001). ROC curves (AOC) analysis yielded:

<table>
<thead>
<tr>
<th>Value (%)</th>
<th>Value (%)</th>
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<tbody>
<tr>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>BNP</td>
<td></td>
</tr>
<tr>
<td>480</td>
<td>585</td>
</tr>
<tr>
<td>210</td>
<td>76.6</td>
</tr>
<tr>
<td>58</td>
<td>59.4</td>
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</table>

Conclusion: BNP also distinguishes between etiologies of L.V.S.D. Patients who died from ischemic causes (N=26) had lower BNP values (1096 + 194 pg/mL) than those patients (N=18) who died of non-cardiac causes (127 + 31 pg/mL, p = 0.0001).

Sequencial Measurement of Natriuretic Peptides to Monitor Progression of Heart Failure

Tina Stenbæk, Ygul M. Pinto, Frans Boomsma, Dirk Jan van Weltens, University Hospital, Groningen, The Netherlands

Background: Early identification of chronic heart failure (CHF) patients at high risk for progression of CHF may allow for a change in strategy before symptoms ensue. Although it is known that elevated levels of N-terminal natriuretic peptides (NT-proBNP) are found in patients with CHF, it is unknown whether sequential N-proBNP measurement identifies patients at high risk for progression of heart failure.

Methods: We studied 280 patients with advanced CHF (NYHA functional class III-IV, mean left ventricular ejection fraction 0.22 (±0.07), NT-proBNP (mg/ml) was determined at baseline and after 1 and 3 months. Patients were stratified into 4 groups: 1) baseline NT-proBNP >1000 and subsequently increasing, 2) baseline NT-proBNP >1000 and subsequently decreasing, 3) baseline NT-proBNP <1000 and subsequently decreasing, and 4) baseline NT-proBNP <1000 and subsequently remaining constant.

Results: The highest risk ratios for progression of CHF (p=0.002, risk ratio 1.56 [1.88-16.47]) was found in patients with a high baseline NT-proBNP, who increased further, according to Cox proportional hazard’s model. This was independent of other baseline characteristics. Of all cases of worsening HF(123 cases), occurred in these patients. No significant increases of risk were observed in any of the other subgroups. Finally, patients in this group had the poorest survival outcome (figure, p=0.001, compared to the other groups).

Conclusion: A high and further increasing NT-proBNP powerfully predicts worsening of CHF, and predicts a poor outcome. Therefore, sequential NT-proBNP measurement could be of value to monitor CHF and to direct treatment.

Superiority of Plasma BNP to Echocardiography in Assessing the Impact of Therapy Upon NYHA Class in a Heart Failure Clinic

Shang-Chiu Lee, Sharon M. Sandberg, Denise M. Heublein, Susan M. Nelson, Margaret R. Paull, John C. Bumett, Mayo Clinic. Rochester

Background: BNP has recently been reported to serve as a guide for CHF therapy. It remains however uncertain if changes in plasma BNP correlate with symptoms following therapy. We compare the utility of plasma BNP to echocardiographic measurement of ejection fraction (EF) in assessing the impact of therapy upon NYHA classification.

Methods: Ninety-eight subjects with known heart failure (HF) were evaluated (56% NYHA I = 17; NYHA II = 38; NYHA III = 29; NYHA IV = 14). Baseline EF measured with 2-D and M mode echocardiography and plasma BNP measured with radioimmunoassay (Shionogi) were obtained. NYHA class was determined independently by attending HF specialists, who were blinded to the study. Forty-one subjects were reassessed during a 6-12 month follow-up period during which drug therapy was optimized by the attending HF specialists.

Results: Based on plasma BNP and EF correlated positively with NYHA class (correlation coefficient: r = 0.78), P = 0.00002, respectively. Plasma BNP was a more sensitive and specific marker for NYHA class when compared to EF by ROC analysis (area under ROC curve 0.90 vs. 0.73, respectively). At follow-up, only changes of BNP correlated to changes of NYHA class after optimizing therapy (P = 0.02) while changes in EF did not correlate (P = 0.78). When comparing the two visits, BNP decreased (45% +/- 12%, N = 14, P = 0.002) in subjects whose NYHA class improved while BNP remained unchanged (1% +/- 10%, N = 25, P = 0.95) in those whose NYHA class remained stable. In two patients whose NYHA class deteriorated, BNP tended to increase (+58% +/- 5%, N = 2, P = 0.008). There was no change in EF in subjects whose NYHA class remained unchanged (-40% +/- 22%, P = 0.09) and (414% +/- 7%, P = 0.05, respectively).

Conclusion: Further analysis, the absolute change in BNP in those who improved NYHA class was...
also greater than in patients whose NYHA class remained unchanged (-92.0 +/- 28 vs -61.8 +/- 29 mg/dL, P = 0.02). Conclusion: This investigation demonstrates the superiority of plasma BNP compared to EF by echocardiography in assessing the impact of therapy on New York Heart Association status.

837-3 Coronary and E Retard the Progression of Transplant Associated Coronary Arteriosclerosis-Impact of Baseline Endothelial Function
Domiok Behrendt, Marco Wannstein, Peter Gavr, Scott Kimley, James C. Fang, Brigham and Women’s Hospital, Boston, MA. Icahn School of Medicine, Brooklyn, NY
Background: In heart transplant patients, excessive vascular oxidative stress may predispose to transplant associated arteriopathy (TAxA). Endothelial dysfunction is associated with more rapid development of TXAA, but we have shown recently that treatment with anti-oxidant vitamins C and E retards progression of TXAA. Whether coronary endothelial dysfunction soon after transplantation determines the response to antioxidant vitamin therapy is unknown. Methods: in a double blind prospective study, 38 patients (2 years post cardiac transplantation) were randomized to combined treatment with vitamin C 500 mg tid and E 400 IU tid (n=19) or placebo (n=19) for 1 year. Coronary vasomotor responses to acetylcholine (ACh) and methacholine (MeACh) were evaluated in 56/60 to identify patients with normal (dilation to ACh) versus abnormal (contraction to ACh) endothelial function. The average intimal index obtained from 10 random sites during IVUS pullback was used as a primary endpoint to evaluate the progression of TXAA. Results: Over 1 year, intimal index increased 6.7+1.5% (p<0.001) in the vitamin group, but remained unchanged (2.4% ) in the vitamin group (p=0.001). In the placebo group, patients with abnormal endothelial function at baseline (n=12) demonstrated a greater increase in intimal index than patients with normal endothelial function (n=26) (11.1+1.0% vs 5.4% , p<0.05). In the vitamin group, intimal index remained unchanged in patients with both normal (n=6) and abnormal (n=12) endothelial function (1.0% and 1% , p=0.05 respectively). Conclusion: This preliminary study with antioxidant vitamins C and E retards the progression of transplant coronary arteriopathy. In the placebo group, endothelial dysfunction identifies patients who are at increased risk for TXAA. Antioxidant vitamin treatment prevented progression of TXAA especially in patients at high risk with endothelial dysfunction at baseline.

4:45 p.m.

837-4 Intimal Thickening One Year After Cardiac Transplantation to a Strong Predictor of Long Term Clinical Outcome: A Serial Intravascular Ultrasound Study
Ranish Sachar, Samir R. Kapadia, Khaled M. Zada, Navdeep Boparai, Luba Platt, Timothy Q. Crowe, Robert E. Hobbis, Steven E. Nissen, E. Murat Tuzcu, The Cleveland Clinic Foundation, Cleveland, OH
Background: Intravascular ultrasound (IVUS) is a sensitive method for evaluating atherosclerotic vascular disease after transplantation, but the ability of IVUS to predict long term clinical outcome remains uncertain. Methods: From 1992 to 1997, IVUS was performed after transplantation in 259 vessels in 143 patients (2.1+0.7 arteries/patient). Intimal thickness was measured at 2 time points, baseline (1.0+0.5 months) and 1 year (12.0+0.5 months). For each coronary segment, the sites with the minimum and maximum thickness were identified. Abnormal thickness was defined as >0.5 mm. Paired analysis of 1069 matched sites at 1 year measured the change in intimal thickness. Two criteria were identified; patients with "rapid progressive" vascular disease, defined as an increase in thickness >0.5mm at 1 year at any site, and patients with "minimal progression," no sites increasing >0.5 mm. Donor transplant arteriosclerosis was also assessed at baseline. Patients were followed for a composite endpoint of all cause mortality, new segmental left ventricular dysfunction, new Q-waves, and/or a fall in ejection fraction <30%.
Results: Ultrasound at 1 year demonstrated rapidly progressive vascular disease at one or more sites in 54/143 (37%). At a mean follow-up of 59+18 months (range 30-90), composite adverse outcomes occurred more frequently in the rapidly progressive group than the minimal thickness group (30% vs 17%, p=0.03). Although intimal thickness at 1 year was greater (1.6+0.5mm vs 0.8+0.3mm, p=0.002) in patients with "minimal progression," no sites increasing >0.5 mm, donor transplant arteriosclerosis was also assessed at baseline. Patients were followed for a composite endpoint of all cause mortality, new segmental left ventricular dysfunction, new Q-waves, and/or a fall in ejection fraction <30%.
Conclusions: Rapidly progressive transplant vascular disease, defined as >0.5mm increase in intimal thickness within the first year after transplantation, is a powerful predictor of adverse survival.

5:00 p.m.
formed immunofluorescent analysis of the transcription factors GATA4 and GATA6 and the growth factors BMP4 and BMP2 during murine cardiogenesis to ascertain which factors may be inductive and which were induced. GATA4 was detected first at day 6.0 p.c. cardiomyocytes by day 10.5 but by day 15.5, neither BMP2 nor BMP4 could be detected at no time could Nkd.5 be detected. We conclude that the formation of cardiomyocytes requires the ordered expression and induction of both growth factors and transcription factors, highlighted by the markers BMP2, BMP4, GATA4 and GATA6 that are carefully regulated both temporally and according to cell type during cardiac development. The expression of these processes by more numerous cells must be carefully considered if we are to render the cardiac phenotype via myogenic transformation after transplantation in damaged myocardium.

837-6 Successful Satellite Cells Grafting Following Myocardial Infarction in Rabbits

Alex Blatt, Dror Robinson, Zvi Nevo, Gad Cotter, Edo K&ski, ZVI Vered. Assaf Harohe Medical Center, Tzrifin, Israel, Tel-Aviv University, Tel-Aviv, Israel

Background: Cell grafting by mature skeletal myofiber, known as satellite cells, is a promising approach to prevent heart failure post myocardial infarction. We suggest a new experimental rabbit model utilizing a more physiological setting without sudden and persistent total main artery occlusion. Methods & Materials: 1- 14 Rabbits Cardiac Injury Model: New Zealand white rabbits, weighing 3.0 to 4.0 Kg were anesthetized with IV Pentobarbital. The heart was exposed via median sternotomy and the marginal sinus artery was ligated to 1.5 cm above the apex. 2- Skeletal Myoblast Isolation and Culture: Muscle pieces, which were left dry for attachment to vertical standing culture dish. After a 3 weeks the cells were expanded by 2-3 orders of magnitude. Cell's phenotype was characterized by immunofluorescence and by autoradiography. Results: ECG and echocardiography documented the presence of myocardial infarction. After sacrifice, in histological section macro and microscopic measurements were obtained. The results showed that the cell transplants consistently showed reduced infarct size and improved recovery of myocardial function. Conclusion: Satellite cells, can be successfully grafted and can be expanded in vitro, providing a possible new option for the treatment of myocardial infarction.

485 Beta-Blocker Therapy for Heart Failure: New Results

Tuesday, March 20, 2001, 8:30 a.m.-10:00 a.m. 
Orange County Convention Center, Room 230B

8:30 a.m.

Baseline and Three Month Change in Systemic Venous Norepinephrine as Predictors of Clinical Outcomes in the BEST Trial Investigators.

Michael R. Blustein, R. Zeldis. VIT Cooperative Clinical Trials Center, Palo Alto, CA, NHLBI, Bethesda, MD

The BEST (Biberlook Evaluation of Survival Trial) trial compared the third generation, non-selective beta blocker bisoprolol to placebo for the prevention of cardiovascular death and hospitalization for heart failure in 2,188 patients with left ventricular dysfunction. In BEST 2186 of the 2708 randomized subjects also had baseline systemic norepinephrine (NE) measurements performed by HPLC, and 1674 of these subjects had follow-up measurements after three months of treatment. Compared to placebo, bisoprolol lowered NE by 19% (p<0.01) at 3 months. In agreement with previous studies, baseline NE was a stronger predictor of mortality, with the low and high tertile groups having hazard ratios (HRs) plus 95% confidence intervals (CIs) compared to the intermediate group of 0.56 (0.38, 0.86) and 2.06 (1.70, 4.15) respectively. For change in NE, which in a large heart failure clinical trial has not previously evaluated as a predictor of outcome, a surprising nonlinear effect was observed. Compared to the intermediate or

845-4 Prospective Randomized Double-Blind Comparison of the Effects of Carvedilol Versus Metoprolol on Endothelial Dysfunction and Hemodynamic Parameters in Chronic Heart Failure

Nina Scherma, Christine Kieker, Sonnta Ertz, Stephan Gejhan, Carsten Waagstein, Ake Toft, Gerhard Schuler, Rainer Hambrecht. University of Leipzig - Heart Center GmbH, Leipzig, Germany

Background: Recent clinical trials have shown similar beneficial effects of metoprolol to carvedilol. In the SELECT study, carvedilol produced a greater than 30% increase in plasma endothelin compared to metoprolol. A possible explanation is that the relation between plasma endothelin and heart failure is adverse, which suggests that metoprolol is less harmful than carvedilol. Aims: To evaluate the effects of carvedilol and metoprolol on endothelial function and other parameters of chronic heart failure.

Methods: 84 patients with NYHA class II-IV, EF<40% and afterload reduced taking digoxin and diuretics were randomized in duplicate to receive either carvedilol or metoprolol therapy. Heart rate, blood pressure, NYHA class, 6-minute walking test and quality of life were assessed in all patients at months 0, 6, 12 and 18. Results: Carvedilol more significantly increased nitric oxide production, enhanced flow-mediated dilatation of the radial artery and reduced left ventricular mass compared to metoprolol. Conclusion: Carvedilol was more beneficial than metoprolol on endothelial function and left ventricular mass. Therefore, carvedilol is the preferred beta blocker in patients with chronic heart failure.
Prior Inhaled Beta Agonist Use Does Not Preclude Beta Blocker Therapy for Heart Failure


Background: The benefits of beta blockers in heart failure (HF) have been well established. Their use among patients with chronic obstructive pulmonary disease (COPD) has been limited because of concern that it might worsen chronic obstructive pulmonary disease. However, data from randomized controlled studies in heart failure are limited and do not address primary prophylaxis of heart failure in patients with chronic obstructive pulmonary disease.

Methods: We retrospectively evaluated 139 patients referred to our HF Treatment Program who had received beta blockers. We also evaluated the effect of beta blockers on exercise capacity and left ventricular function.

Results: Beta blockers were used in 102 patients, and 37 patients were followed up for >6 months. In patients treated with beta blockers, there was a significant improvement in exercise capacity (21.8 ± 12.4 vs. 25.6 ± 12.4 METs, p < 0.01). There was also a significant improvement in left ventricular ejection fraction (44.6 ± 10.8 vs. 48.5 ± 10.9%, p < 0.01).

Conclusion: The use of beta blockers in patients with chronic obstructive pulmonary disease and heart failure is associated with significant improvements in exercise capacity and left ventricular function.

Prepared by: John S. Golden, MD, Catherine C. Fairick, MD, Susan J. Mortkau, MD, Donna J. Matesk, MD, Sharon R. Josipson, MD, Mary C. Landford, MD, and Pamela P. Barnett, MD, Kaiser-Permanente Mid-Atlantic States, Fairlax, VA

9:45 a.m.
There were 26 high risk syndromes: age > 54, resting heart rate > 66, heart rate recovery < 4. An example of a low risk syndrome: age < 58, no resting ST-T abnormalities. Syndromes were derived on a training set of 4727 patients and validated on 4727 different patients. There were 85% high risk and 15% low risk syndromes selected in the training set. Results: In the validation data set (mean age 53, 78% male), 156 patients died over 6 years. At least one high risk syndrome was present in 991 patients (21%); 1 low risk syndrome in 774 (16%). One hundred and eighty (3.5%) abnormal heart rate recovery was strongly predictive of death (9% vs. 3%). Hazard ratio (HR) 3.9, 95% CI 2.6-5.2, P<0.0001; see Figure. After adjusting for age, gender, ejection fraction, evidence of ischemia, resting heart rate, exercise capacity, and standard risk factors an abnormal heart rate recovery remained strongly predictive of death (adjusted HR 1.9, 95% CI 1.4-2.6, P<0.0001). Conclusion: Even in the absence of a cool down period and even after accounting for ejection fraction, heart rate recovery is a powerful and independent predictor of death.

Heart rate recovery was defined as the difference between heart rate at end of the test and heart rate at rest. Heart rate recovery ≤ 18 beats per minute was considered abnormal. Results: The median heart rate recovery was 30 beats per minute (25th-75th percentiles 23 to 37). An abnormal heart rate recovery was noted in 805 patients (15%). There were 190 deaths (3.5%). An abnormal heart rate recovery was strongly predictive of death (9% vs. 3%). Hazard ratio (HR) 3.9, 95% CI 2.6-5.2, P<0.0001; see Figure. After adjusting for age, gender, ejection fraction, evidence of ischemia, resting heart rate, exercise capacity, and standard risk factors an abnormal heart rate recovery remained strongly predictive of death (adjusted HR 1.9, 95% CI 1.4-2.6, P<0.0001). Conclusion: Even in the absence of a cool down period and even after accounting for ejection fraction, heart rate recovery is a powerful and independent predictor of death.

Stress echocardiography predicts mortality. Methods: Consecutive patients (N=5785, mean age 56±12, 37% female) who underwent stress echocardiography and who did not have heart failure, valve disease, atrial fibrillation or pacemakers, were followed for 5 years. Heart rate recovery was defined as the difference between heart rate at peak exercise and 1 minute later, based on maximization of the log-odds via square statistic. A heart rate recovery < 18 beats per minute was considered abnormal. Results: The median heart rate recovery was 30 beats per minute (25th-75th percentiles 23 to 37). An abnormal heart rate recovery was noted in 805 patients (15%). There were 190 deaths (3.5%). An abnormal heart rate recovery was strongly predictive of death (9% vs. 3%). Hazard ratio (HR) 3.9, 95% CI 2.6-5.2, P<0.0001; see Figure. After adjusting for age, gender, ejection fraction, evidence of ischemia, resting heart rate, exercise capacity, and standard risk factors an abnormal heart rate recovery remained strongly predictive of death (adjusted HR 1.9, 95% CI 1.4-2.6, P<0.0001). Conclusion: Even in the absence of a cool down period and even after accounting for ejection fraction, heart rate recovery is a powerful and independent predictor of death.

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POSTER SESSION

1197 Cellular and Molecular Mechanisms Causing Heart Failure I
Tuesday, March 20, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 9:00 a.m.-10:00 a.m.

1197-43 Microvascular Integrity Contributes to the Myocardial Remodeling in Pressure Overloaded LV Hypertrophy Following Aortic Banding
Peter Liu, Phyu M. Daukaz, Wenyu Yu, M.D., Joel W. Sedl, Ph.D., Jean L. Moullecue, Dumas J. Stewart. Heart & Stroke/Richard Lewar Centre of Excellence, Toronto, ON, Canada
We have previously demonstrated the presence of microvascular insufficiency (MVI) in cardiomyopathies, and its impact in LV remodeling post myocardial infarction in the rat model. To understand why patients with microvascular diseases such as diabetes or hypertension are prone to heart failure, and to determine how microvascular angiopathy may contribute to the remodeling process in pressure overload hypertrophy, we studied a rat model of aortic banding (AoBd) with or without microvascular angiopathy. Rats (n=21) were randomized to coronary endothelium denudation with intra-arterial ultra low dose Triton-x (0.01%) and temporary aortic occlusion or placebo, and were subjected to individually calibrated aortic banding or sham controls. At 35 days post banding, the animals underwent determinations of in vivo Millar LV systolic pressures (LVP, in mmHg) and perfusion fixed analysis of LV wall thickness (WTh), myocardial cavity area (A, mm²). The results showed (Mean±SEM): p<0.05 vs. Sham and p<0.05 vs AoBd alone)

<table>
<thead>
<tr>
<th>Group</th>
<th>LVP (mmHg)</th>
<th>WTh (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sham</td>
<td>128±15</td>
<td>2.0±0.2</td>
</tr>
<tr>
<td>AoBd</td>
<td>214±64*</td>
<td>2.6±0.3</td>
</tr>
<tr>
<td>Triton-AoBd</td>
<td>189±31.1</td>
<td>2.1±0.2</td>
</tr>
</tbody>
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The Triton treated hearts were more dilated, with thin walls, and showed severe MVI with complete absence of von Willebrand staining, and also had a significantly higher 35 day mortality (0%) vs. without Triton treatment (50%).

We conclude that microvascular dysfunctions contributes to adverse remodeling in pressure overload hypertrophy by inducing LV diastolic dysfunction, decreased wall thickness, increased LV dilatation and mortality. Thus, microvascular angiopathy may contribute to the adverse cardiac remodeling and rapid progression to heart failure following pressure induced hypertrophy.

1197-44 A Polymorphism of the Endothelial Nitric Oxide Synthase Gene Is Associated with Increased Sympathetic Drive in Patients With Congestive Heart Failure
Philip R. Binkley, Ywen Liu-Stratton, Patty S. Halton, Glen Cooke. The Ohio State University, Columbus, OH
Background: Dysregulation of nitric oxide (NO) synthesis is thought to be a determinant of the arrhythmic substrate typical for patients with CHF. A thymidine (T) to cytosine (C) transi-
tion of TGF-β1 promoter polymorphism. Supine electrocardiographic recordings obtained in each subject were analyzed using computer-based techniques (10, 15, 30, 45, 60 mins).

Methods: 21 patients having CHF underwent genotyping for the C/T allele of the eNOS 4a promoter polymorphism. Supine electrometric chronometric recordings obtained in each subject were submitted to special analysis of HRV.

Results: No differences in HRV were noted between patients homozygous for the T allele (TT, n=15) or heterozygous for the T and C alleles (CT, n=6). These patients were grouped together (TT/CT) and compared to the CC homozygous patients (n=6). CC patients were found to have significantly higher sympathetic drive as reflected by an increase in low frequency HRV (p<0.05 vs. 107 heart/min² vs. 107 heart/min²) and a decrease in high frequency HRV (p<0.05 vs. 107 heart/min² vs. 107 heart/min²).

Conclusions: Myocytes from pressure overloaded human myocardium exhibit a loss of CB number and a decrease in CB turnover in the setting of LV hypertrophy. These findings are consistent with the hypothesis that decreases in CB number and a decrease in CB turnover in the setting of LV hypertrophy.
Poster Session C

1198 Cardiomyopathy: The Microcirculation and Other Aspects

Tuesday, March 20, 2001, 9:00 a.m.-10:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 9:00 a.m.-10:00 a.m.

1198-45 Renin-Angiotensin-Aldosterone System Gene Polymorphisms as Predictors of Improvement in Systolic Performance in Dilated Cardiomyopathy

A Tiago, O Skudicky, A Woodwars, GP Candy, R Brooksbank, K Sliwa, P Sareli, GR Norton. Dept Cardiology: Baragwanath Hospital, PO Bertsham, Johannesburg 2013, South Africa; 2 Dept Physiology University of the Witwatersrand, Johannesburg, South Africa, and 3 Dept Cardiology, Bangor Hospital, PO, Bangor, Gwynedd, Ym Moch, 29, Wales, UK

Introduction. Reproducible markers are required to predict the variable improvement in cardiac function that occurs in patients in heart failure on medical therapy. We evaluated whether genetic polymorphisms of the renin-angiotensin-aldosterone (RAA) system predict improvement in left ventricular systolic function subsequent to medical therapy in patients with idiopathic dilated cardiomyopathy. Materials and Methods. 107 Black patients with IDC had LV ejection fraction (EF) determined using nuclear radionuclide ventriculography prior to, and subsequent to initiating furosemide, digoxin and angiotensin-converting enzyme inhibitor (ACE) therapy. The patients were genotyped for the ACE gene insertion/deletion (I/D) polymorphism, the M235T variant of the angiotensinogen (AGT) gene and the C-344T polymorphism of the aldosterone synthetase (CYP11B2) gene. Results. Prior to initiating medical therapy, the I/D polymorphism of the ACE gene was associated with smaller increase in LV EF (p=0.04). Moreover, the 344T allele of the CYP11B2 gene was associated with a smaller increase in LV EF approximately 6 months (r=0.03, p=0.04), 2 years (r=0.05; p=0.02), 2.5 years (r=0.05; p=0.005), and when considering the final LV EF in all patients evaluated (r=0.17; p=0.001), subsequent to initiating medical therapy. Neither the ACE, nor AGT gene variants examined were associated with change in LV EF. Conclusion. The CYP11B2 gene variant is a strong predictor of improvement in systolic performance following medical therapy in patients with IDC.

1198-47 Differentiation Between Ischemic and Non-Ischemic Dilated Cardiomyopathy Based on Left Atrioventricular Plane Displacement During Dobutamine Echocardiography

Konstadina P. Doulik, Theodoros Kallahan, Konstadinos Kosloupoulos, Georgios Tsami, Loukanos Rallidis, Kyriakos Poulopoulos, Takis Xydas, Thomas Apostolou, Evaggelos Stylianou, Nikolas Koutoukidis, Nikos Gkoul, Greece

Background: Previous reports have shown that recording of left atrioventricular plane displacement (LAVPD) during stress echocardiography accurately identifies coronary artery disease in patients without dilated cardiomyopathy (DCM). In the present study we estimated the response of LAVPD during dobutamine echocardiography in patients with DCM and we evaluated the ability of this parameter to identify the ischemic or non-ischemic origin of the disease.

Methods. Forty-seven patients with at least moderate left ventricular dysfunction of ischemic origin and 10 aged-matched healthy volunteers underwent stress echocardiography. The LAVPD was measured at baseline and after low (5-10 mg/Kg/min) and peak doses (0.05-0.1 mg/Kg/min) of dobutamine. All the 47 patients underwent coronary angiography and according to the results they were divided into two groups (ICM group; 25 patients with ischemic cardiomyopathy, 22 patients with non-ischemic cardiomyopathy).

Results. The two groups of patients had similar baseline characteristics. The LAVPD showed significant increases at PD of dobutamine, in ICM group (23.6±1.8mm) and in non-ICM group (22.2±1.7mm), but not in ICM group (2.7±0.1mm).

Conclusion: Assessment of LAVPD during dobutamine echocardiography offers a simple, rapid and accurate non-invasive method for differentiation between ischemic and non-ischemic DCM.

1198-48 Regional Myocardial Flow-Metabolism Relationship in Patients With Idiopathic Dilated Cardiomyopathy

Danilo Neglia, Cecilia Manni, Elena Testa, Oreste Scorsone, Piero Salvadori, Gianmaria Sambuceti, Oberdan Parodi, Antonio L’Abbate. CNR Institute of Clinical Physiology, Pisa, Italy

Background: In patients with idiopathic dilated cardiomyopathy a depressed myocardial blood flow (MBF) either at rest and during pharmacological vasodilatation has been demonstrated. The relationship between regional myocardial flow and myocardial metabolic rate of glucose has not yet been extensively evaluated. Methods: We studied 40 patients (30 males, mean age 58±10 years, LV EF 25±7%) using positron emission tomography with nitrogen-13 ammonia to quantitate regional flow (MBF, at rest and during dobutamine stress) and fluorine-18 fluorodeoxyglucose (FDG) injected, after a glucose meal, within 30’ from i.v. dipyridamole. This protocol was chosen to enhance regional differences in flow and metabolism. Two patients died (one with ischemic myocardial FDG activity and were excluded from analysis. Regional percentage profiles of dipyridamole MBF and of FDG activity were obtained. The percentage of percentage profiles allowing to recognize mismatch (MBF%>90% and FDG%<50%) or match regions (MBF%<90% and FDG%>50%). Results: Out of the 238 segments analyzed, a mismatch was present in 40% (201 segments), in 30% (176 segments) and in 15% (96 segments) of the normal pattern in 126 (55%). As compared with normal regions, mismatch segments showed a similar resting MBF (0.00±0.02 vs. 0.02±0.23 mlimin/lg, ns) and a more significant increase at PD of dobutamine, in NI-DCM group (2.3±0.8 mm) and in ICM class (2.5±0.9 mm). Conclusion: Regional myocardial flow-metabolism mismatch or match patterns are frequent in patients with idiopathic dilated cardiomyopathy. These results suggest the existence of regional myocardial ischemia and depressed viability in these patients.

1198-49 Isolated Ventricular Non - Compaction is Associated With Coronary Microvascular Dysfunction

Philipp A. Kaufmann, Christoph A. Wyss, Erwin Oechslin, Rolf Jennis. Cardiac Care Center, University Hospital, Zurich, Switzerland

Background: Although in isolated ventricular non-compaction (IVNC) the characteristic features (two-layered structure with uniform tissue and a much thicker endocardial layer of trabecular meshwork) are predominantly found in the apical and the midventricular segments, hypokinesia may not entirely be confined to these segments resulting in a decreased global ejection fraction (EF). We studied whether a global microcirculatory dysfunction underlying the IVNC could contribute to explain these discrepancies. Methods: Myocardial blood flow (MBF, mlimin/lg) was measured in 10 patients with IVNC and in 11 volunteers at rest and after adenosine (Ado, 0.14 mg/kg/min over 7 min) and dipyridamole (0.56 mg/kg in 4'). Regional coronary flow reserve (CFR) was calculated as Ado/resting for the apex as well as for 4 (septal, anterior, lateral and inferior) midventricular and basal segments. The CFR values and the status of perfusion scans were compared to the echocardiographic findings (wall motion abnormality, trabeculation) in each segment. Results: In some of the volunteers a defect at the site of dipyridamole-induced CFR was found. A CFR<2 was found in 39% of the 12 segments with normal wall motion but in 70% of the IVNC patients (p<0.05). Conclusion: Global microcirculatory dysfunction underlying IVNC is associated with impaired coronary flow reserve. Thus, IVNC is a marker of impaired coronary microcirculatory function and may contribute to explain discrepancies in IVNC patients.

1198-50 Abnormal Coronary Blood Flow Reserve in Idiopathic Dilated Cardiomyopathy Is Due to Impairment of Both Endothelium-Dependent and Independent Microcirculatory Vasodilatation

Mehran Canetti, Amir Lerman, Ilyes S. Karsaia, Waseem Al Attar, Antarikumar Mehta, Uri Eikamay. LA County University of Southern California Medical Center, Los Angeles, CA. Mayo Clinic, Rochester, MN

Background: Studies in a limited number of patients with new onset nonischemic cardiomyopathy have demonstrated impaired endothelium-dependent coronary vasodilation but suggested preserved endothelium-independent vasodilatation. The purpose of this study was to evaluate mechanisms of impaired coronary vasodilatory capacity in a large number of patients with chronic advanced heart failure due to nonischemic cardiomypathy.

Methods: We studied endothelium-dependent (during intracoronary infusion of 10-4 to 10-8 M of acetylcholine) and endothelium-independent (after administration of 18.98 mcg of dipyridamole) coronary blood flow reserve and calculated changes in coronary microvascular resistance in 25 patients with nonischemic, dilated cardiomyopathy and 25 patients with normal coronary flow, nonobstructive coronary artery disease who were studied for chest pain and were matched by age, gender and serum cholesterol level.

Conclusion: Assessment of LAVPD during dobutamine echocardiography offers a simple, rapid and accurate non-invasive method for differentiation between ischemic and non-ischemic DCM.
.transfer function technique is a well accepted technique for measuring baroreflexes. By using this technique, BRS and phase shift can be calculated. This phase shift indicates graft rejections were detected in the present study group. After HTX, BRS increased from the first year (mean 5*4 months) and second year (mean 20r4 months) after HTX. The response to variations in blood pressure. After cardiac transplantation (HTX) the heart is Background: Baroreflex sensitivity (BRS) measures modulations of heart rate in occurrences remains a matter of debate. We hypothesized that increased BRS reflects auto-

Results: In both sexes and all age groups peak oxygen consumption and workload, sig-

Conclusions: Peak VO₂ is not as predictive of survival in heart failure patients treated chronically with B-blockade. Further studies involving more patients are needed to evalu-

Associated with better survival, compared with non-transplanted patients. In the operated group, as the most severe patients, who die rapidly, were not given the opportunity to be operated on. Methods: We analyzed data from a large cohort of patients (389) put under cardiac transplantation and death. We identified 135 patients meeting the inclusion criteria: (LV Ejection Fraction = 21% ± 9%, Age 53 ± 12, 75%, male) who were initiated on B-blockade between May 1986 and November 1996. Of these, 12 died and 13 were transplanted. Average follow up was 2.4 years. There were 115 patients with peak VO₂ > 14 cc/kg/min and 20 patients with a peak VO₂ ≤ 14 cc/kg/min. Kaplan-Meier curves were not significantly different between groups. Progression of 3 year survival without transplant was worse for patients with peak VO₂ ≤ 14 and 69% in patients with peak VO₂ > 14 (p=0.72).

Conclusion: Peak VO₂ is as predictive of survival in heart failure patients treated chronically with B-blockade. Further studies involving more patients are necessary to evaluate the role of metabolic testing in prognosis.

Baroreflex Sensitivity is a Powerful Tool to Monitor Cardiac Reinnervation After Orthotopic Cardiac Transplantation in Man

G. Tjardesma, Joop D. Lefteroom, John Brugmans, Dirk Jan van Vedelshausen. University Hospital, Groningen, The Netherlands

Background: Baroreflex sensitivity (BRS) measures modulations of heart rate in response to variations in blood pressure. After cardiac transplantation (HTX) the heart is completely denervated and a result, BRS is absent. Whether or not reinnervation occurs remains a matter of debate. We hypothesized that increased BRS reflects autonomic reinnervation after HTX. Methods: Six patients (age 54±6 years) were studied in the first year (mean 5±4 months) and second year (mean 20±4 months) after HTX. The transfer function technique is a well accepted technique for measuring baroreflexes. By using this technique, BRS and phase shift can be calculated. This phase shift indicates whether blood pressure variation is followed by a subsequent change in heart rate and is normally negative. Phase shift was calculated in both periods for all patients. Results: No graft rejections were detected in the present study group. After HTX, BRS increased from 0.5±0.3 (first year) to 2.4±1.3 (second year), p<0.03 (Figure). Phasic tone was positive in 4/5 patients in the first year, however became negative in 5/6 patients 2 years after HTX, indicating a response of heart rate after a change in blood pressure. Conclusions: Our results provide new evidence for the occurrence of reinnervation after HTX as demonstrated by enhanced BRS and a change in phase shift. This change in phase shift indicates that, 2 years after HTX, variations in blood pressure can induce a baroreflex mediated heart rate response.
ABSTRACTS - Cardiac Function and Heart Failure

1201-01 Decreased IL-6 Concentrations as a Marker of Successful Treatment in Patients with Chronic Heart Failure


Background: Chronic heart failure is characterized by persistent immune activation. It has been demonstrated that interleukin-6 (IL-6) is induced via activation of the renin angiotensin system and that ACE inhibitors may result in a significant reduction of IL-6 concentrations. However, the effect of an additional beta-adrenergic blockade (BB) on IL-6 levels in chronic heart failure remains unclear.

Methods: Twenty-one patients with stable chronic heart failure (NYHA class II-III, ejection fraction <40%, mean age 76.3±12.4 years) were included in a prospective, randomized, double-blind, placebo-controlled study. Patients were randomized to receive either placebo or BB (metoprolol) for 12 months. IL-6 concentrations were measured at baseline and after 3 months.

Results: Baseline IL-6 concentrations were significantly higher in the placebo group compared to the BB group (10.6±5.3 vs. 4.4±1.8 pg/ml, p=0.01). After 3 months, IL-6 concentrations were significantly lower in the BB group compared to the placebo group (4.4±1.8 vs. 10.6±5.3 pg/ml, p=0.01), suggesting an inhibition of the renin angiotensin system. In chronic heart failure prior to BB, IL-6 levels were markedly elevated (6.7±3.9 pg/ml in healthy controls vs. 4.4±1.8 pg/ml in chronic heart failure patients).

Conclusion: In patients with chronic heart failure additional administration of beta-receptor blocker may result in a significant reduction of IL-6 concentrations and may improve clinical outcome.

1201-02 Tropomin I Release Pattern and Myocardial Dysfunction After High-Dose Chemotherapy

Domenico Cardinale, Maria Teresa Sandri, Alessandro Martinetti, Alyson Thor, Elena Borghi, Maurizio Creviti, Giuseppe Lamanita, Giovanni Martinelli, Cesare Fiorentini, Carlo M. Gipillo. Istituto Europeo di Oncologia, Milan, Italy

Background: We previously demonstrated that, in patients with aggressive malignancies, even minimal elevation of troponin I (TnI) after high-dose chemotherapy (HDC), is associated with long-term left ventricular systolic dysfunction. However, the time course of the subclinical myocardial damage, as well as the acuity of TnI to determine risk and low-risk groups for development of investigation-driven therapeutic and management pathways, have not been fully elucidated. Methods: In 125 cancer patients (29 men, 96 women; mean age 48±11 years) undergoing HDC, we measured TnI serum concentration using an immunoenzymometric assay (Stratus II, Dade). TnI positivity (+) was considered when values exceeded the >0.4 ng/ml threshold. Samples were obtained soon after HDC treatment (early TnI) and 3 months later (late TnI). Left ventricular ejection fraction (EF) was evaluated by echocardiography before (T1) and 3 (T3) and 7 (T7) months after HDC. Patients were grouped according to TnI results: Group 1: both early and late TnI were >0.4 ng/ml, Group 2: both early and late TnI were normal, Group 3: normal TnI and late TnI were >0.4 ng/ml. Results: We found a significant association between TnI levels and left ventricular systolic dysfunction (Table). The incidence of left ventricular systolic dysfunction was 61.4% among patients with >0.4 ng/ml TnI levels at the time of chemotherapy administration or at 3 months after chemotherapy completion, while only 8.1% of Group 1 patients had left ventricular systolic dysfunction at T7. Conclusion: TnI positivity after HDC predicts a higher incidence of left ventricular systolic dysfunction.
**1201-04 Relationship between interleukin-6 spillover in the lungs and Pulmonary Vascular Resistance in Patients With Congestive Heart Failure**

Nakio Machibe, Takayoshi Tsutamoto, Atsuyuki Wada, Koie Masato, Masaru Hayashi, Takashi Tsutui, Masahito Onoishi, Masahide Sawai, Masanori Fujii, Takemori Matsumoto, Takashi Yamamoto. Gifu University of Medical Sciences, Otsu, Japan.

**Background:** Plasma interleukin-6 (IL-6) levels have been reported to increase in patients with congestive heart failure (CHF) especially in pulmonary hypertension, whether it is produced in pulmonary circulation and the relation between the IL-6 spillover and the pulmonary vascular resistance (PVR) in patients with CHF remain unknown. **Method:** We measured plasma levels of IL-6 and cyclic guanosine monophosphate (cGMP), a second messenger of nitric oxide which stimulate soluble guanylate cyclase. In the main pulmonary artery (PA) and pulmonary capillary wedge region (PC) in consecutive 50 CHF patients and 9 age-matched normal subjects. **Results:** Plasma IL-6 concentrations were significantly higher from PA to PC both in normal subjects and patients with CHF (Normal: PA, 1.0±0.1; PC, 1.2±0.2 pg/ml, mild CHF (NYHA II): PA, 2.2±0.3; PC, 2.7±0.3 pg/ml, severe CHF (NYHA III/IV): PA, 4.6±1.0; PC, 5.7±1.2 pg/ml.). IL-6 spillover in the lung ([P-PA/2]*100%) was elevated in patients with severe CHF compared with normal subjects and mild CHF patients (Normal: 0.5±0.3%, mild CHF: 1.2±0.2%, severe CHF: 3.0±0.6 ng/ml). There was a significant positive correlation between the IL-6 spillover in the lung and PVR (r=0.450, p<0.001), and cGMP production in the lung (r=0.492, p<0.0001). Among the hemodynamic variables, age, sex, and cause of heart failure were all significantly different between the four groups. **Conclusion:** We observed that the IL-6 spillover in the lungs of patients with severe CHF was significantly increased compared with normal controls and patients with mild CHF. Such findings suggest that chronic exposure to circulating endotoxin may be a trigger of inflammatory immune activation seen in these patients. The predictive power of EndoCAb IgM levels on mortality and morbidity in CHF patients warrants further investigation.

**1201-06 Endotoxin and Severity of Chronic Heart Failure**

Mathias Rauchhauer, Wolfram Doehner, Alcin Bizaker, Rainer Shaheem, Andreas, Konstanz, Michael Kemp, Andreas J. Coats, Stefan D. Anker. NHU. Clinical Cardiology, London, United Kingdom, Marin-Luther-Universität Halle-Wittenberg, Klinik für innere Medizin III, Halle/Bayreuth, Germany.

**Background:** Bacterial lipopolysaccharide (LPS, endotoxin), via bacterial translocation across the intestinum, has been suggested to trigger inflammatory immune activation in heart failure. We hypothesized that the plasma levels of bacterial lipopolysaccharide may be related to the severity of CHF and may in part explain the exaggerated inflammatory immune activation seen in these patients. **Methods:** We consecutively enrolled 120 patients with congestive heart failure especially in pulmonary hypertension, whether it is produced in pulmonary circulation and the relation between the IL-6 spillover and the pulmonary vascular resistance (PVR) in patients with CHF remain unknown. **Results:** We measured plasma levels of IL-6 and cyclic guanosine monophosphate (cGMP), a second messenger of nitric oxide which stimulate soluble guanylate cyclase. In the main pulmonary artery (PA) and pulmonary capillary wedge region (PC) in consecutive 50 CHF patients and 9 age-matched normal subjects. **Conclusion:** Plasma IL-6 concentrations were significantly higher from PA to PC both in normal subjects and patients with CHF (Normal: PA, 1.0±0.1; PC, 1.2±0.2 pg/ml, mild CHF (NYHA II): PA, 2.2±0.3; PC, 2.7±0.3 pg/ml, severe CHF (NYHA III/IV): PA, 4.6±1.0; PC, 5.7±1.2 pg/ml.). IL-6 spillover in the lung ([P-PA/2]*100%) was elevated in patients with severe CHF compared with normal subjects and mild CHF patients (Normal: 0.5±0.3%, mild CHF: 1.2±0.2%, severe CHF: 3.0±0.6 ng/ml). There was a significant positive correlation between the IL-6 spillover in the lung and PVR (r=0.450, p<0.001), and cGMP production in the lung (r=0.492, p<0.0001). Among the hemodynamic variables, age, sex, and cause of heart failure were all significantly different between the four groups. **Conclusion:** We observed that the IL-6 spillover in the lungs of patients with severe CHF was significantly increased compared with normal controls and patients with mild CHF. Such findings suggest that chronic exposure to circulating endotoxin may be a trigger of inflammatory immune activation seen in these patients. The predictive power of EndoCAb IgM levels on mortality and morbidity in CHF patients warrants further investigation.

**1201-07 High Tumor Necrosis Factor Factor Levels Are Associated With Exercise Intolerance and Neurohumoral Activation in Chronic Heart Failure Patients**


**Background:** Exercise activation plays an important role in the progression of chronic heart failure (CHF), however little evidence is available of the associations of psychosocial factors and the local immune system with exercise intolerance in these patients. **Methods:** We measured TNF levels in 107 heart failure patients (II 33, III 26, IV 48) using an enzyme-linked immunoassay and HLA-DQ genotyping with PCR. Left ventricular ejection fraction (LVEF) was assessed echocardiographically. **Results:** TNF levels were elevated in CHF patients compared with age and sex-matched normal subjects (8.9±4.8 vs. 3.1±1.8 pg/ml, r=0.53, p<0.01). There were no differences in any heart failure group (II 23.7±4.2, III 23.8±5.0, IV 10.7±4.9 pg/ml) versus the control group (21.4±4.2 pg/ml) or between CHF groups. EndoCAb IgM levels, however, were significantly higher in NYHA class IV patients (54.4±1.6 vs. all other groups (controls 11.2±1.5; p<0.001, II 11.2±1.5; p<0.001, III 7.2±1.3; p<0.001). **Conclusion:** In patients with severe CHF low levels of EndoCAb IgM antibody may reflect consumption of these antibodies due to chronic exposure to circulating endotoxin. This phenomenon may in part explain the exaggerated inflammatory immune activation seen in these patients. The predictive power of EndoCAb IgM levels on mortality and morbidity in CHF patients warrants further investigation.
The HLA-DQBI gene was found in 22% of Group II but in none of Group I patients. Furthermore, there was an inverse correlation between the presence of histidine at position 50 and the levels of serum proctolin. Both sII-2R levels, a marker of T-cell activation, and the levels of serum protein, both sII-2R levels, a marker of T-cell activation, and the levels of serum protein, were significantly lower in Group II compared to Group I (25.4% and 68.0±5mm, respectively, p<0.01) patients. Conclusion: Hyperprolactinemia presents in 25% of patients with CHF and may reflect decreased activation of T-lymphocytes associated with relatively preserved LV systolic function under immune-genetic control at the HLA-DQ locus.

**Methods:** The study group consisted of 53 pts with CHF (LVEF 25.1±4%, age 56.6±9.2 years, NYHA-class II/III/IV: 6/9/1, peak VO2 18.0±2.5 ml/kg/min). Pts with CHF were subclassified in regard to V02max of more or less than 14 ml/kg/min. Results: We confirmed overactive CS in CHF (peripheral CS: 0.71±0.38L/min/1% SaO2, p<0.05). There was a significant correlation between plasma oxLDL and NYHA functional class (r=0.367, p=0.0019). To evaluate the relation between plasma oxLDL and progression of CHF, we followed 75 pts with CHF for 1 year. oxLDL group (oxLDL > 11.8 unit/ml, n=38) compared with a low oxLDL group (oxLDL < 11.8 unit/ml, n=37). Plasma oxLDL was significantly decreased after administration of carvedilol (p<0.05). Conclusion: These results indicate that plasma oxLDL level is a useful marker of oxidative stress in patients with CHF and may assist in the prediction of the progression of CHF.

**Results:** Released TNP levels (p<0.01) and TNFα (p<0.05) were significantly lower in Group II compared to Group I (TNFα 1.7±1.1 vs 2.6±1.2 pg/ml, p<0.05). Conclusion: There was a significant correlation between plasma oxLDL and NYHA functional class (r=0.367, p=0.0019). There was a significant negative correlation between plasma oxLDL and EF (r=-0.367, p=0.0019). To evaluate the relation between plasma oxLDL and progression of CHF, we followed 75 pts with CHF for 1 year. oxLDL group (oxLDL > 11.8 unit/ml, n=38) compared with a low oxLDL group (oxLDL < 11.8 unit/ml, n=37). Plasma oxLDL was significantly decreased after administration of carvedilol (p<0.05). Conclusion: These results indicate that plasma oxLDL level is a useful marker of oxidative stress in patients with CHF and may assist in the prediction of the progression of CHF.
Endomyocardial Cardiac Gene Expression and LV-Mass Index in Patients With Idiopathic Dilated Cardiomyopathy

Marc Vanderheyden, Georg Baumgarten, Douglas Mann, Walter J. Paulus
Cardiovascular Center, OLV Ziekenhuis, Aalst, Belgium, Baylor College of Medicine, Houston, TX

The in vivo functional significance of pro-inflammatory cytokines for the failing human left ventricle (LV) remains underestimated. The present study investigated the relation between endomyocardial gene expression of TNF-a, IL-6 and IL-1b and LV function parameters in patients with non-ischemic dilated cardiomyopathy (DCM) and varying degrees of LV dysfunction. LV microtubus pressures, angiographic volumes, echocardiographic wall thickness and snap-frozen LV endomyocardial biopsies were obtained in 10 patients referred for diagnosis of left-sided heart catheterization. Intensity of LV endomyocardial-TNF-a, IL-6 and LV-1b gene expression was determined using quantitative RT-PCR. IL-6 and TNF-a were closely linked (r = 0.845; p = 0.002). TNF-a correlated with LV mass index and LV wall thickening (r = 0.938; p = 0.012). This correlation improved when TNF-a was normalized for LV mass. TNF-a/LVEF also significantly correlated with LV systolic wall stress (r = 0.875; p = 0.001). Similar correlations were noted for IL-6 and IL-1b with LV mass index.

LV mass index increased in LVNC subjects in the ligation group when compared to shams showed %MI= 49.4±6.6%, reduced %FS (p < 0.05) at 1 week after the operation. TNF-a was not only present in the donor heart. This unique transient cardiac dysfunction of the recipient hearts was significant reversed by treatment of the MI animals with chimeric TNF-a soluble receptor (IL-6 sR), which was measured from EDTA treated plasma samples by ELISA, for comparison with 9 non-cardiac subjects.

Conclusion: The findings were apparently unrelated to age, gender or obesity. While the origin for early LV dysfunction and heart failure is presumably multifactorial, elevated levels of circulating proinflammatory cytokines may contribute to the pathogenesis of LV dysfunction. Enhanced TNF-a receptor levels in hypertensives may be sufficient to limit activity of the cytokine. Conversely, IL-6 increased occurred without an increase in circulating receptor activity of this cytokine may predominate. IL-6 can downregulate sarcoplasmic reticulum calcium ATPase (SERCA2a) gene expression and protein levels (Villegas S. et al., Basic Res Cardiol, 95:47-53, 2000). The cytokine may thus contribute to enhanced diastolic stiffness.

11:00 a.m.

Induction of Tumor Necrosis Factor-Alpha and Left Ventricular Dysfunction in the Remote Donor Heart Following Myocardial Infarction in the Remote Donor Heart Following Myocardial Infarction in a Heterotopic Syngenic Transplant Model: Evidence of a Novel Unique Cyanotic Intrarenal Signaling Pathway

Hiroshi Kakamur, Gordon Moe, George Nisk, Josef Benneter, Phoebe D’Amico, James Chin, Peter Hsu, Hartz & Shrotri/Heimich Center of Excellence, U of Toronto, Toronto, ON, Canada

Activation of neurohumoral and cytokine systems in heart remodeling after myocardial infarction (MI). To examine the crosstalk between these stress responses systems and the host, and confirm whether each factor is intrinsic or extrinsic, we performed syngenic heterotopic renal transplantation and simultaneously induced MI in the donor heart with coronary ligation. Both recipient and donor hearts were evaluated histologically at 1 or 3 weeks after the transplantation. TUNEL-positive heart sections were stained immunohistochemically with anti-TNF-a and anti-IL-6 antibodies. In the donor heart, TNF-a and IL-6 expression was significantly higher in the infarct region of the donor heart. The highest levels of TNF-a and IL-6 expression were found in the left ventricle of the heart. The highest levels of TNF-a and IL-6 expression were found in the left ventricle of the heart.
Textual content not provided
1231-44 Angiotensin-Converting Enzyme Gene Polymorphism Predicts Aldosterone Escape in Chronic Heart Failure Patients

Marilantnietta Gcoza, Luisa Zanolla, Andrea Rossi, Lorenzo Franceschini, Giorgio Golka, Giusi Calzolari, Alario Bonacozzi. Marilantnietta Gciozari, Pietro Zendo. Divisione Clininica di Cardio orpleto, Verona, Italy

Background: A number of chronic heart failure (CHF) patients has elevated serum levels of aldosterone despite utricular administration of angiotensin converting enzyme (ACE) - inhibitors, but the mechanisms of this escape have never been investigated. We have therefore hypothesized that ACE gene (A1166G) polymorphism, which accounts for half of the variance of ACE levels in individuals, might also determine ACE-inhibitors response in CHF patients. Methods: We prospectively studied 134 CHF patients (left ventricular ejection fraction < 45%) in treatment with ACE-inhibitors for more than 6 months presenting at our five Heart Failure Units. Patients with multiplicity, exogenous etiologies, or without data for at least 2 years were excluded from the study. Serum aldosterone levels were determined in a fasting state and after 30 minutes in supine position. Aldosterone 'escape' was defined as serum aldosterone levels above the normal range of our laboratory (> 42 ng/L). Patients were then divided into two subgroups according to the presence (group 1) or absence (group 2) of 'escape'. Genotype analysis was performed by polymerase chain reaction (PCR) with a three-primer system. Result: The prevalence of 'escape' in our population was 10%. The two groups did not differ concerning duration of treatment and dose of ACE-inhibitor, beta-blockers, diuretics and renal function. The distribution of the three genotypes in group 1 and 2 is shown in the table below:

<table>
<thead>
<tr>
<th>Group</th>
<th>D</th>
<th>ID</th>
<th>DD</th>
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<tbody>
<tr>
<td>Group 1</td>
<td>8 (60%)</td>
<td>5 (40%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Group 2</td>
<td>20 (24%)</td>
<td>69 (57%)</td>
<td>23 (19%)</td>
</tr>
<tr>
<td>Total</td>
<td>37 (28%)</td>
<td>74 (56%)</td>
<td>23 (17%)</td>
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Conclusions: CHF patients with aldosterone 'escape' have a higher proportion of DD genotype, ACE gene polymorphism might therefore guide optimization medical therapy in CHF patients.
Heart Failure in the Elderly: Clinical Aspects

Tuesday, March 20, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: Noon-1:00 p.m.

1233-52 Depression and Risk of Heart Failure Among Older Persons

Yale University School of Medicine, New Haven, CT, University of Minnesota Medical School, Minneapolis, MN

Background: Investigators have shown that depression is associated with an increased risk of coronary heart disease. However, it is unknown whether depression is a risk factor for heart failure, independent of its association with myocardial infarction.

Methods: This study examined whether depression was a predictor of incident heart failure among 4589 persons age 60 years and older enrolled in the Systolic Hypertension and the Elderly Program (SHEP). Depression was defined as a score of 16 or more at baseline on the Center for Epidemiologic Studies Depression (CESD) scale. The relationship between depression and heart failure was assessed using Cox proportional hazards regression.

Results: The average follow-up time was 4.5 years. Heart failure developed in 138 (3.2%) of 4571 non-depressed persons and in 18 (8.1%) of 221 depressed persons. After controlling for age, sex, race, history of myocardial infarction, diabetes, angina, blood pressure, cholesterol levels, electrocardiographic abnormalities, smoking, disability, and SHEP treatment group, depressed persons had more than a twofold higher risk of developing heart failure compared to non-depressed persons (hazard ratio 2.82, 95% confidence interval 1.74-4.27; p < .001). Upon additional adjustment for the occurrence of myocardial infarction during follow-up, depressed persons remained at elevated risk of heart failure (hazard ratio 2.82, 95% confidence interval 1.71-4.87; p < .001).

Conclusion: Depression is associated with a substantial increase in the risk of heart failure among older persons, independent of potential confounding factors.

1233-53 Assessment of 30-Day Pre-Hospital Medication Adherence in Elderly Patients With Congestive Heart Failure

Gwen W. Oldenquist, Peter Vlahivou. John Quinn, Susan McLaughan, Carol Brown, Michelle Tayback, Shawn H. Gottlieb, John Hopkins University, Baltimore, MD

Background: Non-adherence (NA) with medication (MED) prescribed for CHF is often noted as a precipitant of admission to elderly patients with CHF. Depression has seldom been documented in an objective and verifiable way in the period just prior to hospital admission. The purpose of this study was to determine the frequency of NA with MED in the 30 days prior to hospitalization; 52%(12/23) of patients had a prior history of CHF and 58% (31/53) had been previously hospitalized for CHF. We aimed to evaluate depression as a predictor of incident heart failure among elderly patients with CHF.

Methods: NA with MED by subjective and objective criteria among elderly patients hospitalized for CHF was assessed using the Center for Epidemiologic Studies Depression (CESD) scale. The relationship between depression and heart failure was assessed using Cox proportional hazards regression.

Results: The average follow-up time was 4.5 years. Heart failure developed in 138 (3.2%) of 4571 non-depressed persons and in 18 (8.1%) of 221 depressed persons. After controlling for age, sex, race, history of myocardial infarction, diabetes, angina, blood pressure, cholesterol levels, electrocardiographic abnormalities, smoking, disability, and SHEP treatment group, depressed persons had more than a twofold higher risk of developing heart failure compared to non-depressed persons (hazard ratio 2.82, 95% confidence interval 1.74-4.27; p < .001). Upon additional adjustment for the occurrence of myocardial infarction during follow-up, depressed persons remained at elevated risk of heart failure (hazard ratio 2.82, 95% confidence interval 1.71-4.87; p < .001).

Conclusion: Depression is associated with a substantial increase in the risk of heart failure among older persons, independent of potential confounding factors.
null
** Integration of Best Practice into Multidisciplinary Care for Heart Failure in the Elderly: New Benefits Realised**

**John M. Cash, Jon Dwyer, Mary Johnstone, Peter Cherney, Brian Macnicol, Mary Ryder, Bronagh Trainer, St. Vincent’s Cardiology Research Centre, Dublin, Ireland, Laboratoires Servier (Ireland) Ltd., Dublin, Ireland.**

**Background:** It is a growing body of data demonstrating the benefits of multidisciplinary care in heart failure, particularly high risk elderly. However, few studies have looked at the first month of discharge, continue to be documented. **Aims/METHODS:** As part of an ongoing, randomised study on the value of multidisciplinary care in a high risk, elderly (mean age 69 years) heart failure population, we examined the effects of incorporation of three best practice issues on previously high (20%) one month readmission rates. Unlike previous studies of best practice, usual multidisciplinary care (MC) and routine care (RC) populations were not cared for the cardiology service. Additionally, all were required to adhere to guidelines regarding fluid and electrolyte therapy. Although no changes in body weight or medication for 48 hours (and 4 h before upjohn) to receive randomized ACE inhibitor prior to discharge. We analysed death and unplanned heart failure related admissions at one month following discharge. **RESULTS:** This is an early report from the first 100 patients (77% male, 71% systolic dysfunction with a mean ejection fraction of 31%). During index hospitalisation (mean length of stay 10.5 ± 5.0 days), 100% of patients were cared for by the cardiology service and complied with discharge candidacy. 54% of this elderly population with systolic dysfunction achieved target or high dose therapy with ACE inhibitor. Complete elimination of one month hospital readmission was observed in both MC and RC groups. This unexpected result represents a dramatic improvement both for this patient cohort and in contrast with available data from multidisciplinary programmes. **Conclusion:** Critical contributors to this improvement appear to be systematic application of the components of the best practice approach described above. More widespread application of this approach may have a dramatic impact on early readmission for CHF in addition to the proven benefits of multidisciplinary care.

**1234-60 Can the Extensive Peer Review Process Provide Adequate Feedback to Sustain the Implementation of the Heart Failure Guidelines by Primary Care Providers?**

**Judith D. Willis, Jaspal S. Samra, Rukhsaya Gill, Prakash C. Deedwania, VA Central California Healthcare System, Fresno, CA, UCSF School of Medicine, San Francisco, CA.**

In a previous study, we have shown that academic detailing and aggressive provider feedback improved the implementation of practice guidelines in the management of patients with HF by primary care providers (PCPs). Data showed a 54% improvement in LV function evaluation and a 38% increase in the use of ACE inhibitors in the treatment of systolic dysfunction. We also showed a 54% increase in the use of ACE inhibitors in the treatment of diastolic dysfunction. The IMPROVEMENT of Heart Failure Survey, an initiative of the Study Group on Diagnosis and Management of CHF, to implement new proven strategies in a timely manner, and to monitor treatment trends in 11 initial centres across Canada. The first formal meeting of the Network members was in July 1996 when, through consensus, a manual of CHF guidelines for management for physicians, nurses, and pharmacists was developed. **Methods:** A computerized database was designed and implemented in Jan 1999 and 883 patients were included in the first 12 months. These patients represent both new patients to the clinic and some previously seen in the clinic but who were being entered into the longitudinal database for the first time. **Results:** Selected mean baseline characteristics of these patients were: age $64$ years, male $72$, isotropic etiology $62%$; NYHA Class I $13.0$, II $34.0$, III $40.6$, IV $11.4$; LV EF $24.4$. Drug utilization changed from the first to the last quarter of 1999 with an increase in randomisation ($27.1$ vs $10.3$%, p=0.0001) while all ACE-I use remained constant ($70.3%$), and systolic dysfunction ($3.5$ vs $5.0$%, p=0.009). Data on the use of ACE inhibitors was $39.3$% vs $73.4$% and $50.0$ vs $52.5$% respectively. The physical patient interview resulted in a change of drug treatment in $46$% of encounters and education regarding medication in $46$, CHF $42$, fluid/salt $42$, home weight monitoring $42$, and exercise $27$ respectively. **Conclusion:** Critical contributors to this improvement appear to be systematic application of the components of the best practice approach described above. More widespread application of this approach may have a dramatic impact on early readmission for CHF in addition to the proven benefits of multidisciplinary care.

**1234-61 Current National Rates of ACE Inhibitor Dosing for Medicare Beneficiaries With Heart Failure: Results From The National Heart Failure Project**

**Frederick A. Masoudi, Edward P. Heavner, Harlan M. Krumholz, Kelly A. Westfall, Pam Vouite, Diana L. Omtm, Colorado Foundation for Medical Care, Aurora, CO, HC, Healthcare Financing Administration, Boston, MA.**

**Background:** Recent studies suggest that ACE inhibitors are more effective when prescribed in the dosages recommended for suboptimal dosages for the elderly. We sought to characterize current national patterns of dosing of ACE inhibitors for elderly patients with chronic HF admitted for hospital treatment. **Methods:** As part of the National Heart Failure (NHF) project, we collected data from 680 Medicare hospital inpatient discharges from 4:95-1996 onwards. Only 1 discharge per patient for each hospital and, Puerto Rico. We assessed the pre-admission ACE inhibitor dosing among patients admitted with HF who had a documented history of HF and LVEF by determining whether proportion of those patients were taking less than 50% of the lowest dose targeted in the clinical trials. **Results:** Of the 37,500 charts that were analyzed, 4,386 (12%) met criteria for inclusion in this analysis. The median state rate of ACE inhibitor dosing that was $10$% of the lowest dose from the trials beta-blocker use was $16$% (range $21.2%$ to $71.4$%). Dosing to the $50$% level or higher was significantly and independently associated with better outcomes, high admission blood pressure and hypotension, but not LV EF; older patients were significantly less likely to be dosed at the $50$% level. **Conclusion:** Among patients with chronic HF who have a clinical deceleration requiring hospitalization, the prescriber dosing ACE inhibitors in comorbidity risk $\geq 50$% the lowest dose was targeted in the clinical trials. Over 1,363 randomly selected primary care physicians (PCP) from 14 ESC Nations were involved. Each PCP kept a record of all patients with heart failure or prior myocardial infarction for 6-8 weeks. A random selection of patients from this list was obtained to determine the effectiveness of ACE inhibitor therapy and represent an opportunity to improve the care of older patients with HF.

**1234-62 Changes in Heart Failure Drug Utilization During 1999: The Canadian CHF Clinics Network Experience**


**Background:** The Canadian CHF Clinics Network was established to improve the current management of UFH, to implement new proven strategies in a timely manner, and to monitor treatment trends in 11 initial centres across Canada. The first formal meeting of the Network members was in July 1996 when, through consensus, a manual of CHF guidelines for management for physicians, nurses, and pharmacists was developed. **Methods:** A computerized database was designed and implemented in Jan 1999 and 883 patients were included in the first 12 months. These patients represent both new patients to the clinic and some previously seen in the clinic but who were being entered into the longitudinal database for the first time. **Results:** Selected mean baseline characteristics of these patients were: age $64$ years, male $72$, isotropic etiology $62%$; NYHA Class I $13.0$, II $34.0$, III $40.6$, IV $11.4$; LV EF $24.4$. Drug utilization changed from the first to the last quarter of 1999 with an increase in randomisation ($27.1$ vs $10.3$%, p=0.0001) while all ACE-I use remained constant ($70.3%$), and systolic dysfunction ($3.5$ vs $5.0$%, p=0.009). Data on the use of ACE inhibitors was $39.3$% vs $73.4$% and $50.0$ vs $52.5$% respectively. The physical patient interview resulted in a change of drug treatment in $46$% of encounters and education regarding medication in $46$, CHF $42$, fluid/salt $42$, home weight monitoring $42$, and exercise $27$ respectively. **Conclusion:** Critical contributors to this improvement appear to be systematic application of the components of the best practice approach described above. More widespread application of this approach may have a dramatic impact on early readmission for CHF in addition to the proven benefits of multidisciplinary care.

**1234-63 Elderly Heart Failure Patients Receive Less Intensive Medical Management**

**Stephanie H. Dunlap, Ricardo I. Vizcusa, Jun Chong, Benjamin J. Bhea, Andrew J. Kraitik, University of Illinois at Chicago, Chicago, Il.**

**Background:** It has been demonstrated in previous studies that elderly patients (pts) are less likely to receive standard therapies for cardiovascular disorders such as myocardial infarction and unstable angina. Reports also describe an association between younger patient age and higher frequency of ACE therapy (bx) in bx pts. The purpose of this study was to investigate the association of the overall quality of care (QOC) in elderly hospitalized HF pts and to compare their QOC to that of younger HF pts. **Methods:** A random sample of 223 pts (53% female, 65% black, 19% Hispanic, 14% white) with mean age of 65±15 years. (SD). 30% of pts included were older than 69 yrs. The elderly pts were less likely to receive ACEI bx compared with younger pts (86% vs 94%, p<0.01), the target dose of ACEI was less frequently reached in elderly pts despite no contraindications for ACEI (40% vs 56%, p=0.01). Digoxin therapy (70.4% vs 86%, p=0.02) and still less and/or fluid restriction (46% vs 60%, p =0.02) was also less commonly prescribed in older pts. No difference in the frequency of systolic dysfunction (74% vs 67%, p=NS), chronic renal insufficiency (53% vs 32%, p=NS), and atrial fibrillation (17% vs 12%, p=NS) was found between groups. **Conclusion:** Elderly pts less frequently receive optimal care based on these 9 clinical QOC indicators especially as regards use of ACEI therapy. This study underscores the need for continued attention to QOC measures, especially in those within the highest risk for HF.
Cardiology Specialist Care of Heart Failure Patients Improves Survival

Maria N. Ansari, All Tutter, Jean Bullard, Barry M. Massie, John R. Teerlink. San Francisco VAMC/LUSF, San Francisco, CA

Background: Both generalists and cardiologists frequently manage patients with chronic heart failure and since practice patterns differ between these groups, we sought to compare outcomes of patients with an outpatient diagnosis of CHF based on provider type.

Methods: Outpatients at San Francisco VAMC with an encounter form diagnosis of CHF between 7/98-12/98 were eligible (n=177); 42 patients were excluded for absence of CHF by Framingham criteria or lack of primary care within the VA. Clinical progress notes, pharmacy profiles and patient status records were reviewed and survival was assessed from 7/98 to 5/00. Patients with any visit to a cardiologist were assigned to the Cardiology group, and all others as the primary care provider (PCP) group. Characteristics of patients in the 2 provider groups were compared and multivariate survival analysis was performed for the total cohort, the reduced LV function group (EF<45%) and the preserved LV function group (EF≥45%).

Results: Most CHF patients were cared for by PCP (60%). Cardiology patients were younger (age 59 vs 73; p<0.001), with a lower EF (34% vs 40%; p<0.001), lower SBP (131 vs 134; p=0.5), and lower HR (75 vs 79; p=0.007). Cardiology patients were also more likely to have had an assessment of EF (p<0.01). Cardiology CHF patients had a higher prevalence of coronary heart disease (CHD, p<0.001), and CAD (p<0.001) compared to the PCP group. In the absence of concomitant lead changes, cardiologists used more beta blockers (99% vs 77%; p<0.001) and ACE I (63% vs 82%; p<0.001) compared to the PCP group. One year and two month survival was 10.8% and 20.5% overall, 13% and 24.4% in the PCP group, and 7.3% and 14.2% in the cardiology group. Cardiology care was a strong independent predictor of survival in the overall group (HR 1.69, 95% CI 1.01, 2.07; p=0.03) and reduced EF group (HR 1.68, CI 1.29-2.19; p=0.03), but not in the preserved LV function group (HR 0.98, CI 1.25-0.99; p=0.15).

Conclusions: Care of outpatients with CHF in our sample was associated with improved survival in the working PF and overall groups. The improved survival may be related to higher rates of appropriate guideline compliance in managing these patients.

International Variability of the Characteristics of Heart Failure Managed in Primary Care: The IMPROVEMENT of Heart Failure Survey

John G. F. Cleland, Kai Swedberg, Ferenc Follath, Jiri Widding, University of Hull, Kingston upon Hull, United Kingdom

Patients managed in clinical practice may differ substantially from patients in clinical trials and this may apply especially to heart failure. The IMPROVEMENT of Heart Failure Survey, an initiative of the study group on the European liability of Cardiology (ESC), was conducted between September 1999 and May 2000. The survey was designed to provide unique international comparative data. Over 1,363 randomly selected primary care physicians (PCPs) from 14 European countries were involved, each PCP kept a record of all patients with heart failure or prior myocardial infarction for 6-8 weeks. A random selection of patients from this list was obtained to investigate their clinical characteristics. A random selection of patients from this list was obtained to investigate their clinical characteristics. A random selection of patients from this list was obtained to investigate their clinical characteristics. A random selection of patients from this list was obtained to investigate their clinical characteristics. A random selection of patients from this list was obtained to investigate their clinical characteristics.

In patients with a higher hct, there was a significant left ventricular mass regression from baseline to 18 months, such a difference was not seen in patients with a subnormal hct. There was no significant difference in cardiovascular mortality between the 2 groups (p=0.3). As expected higher hlv, larger LVEDD and LVESD and lower EF served as markers of mortality in both groups (p<0.05). Thus while a higher hct did lead to LV mass regression it did not have a significant impact on mortality. Further studies are needed to identify a subgroup of patients who might have a survival benefit from a higher hematocrit.
and plateau patterns were recorded at catheterization in both left (LV) and right ventricular (RV) pressure waves, and the left ventricular (LV) pressure-dilation pressure (PDP) curve was analyzed. The LV pressure-dilation pressure (PDP) curve was analyzed.

Methods: In 50 pts with large pericardial effusions (PE) (68 males, mean age 54.2±6.6 years, PE >2 cm anteriorly) pericardiovascular pathophysiology was performed immediately before cardiac catheterization (pericardioscintigraphy/angiography) in large symptomatic PE had cardiac tamponade. Average volume of PE evacuated by pericardiocentesis in 50 pts with tamponade (725±344 ml vs. 649±421 ml: p=0.317). Sensitivity vs. specificity vs. positive predictive value of the 2D-echocardiographic signs of cardiac tamponade were respectively, RA diastolic collapse -> 45 pts (100% vs. 11.9% vs. 17.5%), LA systolic collapse vs. vs. 200 (5.7%), uremia 16/260 (6.2%). No etiological differentiation of infectious pericarditis using pericardial effusion and pericardial/biopsy analyses is possible in the large majority of patients. Contribution of PST molecular techniques is crucial in revealing the specific etiology of the disease. The Kaplan-Meier method was used to estimate overall survival and survival by etiology group. Cox proportional hazards regression analysis was performed to assess the impact of various causes of BP on long-term survival while adjusting for age. Results: The diagnosis of BP was established by surgical removal of pericardial effusion, and pericardiectomy in this group. Kaplan-Meier curves for the subgroups are shown in Figure 1. Idiopathic CP had the best prognosis (10 year survival 90% vs. matched control 85%). Age, risk factors, vs. 1.04, 95% confidence interval (CI) 1.01-1.06; prior cardiac surgery, RR 1.2, CI 1.3-3.9, and mediatinal radiation, RR 6.3, CI 3.2-12.2, were predictors of poor survival. Conclusion: Survival after pericardiectomy for CP is determined mainly by the etiology of constriction and may reflect the prognosis of the underlying condition. The overall long-term survival in the group with idiopathic CP emphasizes the long-term safety of surgical pericardiectomy in this group.

Figure 1: Etiology-Specific Survival

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Survival Rate (%)</th>
</tr>
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<tbody>
<tr>
<td>Idiopathic CP</td>
<td>90</td>
</tr>
<tr>
<td>Previous Surgery</td>
<td>85</td>
</tr>
</tbody>
</table>

Given the fact that many cases of idiopathic pericarditis are infectious in origin, inflammatory response in the pericardium are often correlated with a rub than the non-infectious causes of pericarditis.

Conclusion: Although often suggested by clinicians, we could not identify a correlation between a pericardial friction rub and the amount of PE in this large study. However, inflammatory pericarditis is often associated with a rub suggesting that rather than the rough pericardial surfaces fibrin strings cause the rub, where they may serve as a source.
PERCUENT SEPTAL ABLE TION FOR HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY: THE LATEST DATA

Tuesday, March 20, 2001, 2:00 p.m.-3:30 p.m.
Orange County Convention Center, Hall F5

861-1 Sepral Abation for Hypertrophic Obstructive Cardiomyopathy: An Analysis of the Patients With Unsatisfactory Reduction of the Outflow Gradient

Lothar Fabel, Bernd Wenteleman, Leon Kratzer, Hubert Seggewiss, Dieter Horstkotte, Heart Center North Rhine-Westphalia, Bad Oeynhausen, Germany; Leopoldina Hospital, Osnabruck, Germany

Background and Introduction: In 90% of the patients (pts), with symptomatic hypertrophic obstructive cardiomyopathy (HOCM) the outflow gradient (LVOTG) can signifi- cantly be reduced or removed by invaventral septal ablation (PTSMA). Pts. with a dissatisfactory LVOTG response are not characterized sufficiently.

Results: In 41 pts., re-evaluated 3 months after PTSMA, 32 (78%) had PTSMA fail- ure (P1) defined as less than 30% LVOTG reduction. On average, these pts. were younger (54+18 vs. 59±14; p<0.01) and had a slightly thicker septum (21.7±3.2 vs. 20.5±3.6 mm; p<0.01).

The leading cause for P1 was an insufficient PTSMA scar on 2D-echocardiography (n=16; successful re-PTSMA in 6 pts., spontaneous LVOTG reduction in 3 pts. after 12 months). Suboptimal scar localization, observed in 7 pts., treated before introduction of routine echocardiographic guidance (MCE) for PTSMA and requiring a re-PTSMA in 4 pts. and surgery in 1 pt., was not seen with MCE-guided interventions any more. Another group of pts. with P1 included cases with persisting SAM and LVOTG despite a correctly placed and sufficiently large PTSMA scar due to excessive elongation of the mitral leaflet(s) and/or spontaneous LVOTG elimination in one of them after 12 months. One pt. had consistent fibromuscular subaortic stenosis and underwent successful surgery for this problem.

Conclusions: After exclusion of scar misplacement by MCE, pts. still remain who seem to be less suitable for PTSMA. Furthermore, LVOTG elimination may need up to 1 year. Pre-interventional pt. selection, echocardiographic assessment, and pt. information should take these findings into consideration.

861-2 Evaluation of Left Ventricular Outflow Tract Area After Septal Reduction in Hypertrophic Obstructive Cardiomyopathy: A Real-Time Three-Dimensional Echocardiographic Study

Marta Sitges, Isakaho Shoida, Harry W. Liew, Jian Xin Qin, Fabrice Bauer, Joannina K. Drinco, Deborah A. Agler, Maureen G. Martin, Nicholas G. Smedira, Bruce W. Lytle, Samir R. Kapadia, E. Murat Tuzcu, Mario J. Garcia, James D. Thomas, The Cleveland Clinic Foundation, Cleveland, OH

Background: The comparative impact of percutaneous septal alcohol ablation (PTSMA) and surgical myectomy (MYO) on left ventricular outflow tract (LVOT) area in patients with hypertrophic obstructive cardiomyopathy (HCM) is not well defined. Real-time three-dimensional echocardiography (RT3DE) provides accurate information about the LVOT geometry and shape. We aimed to analyze the change in LVOT area after septal reduc- tion interventions in patients with HOCM using RT3DE.

Methods: 21 patients (mean age 52±17) with HCM undergoing PTSMA (n=12) or MYO (n=9) were studied at baseline and during follow-up with RT3DE. LVOT area was measured after observing the LVOT in the 3-dimensional space as the smallest area during mid-systole. LVOT pressure gradients (PG) were obtained by conventional CW Doppler.

Results: LVOT area increased from 0.96±0.2 to 2.02±0.5 cm2 (p<0.01) and LVOT pres- sure gradient (PG) decreased from 62.4±45 to 18.1±12 mm Hg (p<0.05) after a mean follow- up of 4 months after intervention. Results of PTSMA and MYO groups are shown in the following table.

<table>
<thead>
<tr>
<th></th>
<th>PTSMA</th>
<th>MYO</th>
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<tbody>
<tr>
<td>LVOT area</td>
<td>Pre 0.96±0.2</td>
<td>Post 2.02±0.5</td>
</tr>
<tr>
<td></td>
<td>0.97±0.2</td>
<td>2.03±0.7</td>
</tr>
<tr>
<td>Rest PG</td>
<td>66±48</td>
<td>22±14</td>
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<tr>
<td></td>
<td>73±47</td>
<td>14±6</td>
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*p<0.05 versus Pre, p<0.01 versus PTSMA.

Conclusions: RT3DE demonstrated an effective increase in LVOT area after both PTSMA and MYO. This technique may be useful for assessing the results of septal reduction in patients with HOCM.
At 1 year, all improvements were similar between the 2 modalities.

Results: In addition to the matching variables, there were no baseline differences in cTnI. One death occurred during NSRT (LAD dissection). The incidence of pace-makers and none had concomitant procedures. Endpoints included hemodynamics, exercise tolerance and symptoms class.

Methods: A prospective, randomized, double-blind, placebo-controlled trial. Enrollment targets were 31 patients per arm. Renal function was carefully monitored.

Conclusions: This study is the first to establish the safety and efficacy of a novel, non-invasive approach to the treatment of severe heart failure. Further research is needed to determine the optimal dosing and duration of therapy.

### 1009 Hypertrophic Cardiomyopathy: Clinical Aspects

**Tuesday, March 20, 2001, 3:00 p.m.-5:00 p.m., Orange County Convention Center, Hall A4**

#### 1009-201 Long-Term Changes in Right Ventricular Geometry and Function in Patients With Hypertrophic Cardiomyopathy

Francesco Pecola, Claudio Cisternino, Giuseppe Masiuzzi, Mario Pagliari, Vincenzo Martelli, Monica Mariani, Collaborative Hospital, Rome, Italy

**Background:** Little information is available on the long-term impact of HC on the right ventricle (RV). Over a 10-year period, serial echocardiograms could be obtained in 54 HC pts (35 males, age: 45±19 yrs) who had normal LV and RV size and function at diagnosis. Time interval between the first and last echocardiogram was 4±3 yrs (range: 2-10 yrs). In both LV or RV, the following measures ware derived (apical 4-chamber view): long-axis length (L), transverse midcavitary diameter (T), and end-diastolic (ED) and end-systolic (ES) areas as well as ejection fraction (EF).

#### Results

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Last Follow Up</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>LV enddiastolic diameter (mm)</td>
<td>48±9 vs 48±5</td>
<td>0.52</td>
</tr>
<tr>
<td>LVOTG at rest (mm Hg)</td>
<td>26±8 vs 26±1</td>
<td>0.67</td>
</tr>
<tr>
<td>LVOTG at Valvotomy (mm Hg)</td>
<td>147±56 vs 25±3</td>
<td>0.04</td>
</tr>
<tr>
<td>Maximum workload (Watts)</td>
<td>88±67 vs 122±43</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Conclusions:** PTSA leads to significant and persistent LVOTG reduction and improvement without global left ventricular dilatation or total heart-volume hypertrophy evident during long-term follow up. Spontaneous degeneration of the AV conduction system together with the PTSA-induced damage may lead to conduction problems in individual patients late after the operation is performed.

### 1009-202 Favourable Outcome of Pregnancy in a Non-Referral Based Population With Hypertrophic Cardiomyopathy

Iacopo Olivotto, Carolina Beattissi, Daniela Vargiu, Franco Cecchi, Arzieda Ospedaliera Careggi, Firenze, Italy

The prevalence of complications during pregnancy in patients with hypertrophic cardiomyopathy (HCM) is still uncertain. Aim of this study was to analyse the outcome of patients with HCM during pregnancy. The study was conducted in a non-referral based population of 202 patients followed for 10±5 years, the clinical history of all female patients (n=81) was reviewed. All women had been referred for evaluation during pregnancy and analysed with regard to pregnancy outcomes.

#### Results

- **Total number of pregnancies:** 29 (1.45/100 female yrs)
- **Total number of deliveries:** 29
- **Total number of complications:** 10
- **Total number of complications per pregnancy:** 0.35
- **Overall rate of complications per pregnancy:** 0.13

**Conclusions:** Pregnancy in patients with HCM is a safe event, with a low rate of complications. Continuation of anticoagulation therapy during pregnancy is recommended in patients with HCM, and should be followed by a lifelong follow-up to assess the long-term outcomes.

### 1009-203 Effect of Left Ventricular Outflow Tract Obstruction on Hemodynamic Adaptation to Exercise in Hypertrophic Cardiomyopathy

Quirino Cigliano, Sandro Bocchini, Anna Vincenzi, Fiore Mario, Maria A. Losi, Giulla Silica, Carlo G. Tocchetti, Raffaella Lombardi, Elodio Pozzale, Filippo Ruffino, Alberto Cuocolo, Massimo Chiariello, Federico di University of Naples, Naples, Italy

**Background:** Exercise is considered harmful in patients with obstructive hypertrophic cardiomyopathy (HOCM), despite little evidence in literature. Aim of our study is to assess hemodynamic adaptation to isometric and isotonic exercise by ambulatory radionuclide monitoring of left ventricular function (VEST) in HOCM, in non obstructive hypertrophic cardiomyopathy (NHOCM), and in controls. Methods: We studied 10 HC (age 37±14 yrs, 14 men), 23 NHOCM (age mean 59±15 yrs, 15 men), 9 healthy subjects. During VEST monitoring, they underwent a stress test, consisting of a 3 min exercise by treadmill (Bruce protocol), and isometric exercise by a dynamometer gripped at 75% of maximal voluntary contraction for up to 5 min. VEST data were analyzed at baseline, at 1, 3, 5, 8 min and at peak exercise (Pex) during isotonic exercise, and at baseline, at 1, 3, 5, 8 min and at peak exercise (Pex) during isometric exercise. Choking volume, cardiac output, and systemic vascular resistance were normalized to baseline value and expressed as a %.

**Conclusions:** Isotonic exercise: HOCM and NHOCM showed a significant decrease in stroke volume (figure, left) (p<0.01 by ANOVA) and in cardiac output (p<0.01 by ANOVA), cardiac output (p<0.01 by ANOVA). No documented ventricular tachyarrhythmias was implanted after CPR for unknown reason. One 86-year-old women with chronic AF died from stroke 23 months after PTSMA. No documented ventricular tachyarrhythmias was implanted after CPR for unknown reason. One 86-year-old women with chronic AF died from stroke 23 months after PTSMA. No documented ventricular tachyarrhythmias occurred after surgery. The remaining 11 women complained of palpitations (n=6), mild to moderate dyspnea (n=2), angina pectoris (n=4), retrosternal pain (n=5), atypical chest pain (n=1). In conclusion, pregnancy was well tolerated and associated with favorable outcome in a non-referral population with HCM. Thus, pregnancy should be viewed as a safe event in patients with HCM, with a low rate of complications.
Septal Ablation for Hypertrophic Obstructive Cardiomyopathy: Normalization of an Abnormal Blood Pressure Response

I. Patzer, A. Thiele, M. Huber, M. Wolf, H. Buellesfeld, C. Haverich, Heart Center North Rhine-Westphalia, Bad Oeynhausen, Germany, Leopoldina Hospital, Schweinfurt, Germany

Background and introduction: In patients with hypertrophic obstructive cardiomyopathy (HOCM), an abnormal blood pressure response (BPR) to exercise seems to be a marker for an increased risk of sudden death. Percutaneous septal ablation (PSA) is a new symptomatic treatment for HOCM with unknown long-term effects. Therefore, we analyzed the exercise BPR before and 12 months after PSA.

Methods and results: In 19 pts. studied, mean resting outflow gradient (LVOTG) was reduced from 86±34 to 71±29 mmHg (p<0.005) after PSA. After PSA, both LV inflow velocity (Ei) and flow propagation velocity (FPV) decreased LV outflow obstruction (from 83±42 to 44±40 mmHg, p<0.005) within 12 months after PSA. In 45 of 50 pts. (89%) the initially abnormal BPR was normalized with a significant decrease in diastolic pressure rise from 11±2±8 to 13±2±6 mmHg (p<0.05), while it remained abnormal in 9 of group 1. Lack of BPR normalization was not associated with a higher residual LVOTG.

Conclusions: In symptomatic HOCM, an abnormal BPR seems to be associated with younger age and a smaller, hypercontractile LV. PSA elimination by PSMA results in normalization of an abnormal BPR in the majority of pts. Whether this effect of PSA leads to a long-term benefit, and what factors remain abnormal in some pts. despite successful septal ablation, remains to be assessed by further investigation.

Purpose: The aim of this study is to investigate the effect of CBZ on LV diastolic function in HCM (as compared with bisoprolol).

Methods: Twenty-three patients with HCM (11 pts. HOCM, 12 pts; non-obstructive HCM; NOHCN) were reassessed. Additional ETOH was infused (1 patient) or another septal treated (3 patients). 40-60% septal ETOH localization in the septum. 1.5-2.5 ml of ETOH was infused and Doppler gradient reductions were sustained at follow-up. In 4 patients, the apical tags moved outward. This systolic outward movement may be related to the obliteration of the apical lumen as suggested by BMIPP imaging in patients with apical hypertrophic cardiomyopathy (AHC). We recorded displacement of myocardial tags from end diastole to end systole perpendicular to the long axis of the LV. Wall thickness of the apex and septum was measured from the four-chamber view. We recorded displacement of myocardial tags from end diastole to end systole perpendicular to the long axis of the LV. Wall thickness of the apex and septum was measured from the four-chamber view. Results indicated that the primary lusitropic effect of CBZ rather than afterload and early diastolic mitral annulus velocity (Ea) were measured. Ei/FPV and Ei/Ea were not changed by bisoprolol in HNCM. The effects of CBZ and bisoprolol on LV diastolic function were different in patients with HOCM, whereas bisoprolol did not affect it. It is concluded that the primary lusitropic effect of CBZ rather than afterload reduction on LV might have contributed to the improvement of diastolic function in HOCM.

Conclusion: CBZ improved LV diastolic function in HCM, whereas bisoprolol did not affect it. It is concluded that the primary lusitropic effect of CBZ rather than afterload reduction on LV might have contributed to the improvement of diastolic function in HOCM.
gested by the paradoxic jet flow, which will cause high mural pressure and may lead to myocardial ischemia or damage. Conclusion: Myocardial tagging is useful in detecting the outward movement in AMI and in predicting the occurrence of cardiac events.

Effect Of The Degree Of Left Ventricular Hypertrophy On Hemodynamic Adaptation To Exercise In Hypertrophic Cardiomyopathy

Daniello Ciampi, Sandro Ragionieri, Anna Vincenzo, Finno Manganiello, Massi A. Lecu, Nilla Sca, Carlo G. Toochini, Battista Lonardi, Matteo Pedagrotto, Elghor Campanolo, Mariano Aversa, Alberto Cuocolo, Massimo Chiarabba. Federico II University School of Medicine, Naples, Italy

Background: Massive LV hypertrophy (LVH) in hypertrophic cardiomyopathy (HCM) carries high risk of sudden death. Our study assesses hemodynamic adaptation to exercise by quantitative analysis monitoring LV function (VES31) in animals with different LVH and in controls. Methods: We studied 10 controls and 44 HCM patients; these were divided into 3 groups according to the number of hypertrophied LV segments: 6 with 1 segment (mild LVH), 27 with 2 segments (moderate LVH), 12 with 3+ LV segments (severe LVH). During VES, they exercised on a treadmill (Bruce protocol). VES data were analyzed at baseline, at 3 min and at peak exercise (Pex). Stroke volume (SV) and myocardial performance index (MPI) were expressed as a % of baseline; for evaluation of radeau raw data are supplied. Results: There were no basal differences in age, NYHA functional class, incidence of angina, presence of LV tract obstruction among 3 HCM groups. In comparison to HCM with moderate and severe LVH, those with mild LVH had a lower ejection fraction (74±7, 76±6, 65±9, p<0.01) and a better left atrial fractional shortening, an estimate of LV end-diastolic pressure (22±7, 16±5, 25±6, p=0.00). During exercise, ejection fraction (EF) and SV increased in all groups. A better EF and SV were associated with mild LVH, but change was not different in HCM with mild and severe HCM with moderate and severe LVH (p=0.001 and p<0.001 by ANCOVA, respectively, figure). Pressure-volume product and PFR were similar among the 3 HCM groups. Conclusion: High volumes of LVH excludes wall stress and leads to supranormal systolic function at baseline, while it causes a drop in SV and ejection fraction during exercise, probably related to exercise-induced ischemia. This might be the background for reported high risk of sudden death in HCM with severe LVH.

Poster Session: Mechanism Effecting Myocardial Function

Tuesday, March 20, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall H4
Presentation Hour: 3:00 p.m.-4:00 p.m.

Body Mass Index, Obesity, and Cachexia vs Survival in Chronic Heart Failure: Results From the ELITE 2 Study
Stefan D. Anker, Constantinios H. Davos, Daniel Frey, Robert Segal, Emmanuels Santoro, Philip A. Poole-Wilson, Bertram Pitt, Andrew J. S. Coats. National Heart & Lung Institute, London, United Kingdom, Franz-Volhard-Klinik, Charité Campus Berlin-Buch, Germany

Background: The relationship between survival and body weight and body weight changes has not been studied in a contemporary large scale population of chronic heart failure (CHF) patients. Whether obesity is frequent in CHF and how it relates to survival is not known. Methods: We included in the analysis 3064 patients of the ELITE II study (31% female, age 71±7y, median follow-up 18 months, 513 deaths) in whom body weight and height data were available for assessment of body mass index at baseline (BMI: 25.2±4.4 kg/m2, weight/height2) and at predetermined intervals during the study. Results: Higher BMI was strongly related to improved survival (risk ratio [RR] 0.94, 95% confidence interval [CI] 0.92-0.96). Patients in the 4th BMI-quintile (Q, BMI: 26.8±2 kg/m2) had the lowest mortality (7.2% at 1y, 12.8% at 2y). Compared to patients in the 4th BMI-Q, mortality was significantly higher in obese patients (9th BMI-Q: <0.05 kg/m2, RR 1.39, p<0.13, but higher in the 3rd (RR 1.80, p<0.001), 2nd (RR 1.90, p<0.002), and 1st BMI-Q (mortality 17.2% at 1y, 29.7% at 2y, BMI≥29.3, RR 2.50, p<0.001). The cumulative frequency of weight loss ≥7.5% was 8.6, 19.7, 26.6 and 24.2% at 6, 12, 18 and 24 months, respectively. Survival after the development of cachexia was reduced compared to that in patients without weight loss (p<0.0001). Female sex (RR 1.40, age (RR 0.93, p=0.001), higher baseline BMI and survival of patients with CHF. Milder obesity patients show the best survival. In CHF, a higher BMI may indicate preserved metabolic efficiency and/or energetic reserves, and should not be considered an adverse risk factor.

Poster Session: Valvular-Ventricular Remodeling and Mitral Leafllet Geometry in Dilated Cardiomyopathy

David T. M. Lai, Paul Daggum, Tomasz A. Timko, Frederick A. Tabibayn, David Liang, George T. Daubert, R. Neil Bluhm, J. D. C. Miller. Stanford University School of Medicine, Stanford, CA, Research Institute of the Palo Alto Medical Foundation, Palo Alto, CA

Background: The effect of valvular-ventricular remodeling on mitral leafllet 3-D geometry in dilated cardiomopathy (DCM) is unknown. Methods: In 8 sheep, radiopaque markers were implanted in the mitral annulus, arterial and venous mitral leafllets, papillary tips, and left ventricle (LV). Following recovery, 3-D marker coordinates were obtained by bimale videofluoroscopy and rapid pacing was initiated. At onset of DCM with mild-moderate mitral regurgitation, marker coordinates were compared with control values at end-systole. Nethering distance from papillary tips to mid-anterior mitral annulus, major and minor annular axes, chordae "length" from papillary tips to leafllet edges and midline leafllet length were measured. Leafllet geometry was measured relative to a best-fitter aneurysm plane. Results: There was a significant negative correlation between LV and mitral leafllet diastolic dimension (p<0.01), and exercise ejection fraction (EF, p<0.05) in the HCM patients. Multiple regression analysis including age, gender, and LV mass index (LVM) demonstrated that LA dimension was an independent predictor of LV remodeling and exercise EF (p<0.001, and p<0.005, respectively). Exercise EF also correlated with LVM (<0.5, p<0.05). Patients in group 1 had reduced peak filling rate (PFR) and tended to have lower time to peak filling rate (TPFR) compared with group 2. There was no correlation between LVM and PFR, PFR or LV myocardial perfusion abnormalities were present in 16/20 patients in group 1 and 13/15 patients in group 2 (p<0.05).

LV Volume (ml) 124±45 138±47 #<0.001
Anterior papillary tip tethering (mm) 40±5 41±4 #0.003
Posterior papillary tip tethering (mm) 45±6 46±6 #0.01
Minor annular axis (mm) 28±3 35±3 #0.001
Major annular axis (mm) 38±4 43±3 #0.001
Anterior leafllet length (mm) 21.2±1.8 24.3±2.7 #0.02
Posterior leafllet length (mm) 11.7±2.4 13.3±2.6 #0.001
Posterior papillary to anterior leafllet chordal tendance (mm) 26.0±1.0 26.7±1.6 #0.001
Posterior papillary to anterior leafllet chordal tendance (mm) 28.9±6.6 30.5±6.0 #0.08
Conclusion: Dilated cardiomyopathy perturbed mitral leaflet geometry, with the basal portion of both leaflets being restricted. Most interestingly, despite LV and annular dilatation and increased papillary muscle thickening, elongation of the chordae tendinae and/or leaflets prevented similar restriction of the leading edges of the leaflets. Such chordal/leaflet remodelling is surprising and needs to be taken into account during valve repair.

In-Vitro Delivery of Non-Stimulatory Cardiac Contractility Modulating Electric Signals Improve Intrinsic Contractile Function of Cardiomyocytes Isolated From Dogs With Chronic Heart Failure

Methods: Cardiomyocytes were isolated from 5 dogs with HF. LV ejection fraction (<30%) produced by multiple intracoronary microembolizations. Extent of cardiomyocyte shortening (%), peak velocity of shortening (dL/dt), and peak velocity of lengthening (dL/dt) were measured by edge detection method. Peak (Fmax) and integral (F) of Ca²⁺ transients were assessed from fluo-3 fluorescent measurements. Data were collected at baseline and during CCM signal delivery. For each parameter, the percent change from baseline was calculated.

Results: The results are shown in the table. Application of the CCM signal to isolated cardiomyocytes significantly increased %S, dL/dt and dL/dt as well as Fmax and F (Table).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>CCM Signal</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>%S (%)</td>
<td>6.0 ± 0.6</td>
<td>7.0 ± 0.9</td>
<td>27 ± 5</td>
</tr>
<tr>
<td>dL/dt (µm/sec)</td>
<td>10 ± 0.6</td>
<td>13 ± 0.9</td>
<td>30 ± 5</td>
</tr>
<tr>
<td>Fmax (µv)</td>
<td>19 ± 4</td>
<td>22 ± 5</td>
<td>16 ± 6</td>
</tr>
<tr>
<td>F (µv/sec)</td>
<td>10 ± 0.6</td>
<td>15 ± 1.0</td>
<td>50 ± 6</td>
</tr>
</tbody>
</table>

Conclusion: CCM signals to isolated tailing cardiomyocytes improve intrinsic contractile efficiency and relaxation and enhances Ca²⁺ transients. These observations provide an explanation for the observed improvement of global LV function in dogs with HF receiving CCM signal delivery and reinforces the potential usefulness of this approach as an adjunct to the treatment of chronic HF.

Cardiac Sympathetic Nerve Terminal Dysfunction in Pacing-Induced Heart Failure Is Associated With the Reduction of Nerve Growth Factor

Free radical production and related oxidant stress during ischemia/reperfusion may lead to DNA strand-breakage which activates the nuclear enzyme poly-ADP-ribose synthetase (PARS) and initiates an energy consuming, inefficient repair cycle. The aim of the present study was to investigate the effects of the inhibition of PARS on myocardial and endothelial function during reperfusion after reversible hypothermic ischemia in a rat heart transplantation model. Intrabatricular hectorplastic transplantation was performed in Lewis rats. After one hour of ischemic preservation, reperfusion was started after application of either saline vehicle (control, n = 12) or PJ34 (3 mg/kg) a selective PARS-inhibitor (n = 12). Coronary blood flow (CBF), left ventricular pressure (LVP), its first derivative (dp/dt), end-diastolic pressure (LVEDP), left ventricular relaxation constant (TV) were measured after 60 minutes and 24 hours of reperfusion. Endothelium-dependent vasodilatation to acetylcholine (ACH) and endothelium-independent vasodilatation to sodium nitroprusside (SNP) were also determined. After one hour, CBF was significantly higher in PJ34 group in comparison to control (3.6±0.3 vs 2.8±0.3 ml/min/100 g, p<0.05). The PJ34 group showed a better recovery of myocardial and myocardial function (maximal LVP: 114±3 vs 83±3 mmHg, p<0.05, maximal dp/dt: 410±32 vs 1740±116 mmHg/s, p<0.05, TV: 11.3±1.1 vs 18.2±1.8 ml, p<0.05, intraventricular volume<80 ml). The washout rate of SNP to SNP was similar in both groups, ACH reacted significantly higher in PJ34 group (96±15% vs 51±15%, p<0.05). UEDV was similar in both groups. After 24 hours, there was no difference between the groups in basal CBF. LVP, dp/dt, TV, LVEDP and the response of SNP to SNP were similar in both groups. However, ACH led to a still significantly higher increase in CBF in the PJ34 group (134±38% vs 89±14%, p<0.05).

Thus, PARS inhibition improves myocardial and endothelial function during early reperfusion after heart transplantation and has a preserving beneficial effect against reperfusion induced graft coronary endothelial dysfunction.

The Heparan Sulfate Proteoglycan-Antithrombin Pathway in Postischemic Hearts

Background: The deposition of fibrin and subsequent ischemia within the heart is mainly prevented by the presence of antithrombin in blood vessels and cardiomyocytes. We asked if changes in myocardial antithrombin were directly associated with the outcome of heart transplant recipients and studied whether the antithrombin binding was mediated...
ABSTRACTS - Cardiac Function and Heart Failure 205A

Noninvasive Differentiation of Pseudonormal From Normal Transmitral Flow by Doppler Total Ejection Isovolume (TEI) Index: A Simultaneous Echocardiography-Catheterization Study in Patients With Anteroseptal Acute Myocardial Infarction

Alisa EIDN, Abeidkia, Yutaka Osut, Kenitsu Takasaki, Toshinori Yassin, Eiji Individuals, Hideaki Shiozawa, Takashi Shiozawa, Shinsuke Minagawa, Chieko Tani. Kagoshima University, Kagoshima, Japan

Background: Differentiation of pseudonormal from normal transmitral flow is important in patients with potential congestive heart failure. Patients with pseudonormal mitral flow usually have left ventricular dysfunction as well, which can be estimated by recently proposed echocardiographic diastolic and systolic Doppler index - total ejection isovolume (TEI) index. The purpose of this study was to investigate whether differentiation of pseudonormal from normal transmitral flow by TEI index is feasible or not.

Methods: Subjects consisted of consecutive 26 patients with anteroseptal acute myocardial infarction (AMI) and transmitral Doppler flow E/A ≥ 1. Based on pulmonary capillary wedge pressure (PCWP), patients were divided into pseudonormal group (PCWP > 18 mmHg, n = 12) and normal group (PCWP ≤ 18 mmHg, n = 14). TEI index was measured as (E + A)/B where A is the interval between the cessation and onset of mitral flow and B is the aortic flow ejection time. Results: TEI index was significantly higher in the pseudonormal group compared to the normal group (0.75 ± 0.13 vs 0.49 ± 0.06, P < 0.001). There was also a close correlation between TEI index and PCWP (r² = 0.82, P < 0.0001). By setting TEI index >0.6 as diagnostic criteria of pseudonormal mitral flow, the index differentiated pseudonormal from normal mitral flow with sensitivity, specificity, and over all accuracy of 100%, 93%, and 97%, respectively. Conclusion: TEI index allows simple and noninvasive differentiation of pseudonormal from normal mitral flow in patients with anteroseptal AMI.
**Parallel Systolic and Diastolic Function Abnormalities in Hypertensive Left Ventricular Hypertrophy With Normal Doppler Mitral Inflow: Insights From Doppler Tissue Imaging**

University of Massachusetts Medical School, Worcester, MA; Lehigh Library, Bethlehem, MA

**Background:** Hypertensive LV hypertrophy (LVH) is strongly associated with CHF even when ejection fraction (EF) and standard Doppler mitral inflow velocities (E, A, E/A ratio) are normal. Mitral annulus Doppler tissue imaging (DTI) has been proposed as a relatively load-independent method of assessing LV systolic and diastolic function. Accordingly we investigated whether DTI provided incremental information concerning diastolic dysfunction in pts with LVH, normal EF, and normal E/A ratio.

**Methods:** Data from 18 pts (age 57±14) with a history of hypertension, LVH by echo, normal EF (66±7%), and E/A > 1 were compared with 29 normal controls (C) (age 43±16). No subject had local wall motion abnormalities or significant valvular disease. In addition to A, E, A ratio, deceleration time (DT), and pulmonary vein flow velocities (L, S, S'/U ratio), we obtained LV early (E') late (A') (msec), and E'./E ratio. Fractional shortening at the midpoint (FS(m)) was used as a systolic parameter which accounts for LV geometry (normal wall thickening).

**Results:** LV not different from C with regard to LV and pulmonary vein flow ratio, but the diastolic parameters, only E' determined LVH from C; FS(m) was lower in LVH, despite normal EF.

**Conclusions:** MCE with ATP may be a new modality in the management of patients with IDC.
Conclusions: WC/GR is a significant predictor of cardiovascular mortality in patients with severe LVD and CAD. DSE CR is superior to NPI NV in predicting cardiovascular mortality.

1267-56 Left Ventricular Structure and Function in Morbid Obesity: A Transesophageal Echo Study

Tel W. Koh, Louise Bowles, Peter G. Mills, Martin T. Rothman, Peter Kopelman, Adam D. Timmis. London Chest Hospital, London, United Kingdom; Royal London Hospital, London, United Kingdom

Background: In subjects with morbid obesity (BMI > 40) data on adaptive changes in cardiac structure and function from transthoracic echocardiography (TTE) is often impaired by patient movements. necessc-diazaphagial obesity subjects (mean age 43 ± 7 yrs, 10 male) without hypertension were studied using transesophageal echocardiography (TEE) as part of the baseline investigations of a clinical trial of gastroplasty for treatment of morbid obesity. We compared the findings in a control group (CTL) of 26 subjects of similar age (40 ± 11 yrs) referred for TEE to exclude cardiac source of embolus, who had structurally normal hearts. We recorded transesophageal E-M mode echocardiograms of the LV cavity at the level of the papillary muscle and transtricuspid Doppler. Body weight and BMI for OBS were significantly higher than CTL (150 ± 32 vs 76 ± 19 kg, 52 ± 10 vs 25.3 ± 7.8 kg/m², P < 0.01). Results: M mode echo and Doppler were successfully acquired in all OBS subjects using TEE. TEE was only feasible in 78% and 86% of OBS subjects for recording LV M-mode and mitral Doppler respectively. On TEE, LV cavity size (end diastole and end systole) was greater in OBS than CTL (5.3 ± 0.6 vs 4.3 ± 0.5 cm, P < 0.01). LV mass was greater in OBS compared to CTL even after correction for body surface area (149 ± 34 vs 75 ± 48 g/m², P < 0.01). LV mass correlated significantly with BMI (r = 0.46, P < 0.05). Diastolic indices were abnormal in OBS with increased A wave velocity (0.7 ± 0.2 vs 0.4 ± 0.1 cm/s), reduced E/A ratio (1.2 ± 0.5 vs 2.1 ± 0.9) and prolonged isovolumic relaxation time (84 ± 13 vs 70 ± 14 s, P < 0.01) for all compared to TEE. Baseline function assessed by traditional shortening fraction was preserved in OBS (20 ± 1 vs 24 ± 1 %) vs CTL. Conclusions: Obese, morbid obesity is associated with increased LV muscle mass, disturbances in diastolic function and increased LV cavity size (end diastole and end systole). These adaptive changes especially if therapeutic maneuvers aimed at weight reduction are contemplated in these patients, who are at high risk of cardiovascular complications.

1267-67 Inter-Study Reproducibility of Left Ventricular Structure and Function in Heart Failure Patients With Cine MR Imaging

Prasad M. Patil, Olaf Muehling, Andrey Stebnezhnikov, Yimei Huang, Cory Swingen, Michael Jerosch-Herold, Norbert Wilke, Inder Anand. University of Minnesota, Minneapolis, MN

Background: Serial measurement of ventricular mass, volume and function is important for assessing new drugs considered to attenuate ventricular remodeling. Although cine MRI provides highly reproducible data in normal hearts, in patients with LV dysfunction, low cardiac output and disturbed ventricles, the resolution in anatomic structures is often poor. Values for inter-study reproducibility in such patients are not available. These are required for calculating sample size in drug studies. We report reproducibility data of LV structure and function in patients with a wide range of LV dysfunction.

Methods: Eight subjects underwent MRI of the heart, with a 1.5T Siemens scanner on two occasions, one week apart using the same breath-hold protocol. The entire heart was covered from base to apex in 8 mm slices with 2 mm inter-slice gap, and 15 to 20 phases to include end-diastolic (ED) and end-systolic (ES) phases. An experienced observer manually traced the LV and LV contours using M 2d analysis software version 4.0, to determine the ED volume (EDV), ES volume (ESV), Stroke volume (SV), Ejection fraction (EF) and LV mass.

Results: The standard deviation, correlation coefficient and percent variance for the LV mass, volumes, EF and SV are shown in the table. Percent variability was determined as the absolute value of the difference between the two measurements over the mean of the two measurements. The data are very similar to those described for subjects with normal hearts.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Variability</th>
<th>Std.dev</th>
<th>Coefficient correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDV</td>
<td>3.79</td>
<td>0.1</td>
<td>0.99</td>
</tr>
<tr>
<td>LVESV</td>
<td>8.79</td>
<td>4.72</td>
<td>0.98</td>
</tr>
<tr>
<td>LVMass</td>
<td>4.32</td>
<td>0.37</td>
<td>0.00</td>
</tr>
<tr>
<td>EF</td>
<td>7.46</td>
<td>3.9</td>
<td>0.94</td>
</tr>
<tr>
<td>SV</td>
<td>3.91</td>
<td>0.79</td>
<td>0.94</td>
</tr>
</tbody>
</table>

Conclusion: Assessment of LV remodeling by MRI in heart failure patients is highly reproducible. Therefore, MRI is capable of assessing a given change in LV structure and function with a much smaller sample size as compared with other non-invasive imaging techniques such as echocardiography.

1267-68 NOGA Electro-Mechanical Characteristics of Non-Ischemic Dilated Cardiomyopathy

S. Chu, Weng, Barry Cohen, Stylianos Papakostas, Mark Blum, Mohsen Mabzban, Mark Reisman. The New York Presbyterian Hospital-Cornell Campus, New York, NY, Memorial Sloan-Kettering, New York, NY

Background: Left ventricular myocardial (LV) data from Biosonics NOGAD™ maps can be useful for assessing myocardial viability. Normal myocardium is represented by high unipolar voltage (UV) (14±2 mV) and linear local shortening (LS, 12±5±2%) whereas non-viable myocardium is characterized by low UV and LS concord (<0.7 mV and -6.5±2%) respectively. Currently, the NOGAD™ imaging techniques in pts with non-ischemic dilated cardiomyopathy (NIDC) are unknown.

Methods: We prospectively evaluated the NOGAD™ findings in 12 consecutive pts with NIDC (defined as pts with history of heart failure, prior MI, >30% loss on angiogram and global hypokinesis with LVEF <30%). Results: All 12 pts had hypertension with mean age of 54±12±8 yrs, 30% were smokers, 25% had diabetes and 59% had hypercholesterolemia. The mean LVEF by ventriculogram was 25±17±3%. The mean UV and LS in each of the 12 standard NOGAD™ myocardial segments are:

<table>
<thead>
<tr>
<th>Segment</th>
<th>UV (mV)</th>
<th>Anterior</th>
<th>Lateral</th>
<th>Posterior</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apex</td>
<td>12.8±4.8</td>
<td>12.0±5.1</td>
<td>12.3±4.9</td>
<td>12.5±5.6</td>
</tr>
<tr>
<td>Mid</td>
<td>13.3±3.8</td>
<td>12.6±5.4</td>
<td>11.6±5.5</td>
<td>11.8±4.8</td>
</tr>
</tbody>
</table>

Conclusions: Despite low LVEF, pts with NIDC have preserved UV similar to pts with normal myocardium. 2) NOS with significantly diminished mechanical function with %LS comparable to non-viable myocardial segments. 3) This marked discordance in the electro-mechanical findings, with "normal" UV and "non-viable" LS defines a unique NOGAD™ map for pts with NIDC.
208A  ABSTRACTS  -  Cardiac Function and Heart Failure

POSTER SESSION

1268  Cardiomyopathy: The Genetie Puzzle

Unfts II

Tuesday, March 20, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 3:00 p.m.-4:00 p.m.

1268-70  Association Between 11-Adrenergic Receptor Gene Polymorphism and Ventricular Tachycardia in Patients With Dilated Cardiomyopathy

G. Niwa, I. Shiga, M. Tsujii, A. Yamauchi, M. Watanabe, S. Takahashi, T. Ikeda. Y. Furuta, M. Miyamoto, Masahiko Shimizu, H. Kawada, N. Takekura, Mitsuhiro Yokoyama, Dept. of Internal Medicine, Kobe University School of Medicine, Kobe, Japan.

11-Adrenergic receptor (AR) stimulation plays an important role in the arrhythmogenesis of dilated cardiomyopathy (DCM). 11-Beta-blockers can prevent sudden death due to ventricular arrhythmias in patients with heart failure. Recently, a common functional 11AR gene polymorphism (Arg388Gly; C1166G) has been identified. In vitro functional studies have shown that Arg388Gly increases the activity for the Arg388AR (CC) were much higher than those for the Gly388AR (GG) with agonist stimulation. We hypothesized that this gene variant could be a genetic risk factor for ventricular tachycardia (VT).

Methods: To elucidate whether this genotype variant can be a genetic risk factor for DCM in Japan, we collected a case control study. We evaluated Arg388Gly polymorphism in human 11AR gene in 153 DCM patients and 157 age- and sex-matched control subjects by using polymerase chain reaction and the restriction fragment length polymorphism analysis. We further analyzed 133 DCM patient of whom underwent 24-Hour Holter monitoring. VT was defined as 2 consecutive ventricular ectopic beats. Results: There was no statistical difference of allele distribution between DCM and controls (C allele frequencies 0.71 vs. 0.70, p = 0.51). The logistic regression analysis revealed that the odds ratio of Arg388AR (CC) was 4.75 (p < 0.0001).

Conclusion: Our findings suggest that arg388gly polymorphism in human 11AR gene is associated with VT in patients with DCM. C allele could be a genetic risk factor for VT.

1268-71  Malignant Mutations in Hypertrophic Cardiomyopathy: A Rare Find Indeed

Michael J. Ackerman, David A. Lifton, Bernard J. Gersh, Rick A. Nishimura, A. Jamil Tajik, Mayo Clinic, Rochester, MN

Background: Hypertrophic cardiomyopathy (HCM) is a genetically and phenotypically diverse disease involving the cardiac sarcomere. Previous genotype-phenotype studies have identified three mutations (R403Q, R453C, and R719W) as highly malignant mutations of the beta-myosin heavy chain gene (MYH7). This study was designed to identify mutations in MYH7 and other sarcomeric genes in families with HCM and to determine their clinical significance.

Methods: We screened 249 near-consecutive, unrelated cases (103 female) of HCM by routine clinical screening for these malignant mutations has been suggested to identify members at high risk for sudden death.

Results: Of the 249 patients with HCM, 1268-72  A Common Variant of the AMPD1 Gene Predicts Improved Survival in Patients With Ischemic Cardiomyopathy, but Not Non-Ischemic Cardiomyopathy

Yoshikazu Yazaki, Glaucia Ghafari, Joseph B. Muhlestein, Tami L. Bair, Benjamin D. Home, Dale G. Renlund, Jeffrey L. Anderson, John F. Carlquist. LDS Hospital, Salt Lake City, UT. University of Utah, Salt Lake City, UT

Background: Reduced adenosine monophosphate deaminase (AMPD1) activity may result in increased circulating levels of adenosine. A recent study has demonstrated a survival benefit associated with carriers of a nonsense AMPD1 gene mutation (Gln217Ter) in patients with congestive heart failure (CHF), since adenosine may have cardioprotective actions, leading to increased coronary blood flow and ischemic preconditioning, we hypothesized that this survival benefit may occur preferentially in patients with non-ischemic cardiomyopathy (NIC).

Methods: To test this hypothesis, blood samples were drawn from 390 consecutive patients with a left ventricular ejection fraction (LVEF) ≤ 40% consisting of 210 in NIC and 180 in IC with a group separately.

Results: Of the IC patients, 153 (79.2%) were CC homozygotes, 54 (29%) were CT, and 3 (1.5%) were TT homozygotes. Of the n-IC patients 144 (93.7%) were CC, 31 (17.2%) were CT, and 5 (2.8%) were TT. Overall, mortality was 8.7% for T allele carriers compared to 1.9% for non-carriers (log rank statistic, 4.4, p = 0.036). In IC patients, T allele carriers showed a significantly longer mortality compared with non-carriers (14.0% versus 29.1%, log-rank=4.4, p = 0.036), but this was not the case in n-IC patients (2.8% versus 9.8%, p = 0.211).

Conclusion: The AMPD1 polymorphism predicts future mortality preferentially in patients with ischemic compared to non-ischemic cardiomyopathy. This may be related to the differing underlying pathophysiology of these two disease processes.

1268-73  Prevalence of Carrier Status in Relatives of Naxos Disease Patients

Nikos Protonotarios, Adelaina Tsattopoulou, Aris Anastasakis, Angelis Milios, Elias Bevardis, Angelos Rigopoulos, Artemisa Theopelis, Christofina McCoy, Christodoulos Siemidis, Pavlos Tsivgoulis, Department of Cardiology, University of Athens, Athens, Greece, J. Protonotarios Medical Center, Naxos, Greece

Background: Naxos disease is a syndrome of arrhythmogenic right ventricular cardiomyopathy with autosomal recessive inheritance. The responsible gene pathogenic is that of plakoglobin, a constituent of the cardiac sarcomere. The disease is characterized by a homozygous for the mutated gene, whereas neither the carriers (heterozygous) nor the percentage of gene prevalence in the communities where the disease appears were known until today (isolated communities phenomenon).

Methods: We assessed 58 subjects from 6 families with Naxos disease (4 from Naxos, 2 from Milos). Mean age was 35 years (range 5-86) and the mean number of relatives screened for the Naxos disease gene (plakoglobin) was 8 (range 1-17). We excluded 3 members of the 6 families who did not have Naxos disease as confirmed by exclusion. Screening for the Naxos disease gene (plakoglobin) was performed by a polymerase chain reaction (PCR) with specifically designed primers. Restriction enzyme analysis, using the restriction endonuclease BstBI, verifies the presence or not of the mutation.

Results: Of 86 Naxos disease family members, 14 subjects were affected and 44 had a normal phenotype. Of those 44, 34 were gene carriers. The gene carrier prevalence is up to 77%.

Conclusion: The prevalence of carriers for the Naxos disease gene comes to 77%, if we consider only relatives in Naxos and Milos. NAXOS CARRIERS ARE RISK FACTORS, UNTIL THEY GIVE THE MUTATION OR TO THE NEXT GENERATIONS. SCREENING FOR THE NAXOS DISEASE GENE (PLAKGLOBIN) COULD BE INITIATED IN SELECTED POPULATIONS IN A similar strategy that of β-thalassemia.

1268-74  QT Dispersion in Gene-Affected Members Without Hypertrophy in Familial Hypertrophic Cardiomyopathy Caused by Myosin-Binding Protein C Gene Mutation

Hideo Kitaoka, Toru Kubo, Makoto Okawa, Toshikazu Yabu, Takashi Furuno, Yoshinori Otsuji, Department of Internal Medicine, Niigata University, Niigata, Japan

Hypertrophic cardiomyopathy (HCM) is caused by several gene mutations of the cardiac sarcomere. However, it is unclear whether or not gene-affected members have electrically abnormal myocardium when they have not yet developed left ventricular hypertrophy (LVEH). QT dispersion (QTD) in surface ECG may reflect the abnormality of repolarization and can be a useful marker for electrically abnormal myocardium. QT dispersion, QTD and corrected QT (cQTD) were studied in eleven patients with HCM and sixteen family members (6 family members with positive gene abnormality and negative phenotype and 10 unaffected family members) from five families with HCM caused by myosin-binding protein C gene mutation (exon1BcG374T>C). Results: (1)QTD and QTD in patients with HCM were greater than those in other family members. However, there
were no significant difference in QTd and QTcd between members with positive gene abnormality and unaffected members (Table). There was good correlation between maximal wall thickness and QTd (r=0.86, p<0.001). Conclusion: Although QTd was pro- longed in patients with HCM, it was within normal limits in family members with positive gene abnormality and negative phenotype. QTd in patients with HCM caused by myosin-binding protein C gene mutation may relate to the degree of wall thickness.

**ORAL CONTRIBUTIONS**

872 Gender and Ethnic Differences in Heart Failure

Tuesday, March 20, 2001, 4:00 p.m.-5:00 p.m.
Orange County Convention Center, Room 204A

872-1 Racial Differences in Heart Failure Presentation but Not Therapy: Report From the UNITE-HF Multicenter Heart Failure Database


University of North Carolina, Chapel Hill, NC

Background: Heart failure is an important cause of morbidity and mortality in African-Americans but current clinical characteristics and treatment patterns of this group remain poorly defined.

Methods: To compare clinical aspects and medication use in African-American versus other races, data were analyzed on randomly selected patients seen in HF clinics at 11 institutions participating in the UNITE-HF Database between 11/16/98 - 6/17/00.

Results: Among the 454 patients analyzed to date with respect to race, a significant number were African-American (26%) and female (40%) with a mean age of 56 ± 14 and NYHA class of 2.6 ± 0.7. Left ventricular systolic dysfunction predominated (LVEF ≤ 40%). Medication usage was similar between African-American and other races: for ACE (91 vs 81%), diuretic (91 vs 86%), beta blocker (60 vs 55%) and digoxin (85 vs 89%) but use of calcium blocker was higher (24 vs 12%, p<0.001) in African-Americans.

Contrasts in other clinical characteristics are shown below:

<table>
<thead>
<tr>
<th>Race (N)</th>
<th>NTHA</th>
<th>LVEF</th>
<th>Age</th>
<th>African-</th>
<th>HTN</th>
<th>Etio</th>
</tr>
</thead>
<tbody>
<tr>
<td>African-American (172)</td>
<td>27±8 27±8 52±13</td>
<td>53%</td>
<td>71 78</td>
<td>28 30</td>
<td>2±6 3±6</td>
<td></td>
</tr>
<tr>
<td>Non-Mean/Am (382)</td>
<td>26±8 28±14 50±14</td>
<td>50</td>
<td>41</td>
<td>2±8 2±8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

BMI:body mass index, Etio=% ischemic etiology of HF, F=% female, HTN-% hypertension history

Conclusions: African-Americans with heart failure tend to be younger, more often female, more likely to have history of HTN and less likely to have IHD as origin of heart failure. In contrast to these findings, usage of ACE and beta blockers was similar between African-Americans and Non-African-Americans.

872-2 Differences in Clinical Characteristics and Outcomes Between African American and White Heart Failure Patients

Mark Alexander, Maria N. Ansari, Ali Tutar, Barry Massie, Kaiser Permanente, Division of Research, Oakland, CA, Center for Aging in Diverse Communities, University of California Berkeley School of Medicine, Berkeley, CA

Background: Several studies have noted differences in the characteristics and outcomes of African Americans (AA) with CHF compared to whites, including higher rates of hospitalization and (more variably) mortality in AA. However, these data were mostly derived from hospitalized patients or clinical trials with highly selected subjects. Relatively little is known about racial differences in unselected outpatients, particularly in populations where access to care is similar.

Methods: We identified a cohort of patients in the Northern California Kaiser Permanente Medical Program with new outpatient diagnoses of CHF between 7/1/96 and 8/31/97. Pts with prior CHF diagnosis or hospitalization or severe comorbidities (such as terminal cancer, ESRF, or dementia) were excluded. Hospitalization and mortality data were collected for up to 2 years (mean 21 months following the initial CHF diagnosis).

Results: The cohort included 361 Pts (13.3% AA, 86.7% whites). There was no racial difference in the age of men (68 yrs), but AA women were significantly younger than white women (60 vs 73 yrs), hypertension and diabetes were more frequent in AA, whereas CAD and atrial fibrillation were more common in whites. Similar numbers of AA and whites were treated with ACE inhibitors (81.3% and 80.2%) and beta-blockers (31.3% and 32.8%). Involvement of cardiologists was also similar. Proportional hazards models found there were no significant ethnic differences in 2yr cardiovascular mortality (AA 29.2%, whites 31%) or deaths (AA 12.5%, whites 12.1%). Risk of the composite endpoint of death or cardiovascular hospitalization was not different (HR=0.83, 95% CI=0.68-1.02).

872-4 Gender Differences in Heart Failure Clinical Characteristics and Therapy: Report From UNITE-HF Multicenter Heart Failure Database


Background: Potential differences in the clinical characteristics and outcome of males (M) and females (F) with cardiovascular disease remain of significant interest. Heart failure is an important cause of morbidity and mortality in F but current clinical trial data provide limited information concerning the characteristics and treatment patterns of M with heart failure.

Methods: The UNITE-HF investigators randomly enrolled 454 patients from their heart failure specialty practices between 11/16/98 - 6/17/00. Demographic, clinical and medication data were collected through a standard form set and analyzed through a computerized database.

Results: A significant number of patients enrolled were F (40%) and African-American (28%) with a mean age of 56 ± 14 and NYHA class of 2.6 ± 0.7. Left ventricular systolic dysfunction predominated (LVEF ≤ 40%). Medication usage differed between F and M with ACE (78 vs 84%, p=0.066) and digoxin (83 vs 91%, p=0.024) being less used, diuretic given more frequently (92 vs 86%, p=0.003) and beta blocker (57 vs 56%, p=NS) to a similar degree. Contrasts in other characteristics are shown below:

<table>
<thead>
<tr>
<th>Gender (N)</th>
<th>NTHA</th>
<th>LVEF</th>
<th>Age</th>
<th>African-</th>
<th>HTN</th>
<th>Etio</th>
</tr>
</thead>
<tbody>
<tr>
<td>M (273)</td>
<td>26±12 16±12</td>
<td>54±13</td>
<td>50</td>
<td>60</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>F (181)</td>
<td>26±12 16±12</td>
<td>54±13</td>
<td>50</td>
<td>60</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>NS</td>
<td>&lt;0.001</td>
<td>NS</td>
<td>0.35</td>
<td>0.045</td>
<td>&lt;0.01</td>
</tr>
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</table>

Ethnic% ischemic etiology of heart failure HTN-% hypertension history

Conclusions: Although previously described differences in comorbid conditions were present between AA and whites, there were no significant differences in adjusted hospitalization or mortality rates. This may have reflected more similar access to care and ACE inhibitor and beta blocker use in this UNITE HF outpatient cohort.
Conclusions: M and F with heart failure suffer in baseline characteristics and treatment patterns. LVEF was significantly higher in F. Females were less likely to receive ACEI and digoxin, but more likely to be on diuretic than M. Beta blocker use was similar. Potential impacts of these differences on outcomes will be explored.

ORAL CONTRIBUTIONS

877 Identification of Patients With Diastolic (Or Nonsystolic) Heart Failure

Wednesday, March 21, 2001, 8:30 a.m.-10:00 a.m.
Orange County Convention Center, Hall F4

8:30 a.m.

877-1 Autopsy Findings in Patients With Diastolic Versus Systolic Heart Failure
Shen-Li Tan, Hong H. Chen, William D. Edwards, Michele Senni, Margaret M. Redfield, Mayo Clinic and Mayo Foundation, Rochester, MN

Background: Heart failure (HF) is associated with normal systolic function in ~40% of cases. This study compared autopsy findings in patients with a diagnosis of diastolic HF (DHF) to those of pts with HF and systolic dysfunction (SHF) to evaluate differences in structure or histology. Secondly, as pts with DHF are less likely to have a clinical dx of coronary artery disease (CAD), we sought to determine if clinically unrecognized CAD was common in DHF.

Methods: Pts previously identified in two population-based studies of HF in Olmsted County, MN in 1991 (SHF and DHF) and 1996-1997 (DHF only) who had cardiac autopsies were included in this study. Of the 78 pts with SHF, 11 had autopsies. Of the 164 pts with DHF, 17 had autopsies.

Results: Patients with DHF who were older at dx (median age = 80 yrs, vs 72 yrs for SHF; p<0.05) and more likely to be female (50% vs 36% for SHF; p<0.01) had mean ejection fraction (EF) at dx of 52±10% in DHF and 24±4% in SHF. Clinical dx of CAD was present in 35% of DHF vs 45% of SHF. Hypertension was present in 75% of DHF vs 38% of SHF (p=0.001). Mean time from dx to death was 16 months (DHF) and 17 months (SHF). Of the 17 subjects with DHF, 8 had repeat echo prior to death with EF=45% confirmed in 7. Immediate causes of death (CAD, HF, intxn, pulmonary embolus, arrhythmia) were similar in DHF and SHF. Of the 8 pts with SHF and Grade III/IV CAD, 4 (50%) had no clinical dx of CAD. Of the 11 pts with DHF and Grade III/IV CAD, 5 (45%) had no clinical dx of CAD.

Autopsy results

<table>
<thead>
<tr>
<th>SHF (n=11)</th>
<th>DHF (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart weight (g)</td>
<td>464±343 vs 577±139</td>
</tr>
<tr>
<td>LVH</td>
<td>73% vs 82%</td>
</tr>
<tr>
<td>LV dilatation</td>
<td>73% vs 72%</td>
</tr>
<tr>
<td>Atrial dilatation</td>
<td>50% vs 57%</td>
</tr>
<tr>
<td>Diffuse fibrosis</td>
<td>45% vs 35%</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>8% vs 6%</td>
</tr>
<tr>
<td>Grade III/IV CAD, (%)</td>
<td>8 (73%) vs 11 (65%)</td>
</tr>
</tbody>
</table>

*p<0.05 vs SHF; Left ventricular hypertrophy (LVH). Left ventr. (LV) conclusion: At autopsy, pts with DHF have less LV dilatation but similar prevalence of LVH, atrial enlargement, and CAD. DHF was not associated with a higher incidence of diffuse fibrosis or amyloid deposition. Clinically unsuspected CAD was common in both groups. While other age related morphologic changes can not be excluded, concentric LVH and CAD are the primary structural abnormalities associated with DHF.

8:45 a.m.

877-2 Can We Diagnose Diastolic Heart Failure by Transthoracic Echocardiography?

Mark C. Petrie, Lynne Ceranosa, John J. V. McMurray, Western Infirmary of Glasgow, Glasgow, United Kingdom

Background: Though it is often assumed that a high proportion of patients with heart failure but preserved left ventricular (LV) systolic function have "diastolic heart failure" it is not clear how diastolic function should be measured. A variety of echocardiographic criteria have been proposed. Our aim was to determine the concordance of different "diagnostic" criteria for diastolic dysfunction in patients with suspected heart failure but preserved LV systolic function.

Methods: The Concordance of different "diagnostic" criteria for diastolic dysfunction were compared. The discordance of criteria was determined by the number of pts with a discordant dx, the number of pts with a concordant dx with different criteria, and the number of pts with a concordant dx with all criteria.

Results: 103 consecutive pts referred for general practitioners and long term treatment, and 103 consecutive pts referred for general practitioners with suspected heart failure to an outpatient-based direct access echocardiography service were studied. Each patient had a transthoracic echocardiogram. All patients had assessment of LV systolic function (both qualitative and quantitative [Kilson's biplane and M-Mode]) and the following putative indicators of diastolic dysfunction measured: E/A ratio, IVRT, AFF and E/A/T. Reference ranges for these diastolic indicators were taken from recently published studies (Mantero et al, Framingham and the European Working Group). The concordance of values out-with these recommended ranges was sought. Results: 109 of 159 participants had suspected heart failure in the absence of left ventricular systolic dysfunction, valvular heart disease or AF. Concordance of abnormalities of putative indicators of diastolic dysfunction was poor (see Table). Conclusion: There is poor concordance of putative indicators of diastolic dysfunction in patients with suspected heart failure but preserved LV systolic function. As yet there are no ref-}

2-D Findings

<table>
<thead>
<tr>
<th>E/A</th>
<th>IVRT</th>
<th>AFF</th>
<th>E/A/T</th>
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<tbody>
<tr>
<td>Mantero</td>
<td>40-1/5/8; IVRT</td>
<td>1/5/8; Aff</td>
<td>40-1/5/8; E/A/T</td>
</tr>
<tr>
<td>Framingham</td>
<td>40-1/5/8; IVRT</td>
<td>1/5/8; Aff</td>
<td>40-1/5/8; E/A/T</td>
</tr>
<tr>
<td>Orange County</td>
<td>40-1/5/8; IVRT</td>
<td>1/5/8; Aff</td>
<td>40-1/5/8; E/A/T</td>
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Doppler Findings

<table>
<thead>
<tr>
<th>E/A</th>
<th>IVRT</th>
<th>AFF</th>
<th>E/A/T</th>
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<tbody>
<tr>
<td>Mantero</td>
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<tr>
<td>Framingham</td>
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<td>Orange County</td>
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9:15 a.m.

877-4 BNP Can Differentiate Normal LV Function From Diastolic Dysfunction in Patients With Clinical Congestive Heart Failure

Pedra B. Krishnaswamy, Emily Lubien, Ramnik Kastanopoulos, Judy Hope, Alan S. Maisel, VA San Diego Health Care System, San Diego, CA

Background: As many as 30% - 40% of patients who present with symptoms of congestive heart failure have normal LV systolic function. A definite diagnosis of CHF in the presence of preserved systolic function is difficult, especially in an elderly population with chronic lung and renal disease. We hypothesized that BNP can be used as a diagnostic test in these patients who have signs and symptoms of heart failure, but a normal ejection fraction. Methods: 400 patients with either known or unknown LV function were recruited over a period of one year. Patients were determined to have congestive heart failure based on Framingham criteria, hospitalization for CHF, and response to treatment. BNP levels were measured by a point-of-care immunoassay (Biosite Diagnostics, La Jolla, CA) and echocardiogram was performed. Results: 25% of the patients (n=86) had diastolic dysfunction by standard echocardiographic criteria. 41% of the patients with diastolic dysfunction (n=46) had clinical congestive heart failure. The BNP levels in this group of patients was 475±65 pg/ml compared to BNP levels in patients who had clinical congestive heart failure (n=41) vs patients with normal LV function (n=30). Conclusion: Thus BNP is able to reliably delineate patients with diastolic dysfunction in patients presenting with clinical CHF.
Diastolic Heart Failure or Misdiagnosis?
Mark C. Petrie, Lynne Caruana, John J. V. McMurray. Western Infirmary of Glasgow, Glasgow, United Kingdom

Background: Patients with suspected heart failure but preserved left ventricular systolic function are often thought to suffer from "diastolic heart failure". We sought to characterise the clinical features of this patient group to determine if they had other potential causes for their symptoms. Methods: 159 consecutive patients referred by general practitioners with suspected heart failure to an outpatient-based direct access echocardiography service were studied. A full clinical history (including shortness of breath, ankle oedema, paroxysmal nocturnal dyspnoea, angina and chronic pulmonary disease) was taken. Each participant also had a transthoracic echo recording, an electrocardiogram and measurement of body mass index and pulmonary function tests. Results: 159 of 159 participants had suspected heart failure in the absence of left ventricular systolic function, valvular heart disease or AF. Of those 100, a third of patients were either obese or very obese. Half had a significant reduction in FEV1 (70 per cent or less) and 89 per cent had a PEFR less than or equal to 70 per cent of normal. 30 per cent patients either had a history of angina, a myocardial infarction or had undergone coronary artery bypass grafting. Only 7% of the patients in this study with a diagnosis of heart failure but preserved left ventricular systolic function had sufficient alternative explanations for their symptoms eg obesity, lung disease and myocardial ischaemia. For that reason the diagnosis of "diastolic heart failure" need not be invoked and management should target these alternative conditions.

At the Orange County Convention Center, Hall A4

1308-6 Screening for Diastolic Heart Failure Among Elderly Patients: Experience From a Randomised, Multicentre, Clinical Trial Comparing Perindopril and Placebo: The PEP-CHF Study, UK Centres
Jackie Taylor, John G. F. Cleland, Michael Levy, Christopher Gray, Tumpa Ramnath, Eve Shannon, Nick Wnisnioti, John Buxton, Emma Owen, Annie Spinksley, Anita Dinin. University of Hull, Kingston upon Hull, United Kingdom, Royal Infirmary, Glasgow, United Kingdom

Several multicentre studies are investigating the effects of treatment on patients with heart failure thought to be secondary to diastolic dysfunction. Most of these studies define 'diastolic heart failure' as a clinical diagnosis of heart failure in the absence of left ventricular systolic dysfunction. Recent reports have suggested that many such patients may not have cardiac disease as the cause of their symptoms and signs. The Perindopril in Elderly People - Chronic Heart Failure (PEP-CHF) trial aims to randomise 1,000 patients aged >70 years who have had a recent cardiovascular hospitalisation, who exhibit at least 3 pre-specified clinical features of CHF and who fulfil at least two out of four echo criteria confirming the presence of cardiac disease, including: a) mitral regurgitation, b) left atrial dilatation, c) left ventricular hypertrophy, and d) Doppler criteria, with atrial fibrillation being regarded as equivalent to a positive Doppler finding. Thus PEP-CHF in contrast to other studies of 'diastolic heart failure' requires evidence confirming cardiac dysfunction rather than merely the absence of systolic dysfunction. We screened a total of 1568 consecutive patients of which 773 had echocardiograms resulting in the randomisation of 68 patients by August 2000: 96% of patients were excluded. 96% because heart failure was excluded on further evaluation, 25% because they were too frail to walk even with a walking aid, 35% patients were excluded because they had significant systolic dysfunction (WM<1.4). 172 had valvular disease or uninterpretable echocardiograms, serious co-morbid disease excluded 153 patients and 78 patients had major cognitive impairment. Some patients had >1 exclusion criterion. This report highlights the difficulties encountered in studying a frail elderly population with heart failure. Using "positive" echo criteria for diastolic dysfunction rather than simply the absence of systolic dysfunction greatly reduces the proportion of patients with diastolic heart failure compared to that reported in some series. More studies in older, more representative patient populations are required.

1308-4 Aortic Distensibility is Independently Correlated With Exercise Tolerance in Patients With Dilated Cardiomyopathy
Stefano Biondace, Marilantonietta Cisoia, Lorenzo Franceschin, Luisa Zanolla, Giorgio Golia, Piero Zardini, Andrea Ross. Universita' di Verona, Verona, Italy

Background: Peak exercise oxygen consumption (VO2) is crucial for the prognostic assessment of patients with congestive heart failure, but its hemodynamic determinants are still poorly understood. Aortic elastic properties play an essential role in determining left ventricular (LV) function. An increased aortic stiffness rises LV afterload leading to an increased LV work. Aim of this study was to assess the relationship between aortic distensibility measured by pulse wave velocity (PWV) and exercise tolerance expressed by peak VO2 in patients with dilated cardiomyopathy. Methods: 34 patients with clinical diagnosis of dilated cardiomyopathy (age 61.5±14 years, 25% female, mean exercise tolerance (EF) 24±12%) were selected. LV stroke volume (SV), LV volumes and EF, mitral E, E/A and E wave deceleration time (DT) were measured by Doppler-echocardiography. PWV was calculated as the time (t) taken by the pulse wave to travel from the descending thoracic aorta to the abdominal aorta by Doppler flow recordings and the distance (d) travelled by the pulse wave was measured over the body surface as the distance between the two recording sites: PWV=t/d (m/s). To measure peak VO2 bicycle exercise testing with expiratory gas exchange monitoring was performed. Results: In 34 patients with dilated cardiomyopathy aortic distensibility (r=0.45, p=0.008) and exercise tolerance (peak VO2, r=0.45, p=0.008) were independently correlated with peak VO2 (R2=0.32). Conclusion: Aortic distensibility affects peak VO2 in patients with dilated cardiomyopathy. The degree of aortic distensibility impairment might independently predict the exercise tolerance in these patients.

1308-47 A Short Course of L-Arginine Improves Exercise Capacity and Endothelial Function in Chronic Heart Failure: A Prospective, Randomised, Double Blind Trial
Mohamed Youssifudin, Marcus Fatthi, Walid Shamiun, Zahir Yousef, Michael Makber, Mohammd Aamran, Nicholas Banner, Michael Kemp, James Hooper, Andrew J. S. Coats. National Heart and Lung Institute, London, United Kingdom, Kings College, London, United Kingdom

Background: L-arginine, a precursor of nitric oxide, has been shown to improve endothelial function. The effects of l-arginine in patients with chronic heart failure (CHF) are not known. Methods and Results: In this prospective and double-blind study we ran...
chronotropic incompetence was present in 87 patients (59%). Results: Cardiopulmonary exercise capacity was higher in CHF-pts on chronic BB therapy with a %-year mortality of 2.4±0.1 vs 2.1±0.5, p<0.05). Maximal respiratory exchange ratio did not differ between the groups (2.0±0.5, 2.1±0.5; p=0.6), medications, resting heart rate (71±10, 68±13; p=0.42), mean blood pressure (81±14, 80±14) left ventricular ejection fraction (46±12, 57±19%: p=0.89), and baseline brachial artery diameters (5.75±0.68, 5.26±0.76mm: p=0.56) were similar in both l-arginine and placebo groups. A one-week treatment with l-arginine has resulted in a significant increase in exercise duration (49±8 vs 44±8: p=0.04 vs 81±65 vs 51±22: p=0.03), anastomotic threshold (12.3±3.1 vs 13.5±3.6: p=0.04) VO2AT (21.5±5 vs 24.3±9: p=0.01 vs 21.5±7 vs 22.6±7: p=0.24) and flow-mediated dilatation of the brachial artery (2.3±2.3 vs 3.2±1.1: p=0.005) vs 1.5±2±2.2 to 2.3±2.2: p=0.1) in l-arginine group compared to placebo. Conclusion: Improved exercise function with l-arginine is associated with improved endothelial function.

**1308-48** 
**Chronic**[T]ropic Incompetence Is Related to Reduced Exercise Capacity and Increased Mortality in Congestive Heart Failure

Hans P. Brunner-La Rocca, Christoph Scharf, Christoph Schalcher, Erwin Oechslin, Wolfgang Kwonkiewicz. Cardiology, University Hospital Zurich, Zurich, Switzerland

**Background:** Heart rate response to exercise has been shown to be reduced in patients with chronic heart failure (CHF). However, results are controversial regarding its effect on exercise performance. In addition, no data are available whether chronotropic incompetence is related to mortality in CHF.

**Methods:** 147 patients with CHF (EF<40%, age ≥60 years) were evaluated during an exhaustive cardiopulmonary exercise testing. Chronotropic response was defined as percentage of predicted maximal heart rate (220-age) achieved. Chronotropic incompetence was defined as maximal heart rate <75% of predicted maximum. Patients were followed up prospectively for 21±1 months. Results: Chronotropic incompetence was present in 67 patients (59%). There was no clear relation to medication including beta-blockade. Patients with chronotropic incompetence had a 2-year survival of 75% which was significantly worse compared to patients with normal baseline heart rate response to exercise (89%, p<0.05). These results were not influenced by the presence of diabetes and ischemic etiology or by the use of ACE inhibitors (93.9% vs 85.1%, p=0.1368). Conclusion: Chronotropic incompetence is related to mortality in CHF.

**1308-49** 
**Different Prognostic Value of the Oxygen-Uptake and the Ventilatory Efficacy in the Risk Stratification of Heart Failure Patients With and Without Chronic Betablocker Therapy**

Anneli K. Gitz, Caroline Bergmeyer, Armin Schwarz, Andreas Klöckowski, Thomas Kleemann, Matthias Bangert, Jochen Songs, Herzcenter Ludwigshafen, Ludwigshafen, Germany

**Background:** The maximal oxygen-uptake (peak VO2), the oxygen-uptake at the anaerobic threshold (VO2 AT) and the ventilatory efficacy (VE/VCO2-Slope) are used in the risk stratification of patients (pts) with chronic heart failure (CHF). It is unknown if the prognostic value of these parameters is influenced by the beneficial effect of chronic betablocker (BB) therapy in CHF. Methods: During 1996 and 1998 we performed cardiopulmonary exercise tests with gas-exchange-measurements in 227 CHF pts (age 63±10 years, LVEF 29±8%, NYHA 3±3, IIb: 38%: 112 CAD: 91 dilated cardiomyopathy: 24 others) who consecutively had been included in a heart failure registry. We measured peak VO2 breath-by-breath (mll/kg/min), the anaerobic threshold (VO2AT, ml/kg/min) and the ventilatory efficacy (VE/VCO2-Slope). We selected peak VO2>14 ml/kg/min, VO2AT<11 ml/kg/min and VE/VCO2-Slope>35 as threshold values for high risk.

The median follow-up time was 651 days. We evaluated the prognostic value of these parameters in CHF-pts who did (56/227, 24%) or did not (171/227, 76%) receive chronic BB therapy. Results: Cardiovascular exercise capacity was higher in CHF pts with BB as compared to those without BB therapy (peakVO2= 16.5±4 vs 14.6±2.5 ml/kg/min, p=0.002 and VO2AT= 12.1±3.5 vs 11.0±3.5 ml/kg/min, p=0.01). In CHF-pts without BB therapy the oxygen uptake and the ventilatory efficacy discriminated patients with high risk for early death within 6 months. The combination of VO2AT and the VE/VCO2-Slope identified high risk CHF pts without chronic BB without therapy with a 3-year mortality of 38.4%. In CHF-pts with BB therapy these prognostic factors did not identify patients with increased 3-year mortality.

**1/2 year mortality in CHF**
Hormone Replacement Therapy Predicts Outcome in Women With Advanced Heart Failure.

JoAnn Lindenfeld, Jalal K. Ghali, Heidi J. Krause-Steinrauf, Surai Thaneemit-Chen, Rhonda L. Larsen, Brian D. Loeser, Yves D. Rosenberg, For BEST Investigators.

University of Colorado Health Sciences Center, Denver, CO

Background: The effect of hormone replacement therapy (HRT) on prognosis in heart failure in women is unclear. We sought to determine if the use of HRT predicts an improved outcome in women with advanced heart failure when other important risk factors for mortality are included in the analysis. Subjects and methods: A total of 232 women aged 50 or older. Of these, 95 (22%) were using HRT at baseline. HRT was a predictor of survival when adjusted for known baseline risk factors: New York Heart Association (NYHA) functional class, coronary artery disease (CAD), left ventricular ejection fraction (LVEF), history of diabetes, creatinine, and plasma norepinephrine (PNE). Age, race, and diabetes were not predictive of survival.

Conclusions: HRT predicts improved survival in women with advanced heart failure even when accounting for other known important predictors of prognosis. These data suggest the need for a prospective study of the use of HRT in women with heart failure.

Predicators of Survival in Women With Advanced Heart Failure

Jalal K. Ghali, Heidi Krause-Steinrauf, Yves Rosenberg, Rhonda Larsen, Brian D. Loeser, JoAnn Lindenfeld. Cardiovascular Institute of Louisiana, Shreveport, LA

Background: Limited data are available on survival of women with advanced heart failure. Women Interestingly, age, race and the presence of diabetes do not appear to affect survival.

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Prevalence and Clinical Characteristics of Hypertrophic Cardiomyopathy Caused by Actin Mutations

Saad A. Mohiddin, Judith Weikel, Elieha M. McMan, David A. Begley, Lamie Fonarowicz. NIH, National Institute of Health, Bethesda, MD

Introduction: Hypertrophic cardiomyopathy (HCM) is caused by mutations in one of nine sarcomeric genes. Actin is a critical component of the thin filaments of the contractile apparatus of the heart; 80% are encoded by the cardiac actin gene (ACTC) and 20% by the ACTN3 gene (dystrophia myotonica which has 90% homology with cardiac actin). Mutations in cardiac actin (ACTC) may interfere with either generation or transmission of contractile force to result in HCM or dilated cardiomyopathy. We examined the frequencies with which mutations in ACTC and ACTN3 cause HCM.

Methods: DNA from 372 unrelated HCM patients was screened for mutations in ACTC and ACTN3 by single-stranded conformation polymorphism. Non-consomers were sequenced. Following mutation detection, further family members were evaluated by echocardiography and magnetic resonance imaging.

Results: Two novel missense mutations were detected in highly conserved regions of ACTC. Both mutations were absent from DNA in 200 unrelated normal subjects (400 chromosomes); a Val606 substitution was sporadic (absent in both parents) and a Leu219His substitution was present in several affected family members. No sporadic and familial cardiac actin mutations were associated with an unusual and previously undescribed HCM morphology characterized by apical hypertrophy and trabeculation. The distinctive morphoscopy resembles venous non-compliance that may result from impaired ventricular development. Several nucleotide substitutions were detected in the 6 exons of ACTC: none, however, altered translation.

Conclusions: (1) ACTC mutations cause spontaneous and familial HCM; (2) ACTC mutations are responsible for about 1% of HCM, but should be suspected in patients with apical HCM; (3) ACTC may be critical for normal myosin filament contraction during development; and (4) ACTC mutations are not a common cause of HCM.

The Val606Met Mutation of the Cardiac B-Myosin Heavy Chain Gene in Patients With Hypertrophic Cardiomyopathy Is Associated With a High Risk of Sudden Death at Young Age

Ole Haustrup, Henning Blundgaard, Paul S. Andersen, Lars A. Larsen, Jens Vuust, Michael Christensen, Keld Kielso. National University Hospital, Copenhagen, Denmark, Statens Serum Institute, Copenhagen, Denmark

Objectives: The purpose of this study was to identify families with hypertrophic cardiomyopathy (HCM) associated with the cardiac b-myosin heavy chain (MYH7) gene Val606Met mutation, and characterise the phenotype with specific focus on the prognosis associated with the mutation. Background: The insertion/deletion (I/D) angiotensin-I converting enzyme (ACE) gene polymorphism is associated with increased plasma ACE levels and increased left ventricular hypertrophy (LVH) in hypertrophic cardiomyopathy (HCM). We sought to determine the influence of the I/D genotypes on LV mass, systolic and diastolic function, and myocardial perfusion by exercise thallium scintigraphy.

Methods: Case-control study of Myosin and ACE genotypes in patients with typical HCM and normal hearts. Patients with HCM were randomly divided into 2 groups. Group 1 patients were genotyped for I/D polymorphism (p<0.05). Group 2 patients were genotyped for the Val606Met mutation (p<0.05). LV mass-index (LVMI) was not significantly different between the groups. LV mass-indexes were present in 111 (79%) patients in group 1 and 131 (87%) patients in group 2 (p<0.05). There was a significantly greater proportion of the DD genotype in group 1. Patients with DD genotypes (p<0.05) had lower exercise ejection fractions (67±10% vs. 83±13%, p=0.05), and lower MVO2 (17±5 vs. 25±9, p=0.05) compared to patients with WT genotypes. Patients tended to be younger (41 ±10 vs. 51 ±14, p<0.05).

Conclusions: ACE DD genotype is associated with impaired exercise systolic function and exercise performance. The etiology of the LV dysfunction is uncertain but does not appear to be directly related to LV mass. Further studies are necessary to determine if the findings are due to ACE-induced increased myocardial fibrosis and fiber disarray, and whether ACE inhibition reverses the abnormalities.

Isoproterenol-Induced Sudden Deaths in Transgenic Mice Expressing a Troponin T Mutant Linked to Familial Hypertrophic Cardiomyopathy


Background: The cardiac troponin T (TnT) 79N mutation has been linked to familial hypertrophic cardiomyopathy and a high incidence of sudden death in humans, despite causing little or no cardiac hypertrophy. To study the mechanisms of sudden death caused by this mutation, we generated transgenic mice in which mouse TnT 79N was replaced with either human wild-type (WT) or mutant (79N) TnT. In vitro skinned fiber studies showed that the 79N mutation caused higher Ca2+ sensitivity of force. Here we examine the cardiac contractility and ultrastructure of this mutant FHC model in vivo. Methods: TnT knockout mice (n=43) and TnT 79N mice (n=37) were evaluated for cardiac contractility at 3 months, ECG, 1.5-Doppler echocardiography at baseline and after high (1.5 mg/kg) or low (0.3 mg/kg) isoproterenol (ISP). Results: 79N mice had a lower heart rate (79N 322±7 vs. WT 660±10 bpm, p<0.05) but similar blood pressure (112±2 vs. 116±2 mm.Hg, p=ns). In WT mice, we observed isolated systolic and diastolic function. The 79N mice showed depressed cardiac contractility in response to ISP (1.5 mg/kg) compared to WT mice. Conclusion: 79N mice exhibit significant cardiac contractility changes in response to ISP.

The 79N Mutation Results in Hypertrophic Cardiomyopathy

Michael Christiansen, Keld Kjeldsen. National University Hospital, Copenhagen, Denmark

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**UVEO (mm)**
- 3.5 ± 0.2
- 3.8 ± 0.1
- 4.6 ± 0.2
- 5.4 ± 0.1 * 0.48

**UVEO (mm)**
- 2.1 ± 0.1
- 2.3 ± 0.1
- 3.3 ± 0.1 * 0.83

**IVS+PW (mm)**
- 1.1 ± 0.1
- 1.3 ± 0.1
- 1.9 ± 1
- 1.9 ± 1 * 0.1

**VCF (sec-0.5)**
- 2.7 ± 0.2
- 2.9 ± 0.2
- 2.2 ± 0.2
- 2.5 ± 0.1 * 0.82

MMO = mean arterial pressure, **W**t = whole body weight, **L**v = left ventricular weight, **IVS** = interventricular septum, **PW** = posterior wall thickness, **VCF** = rate corrected velocity of circumferential shortening, *p < 0.05 compared to respective Sham groups, #p < 0.05 compared to nonoperative **1** group, **A** = p value, interaction between **A**CF and genotype by **3** way ANOVA, n = 6-8.

This finding supports the hypothesis that ANP protects the heart from developing both LV and RV enlargement in response to volume overload. Echo data indicated that cardiac function did not differ between two genotypes in either sham or ACF mice.

1310-01 Effects of Xylazine/Ketamine Versus Avertin Anesthesia on Left Ventricular Structure and Function in Normal Mice

Chari V. T., Hart, John C. Barnett, Jr., Maroant Redfield, Mayo Clinic Rochester, MN

**Background:** Assesment of cardiac function in murine models with altered genotype is crucial if the influence of genetic manipulation on cardiovascular physiology is to be fully appreciated. Evaluation of left ventricular (LV) function in the conscious state is not yet well established.

**Objectives:** While advances in murine transgenic technology offer an opportunity for the development of novel experimental models to characterize diverse aspects of chronic post-infarct myocardial remodeling and its relation to function, we have established this mouse model of chronic heart failure.

**Methods:** Eight weeks after ligature of the left coronary artery or sham operation (S), 3- to 5-month-old male Swiss Webster mice were subjected to echo-cardiographic examination under tri-ketone (LV pressure/volume (PV) conductance catheter. Results: The total mortality at 8 weeks was 17%, which of the early post-operative mortality was 7%. Among surviving animals at 8 wks, two distinct LV remodeling phenotypes with distinctly different functions were identified: hypertrophic (H) and dilated (D) hearts. Compared to S: LV mass/chamber volume index was increased by 134% and decreased by 35% in H and D respectively, and LV volume was reduced by 42% and increased by 100% in H and D respectively. Stroke volume (SV) and ejection fraction (EF) were reduced in both H and D (Table). The current study tested the hypothesis that ANP protects the volume overloaded heart. The current study tested the hypothesis that ANP protects the volume overloaded heart.

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**Conclusions:** XK results in non-physiologic heart rates in the mouse. This bradycardia is associated with increases in preload (LV end-diastolic dimension) and increases in load-dependent indices of systolic function. As murine cardiovascular physiologic assessment matures, increased attention to methodology is needed to ensure that data are collected under (near) physiologic conditions.

**1310-05 Comparison of Two Methods to Determine Left Ventricular Pressure-Volume Relationships in Mice**

Marc D. Feldman, Rebecca Blackwood, Danny Escobedo, Gregory L. Freeman, University of Texas Health Science Center, San Antonio, TX

**Background:** The generation of left ventricular (LV) pressure-volume relationships in the in situ murine cardiovascular system is important to define functional phenotype. There are two methodologies to generate this information, dual frequency conductance (volume) and 2-dimensional crystals. There have been no comprehensive studies of these two methods.

**Methods:** Open-chest C57Bl mice (n=12) were mechanically ventilated. The LV was instrumented with epicardial 2-dimensional crystals and a dual frequency pressure-volume (conduction) catheter. A flow probe was placed on the thoracic aorta. Baseline pressure-segment and volume relations were acquired at steady state and during transient occlusion of the inferior vena cava.

**Conclusions:** Heart rate was 477 ± 6 bpm, maximal LV pressure was 73 ± 9 mmHg, and end-diastolic pressure was 6 ± 2 mmHg. A comparison of the conductance and crystal derived data is shown on the table and includes V0, V0 (end-diastolic volume, µl), V0 (end-systolic volume, µl), SV (stroke volume, µl), E (end-systolic elastance, mmHg/l), and E (end-diastolic elastance, mmHg/l), and V0 (extrapolated volume intercept, µl). Although the mean E0 and E0 were similar, there were poor correlations of individual mice between the two methods (SV m=0.45, E0=0.26).

**Conclusions:** Volume detected with the 2-dimensional crystals are greater than conductance method volume detected under the pressure of their respective methods. Although the mean E0 was similar between the techniques, individual values did not correlate.

**1310-06 Cardiac Enlargement in Response to Volume Overload is Exaggerated in Mice with Homozygous Deletion of the Atrial Natriuretic Peptide Gene**

Istvanhely M., Gilbert J. Henry, Ji An Heng, Suzanne Upari, Yu-Fu Lin, University of Alabama at Birmingham, Birmingham, AL

Atrial natriuretic peptide (anp) is overexpressed in the heart of cardiac hypertrophied mice and is thought to have an antihypertrophic effect in heart. The current study tested the hypothesis that anp protects the volume overloaded heart from developing hypertrophy. Ablation of anp (anp−/−) mice and mice with homogenously deletion of the anp gene (anp0/0) underwent placement of an aorto-caval fistula (Acf) or sham surgery (Sham) and were subjected to echo-cardiographic examination under tricloporan anesthesia at 2 weeks. ACF shunting assessed by a microalterior technique was similar at 1/1.0.

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Background: Measurements of LV function in large mammals are well described but these sophisticated techniques are often overlooked in murine studies which have near a nullifiy of analyzing the effects of genomic manipulation on cardiac function. The goal of this study was to address which indices of LV function were most sensitive to change in various conditions.

Methods: LV function was assessed in vivo in isolated mouse hearts by echocardiography and also by LV catheterization using 1.4 MHz tipped, biplane, continuous wave Doppler transducers (39 MHz for LV systolic function) and during atrial pacing at a 1HF (1 kHz/30 G Hz beats/min) which we used to increase inotropy by augmentation of the force-frequency relation. Preload independent parameters, such as stroke volume (MaxS) and slope of dp/dt max-EDV relation (dp/dt EDV), were measured during preload reduction by IVC occlusion as well as standard parameters.

Results: See the table.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MaxS</th>
<th>dp/dt EDV</th>
</tr>
</thead>
<tbody>
<tr>
<td>5F</td>
<td>4.12±0.2</td>
<td>0.62±0.2</td>
</tr>
<tr>
<td>13F</td>
<td>7.63±0.4</td>
<td>1.02±0.2</td>
</tr>
</tbody>
</table>

Conclusions: These studies demonstrated that independent indices of LV function were most sensitive to change in LV contractility in mice and ZPS failed to show this significant change. Moreover, HR has a substantial effect on murine LV performance and must be considered in the evaluation of cardiac function.
pressure and systolic blood pressure may be particularly beneficial. After controlling for diastolic blood pressure and other risk factors, pulse pressure was not well as with a 23% increase in risk of heart failure and a 19% increase in risk of stroke among older adults being treated for isolated systolic hypertension. In those patients, monitoring of pulse pressure during anti-hypertensive treatment should be a useful tool for risk stratification, and utilizing therapies that lower both pulse pressure and systolic blood pressure may be particularly beneficial.

1311-72

Is Aortic Valve Sclerosis a Manifestation of Atherosclerosis?

Jignesh S. Shah, Michael J. Wade, Abul Huissain, Ajqul Ahmed, Paul Sheahan, Paul Krier, Prabhakara S. Hegdejar, Veterans Affairs Medical Center, Syracuse, NY, SUNY Upstate Medical University, Syracuse

Background: Prior studies have shown that aortic valve sclerosis (AVS) is associated with increased cardiovascular events. It has been suggested that AVS is a manifestation of atherosclerosis. However, its association with atherosclerotic diseases such as peripheral vascular disease (PVD) or cardiac artery stenosis (CAS) has not been studied.

Methods: We assessed 2411 consecutive echocardiograms performed at our institution between January 1994 and December 1995 for the presence of AVS without clinical information. Of the 805 patients with AVS for whom information on predefined variables was available, 280 had low coronary artery disease (+AVS+CAD) and 525 did not (+AVS-). We compared the prevalence of PVD and CAS between the above two groups and also 244 age matched controls with neither AVS nor CAD (+AVS-)

Results: There was no difference in the prevalence of symptomatic PVD among the +AVS+ and +AVS- groups (11.5% vs. 11.0%, p=.96). Similarly, the CAD rate between the two groups was not significantly different (+AVS+CAD-0.2%, +AVS- 

Conclusion: These results indicate that pulse pressure is a useful marker of risk for heart failure and stroke among older adults being treated for isolated systolic hypertension. In those patients, monitoring of pulse pressure during anti-hypertensive treatment should be a useful tool for risk stratification, and utilizing therapies that lower both pulse pressure and systolic blood pressure may be particularly beneficial.

OR AL CONTRIBUTIONS

886

Tachycardia-Mediated and Other Cardiomyopathies: Toward a Better Understanding

Wednesday, March 21, 2001, 10:30 a.m.-Noon
Orange County Convention Center, Hall F5

886.1

Reduced Longitudinal Myocardial Contraction and Relaxation Are Related to the Onset of Congestive Heart Failure Patients With Primary Cardiac Amyloidosis

Jun Koyama, Patricia A. Ray, Rayn Davidson, Rodney H. Felix, Boston Medical Center, Boston, MA

Background: Cardiac amyloidosis is an infiltrative cardiomyopathy characterized by heart failure (CHF) with normal or near normal fractional shortening. It is generally thought that CHF is due to diastolic dysfunction, but it is possible that systolic dysfunction is underestimated by standard echocardiographic measurements.

Methods: Twenty-seven consecutive biopsy-proven patients with primary amyloidosis were examined by pulsed Doppler tissue imaging (DTI). Eighteen had evidence of heart involvement, of whom 9 had clinical LVH. Nine patients had non-cardiac amyloidosis. Sample volumes were placed on basal and mid-posterior walls in parasternal long-axis view, and were placed on basal and mid-ventricle at interventricular septal, lateral, infero-

Results: With TIC, MAA, S-L, and C-C at ED increased by 36±1456, 25±12%, and 9±230 min. for 15i6 days) sufficient to develop tachycardia induced cardiomyopathy (TIC) and MR. MA segmental contraction was defined as percent difference between max and min length. MA area (MAA) and MA septal-lateral (S-L) and commissure-commissure (C-C) diameters were computed from 3-D marker coordinates at end-diastole (ED) and end-systole (ES). MAA area increase in TIC was primarily due to S-L diameter augmentation; excessive chronotropic demands require compensatory reductions in contractility in order to balance energy requirements.

Results: Despite a normal fractional shortening in each group, the L-MVG of S-w was increased in CHF compared both to normal and cardiac amyloidosis without CHF. In contrast to the S-w, L-MVG of E-w differed significantly among all 3 groups of patients (+p<0.05) and was slightly increased in CHF patients.

Conclusion: In amyloidosis, decreased tissue Doppler E-w is an early sign of cardiac involvement. The causes of CHF is associated with a significant impairment of longitudinal myocardial contraction despite normal fractional shortening indicating that traditional measures of systolic function underestimate the co-existence of systolic and diastolic dysfunction in heart failure.

L-MVG S-w

Fractional Shortening (%)

Normal No CHF CHF

40±4 36±7 34±9

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10.43 a.m.

886.2

3-D Mitral Annular Dynamics in Tachycardia Induced Cardiomyopathy

Tomasa T. Impe, Paul Dagum, David T. Lai, David Liang, George T. Daughters, Neil B. Ingles, III, T. Miller, Stanford University, Stanford, CA. Research Institute of the Slath Medical Foundation, Palo Alto, CA

Purpose: Annual dilatation accompanied by mitral regurgitation (MR) often occurs in dilated cardiomyopathy (DCM), but the mitral annular (MA) geometry perturbations associated with MR have not been well characterized.

Methods: Eight radionuclide markers were added to the MA creating 6 distinct annular segments, 14-c anterior MA, 13-c posterior MA) in sheep. Simultaneous biplane videodensitometry and TEE were performed before and after rapid pacing (180-230 min) for 156 days sufficient to develop tachycardia induced cardiomyopathy (TIC) and MR. MA segmental contraction was defined as percent difference between max and min length. MA area (MAA) and MA septal-lateral (S-L) and commissure-commissure (C-C) diameters were computed from 3-D marker coordinates at end-diastolic (ED) and end-systolic (ES) volumes.

Results: With TIC, MAA, S-L, and C-C at ED increased by 23% (p<.01), 23%, 12%, and 5%, respectively (p<.01). MRA increased from 0.3 to 22.1 to 9.9 (p<.001). Table 1

Table 1

Segment (cm)

Control TIC TIC

Diameter (cm)

ED Length (cm) Control TIC TIC

S-L 13.3±3.6 15.0±4.3** 7.3±2.1

C-C 11.4±2.2 12.2±2.2* 8.5±3.4

S-L 15.6±3.1 15.5±3.5 6.5±3.1

C-C 13.2±1.5 14.7±2.2 10.7±3.0 9.3±3.4

S-L 11.0±2.7 13.0±3.1*** 13.3±2.9 8.4±3.5

C-C 19.9±4.9 16.4±5.4*** 16.4±4.1 9.4±4.1

S-L 18.4±3.2 19.6±3.5*** 14.0±5.9 8.0±3.0

C-C 14.8±5.4 15.6±5.8*** 13.8±5.7 7.4±1.4* Conclusion: MA areas increase in TIC is primarily due to S-L diameter augmentation; additionally, greater segmental dilatation and decreased segmental contraction occurred in the posterior annular segments. These experimental findings have direct implications relevant to clinical surgical approaches for patients with DCM and MR.

886.3

Mechanisms Whereby Rapid Ventricular Pacing Causes LV Dysfunction

Lazarus A. Neelakhan, Young Shin, Aaron Vorobyev, Teresa Hernandez, Rhonda Huebner, Richard G. Shannon, Allegheny General Hospital, Pittsburgh, PA

Background: Rapid ventricular pacing (RVP) induces dilated cardiomyopathy in experimental models, yet the mechanisms are not well understood. We hypothesized that excessive chronotropic demands require compensatory reductions in contractility in order to balance energy requirements.

Methods: We studied 18 conscious, chronically instrumented dogs during RVP (240 bpm) for 4 weeks. DTABLES were instrumented with LV pressure transducers (LV Pd), coronary sinus catheters to calculate MVO2. We measured the transmyocardial production of nitric oxide (NOx) and the cardiac respiratory quotient (RQ).

Results: Inflation of RVP (10 min) was associated with significant decreases in CBF/beat and MVO2/beat and comparable decreases in LVdP/dt (p<0.001), consistent with hibernating myocardium (flow-function matching). The matched decline in flow and function persisted over the first 72 hours and was associated with increased cardiac NO production (+4.7 µM from -0.9 µM). Thereafter, CBF/beat and MVO2/beat increased to levels greater (p<0.05) than those seen during acute pacing (10 min), yet LV dP/dt continued to decline (p<0.001), consistent with flow-function mismatch or stunning. Cardiac NO production was lower (-2.9 µM from -1.7 µM) over 21 days, while RQ progressively increased (0.61±0.06 to 0.79±0.06, p<0.003).

Conclusion: MA areas increase in TIC is primarily due to S-L diameter augmentation; additionally, greater segmental dilatation and decreased segmental contraction occurred in the posterior annular segments. These experimental findings have direct implications relevant to clinical surgical approaches for patients with DCM and MR.

11:00 a.m.

10.45 a.m.
Improved Cardioprotection With the Oral Iron-Chelator L1, Over Standard Therapy With Subcutaneous Deferoxamine in Iron Overload Cardiomyopathy

Lazaros A. Nikolaidis, Josephine M. Egan, Dariush Elahi, Richard P. Shannon. Allegheny General Hospital, Pittsburgh, PA, Massachusetts General Hospital, Boston, MA

Background: Thalassemia major. The only widely available iron-chelation therapy is deferoxamine, with approximately 50% having excess myocardial iron deposition and 50% still die before 35 years in the UK. Early results with the new oral chelator L1, appeared promising, but its long-term efficacy and safety has recently been questioned due to low levels of liver iron in some patients.

Methods: We compared myocardial iron, liver iron and cardiac function in patients receiving L1 with age-, sex- and ferritin-matched controls receiving subcutaneous deferoxamine. Thalassemia major patients receiving L1 were selected from our database and matched using propensity score analysis.

Results: L1 group was 38% larger than the control group and had a mean serum ferritin levels (p=0.83, mean difference 15.7ng/l, 95% CI -140 to 17lng/l). Mean liver iron was (33±2 w 48±6 ml*) causing 32% fall in CO*. Diastolic filling period did not change (23±4 frames/sec) and Doppler echocardiography at rest and after staged treadmill Ex [5' incline, 6 meters/minstage) showed no change in CHF (p>0.05 vs. controls). Ex was terminated when the mouse preferred a noxious stimulus [tail shock] to Ex. Left ventricular (LV) mass and volumes were measured using the area-length method, previously validated (Th5, 65% vs. 1.1 for L1 LV mass). Heart rate (HR) was measured by frame count analysis.

Conclusion: LV mass, ejection fraction (EF), LV end-diastolic volume (EDV) and cardiac output (CO) were normal in rest in L1 mice (p>NS vs. WT), but Ex time was delayed/reduced (5.62 min vs 12.93 min in WT, p<0.05) (48% vs. 60% were immediately post-Ex (first image <15 sec) and L1 mice had no change in HR (58±4 vs 63±1 min 19 min 18; 0.05 or Ex 0.42±0.02 vs 0.32±0.07) but EDV fell (53±2 vs 48±4 ml m2) causing 15% fall in CO. LV function during treadmill heart rate range (21±4 vs 24±2 sec/min) but LV shortening efficiency (S1) (43±3 vs 26±2%) - indicating LV diastolic dysfunction - which explains the fall in EDV and CO. At 3 min post-Ex, L1 mice developed LV dilatation (PW 67±10 mm, p<0.01 vs immediate) and decreased EF (1.2±1.5); One L1-Sgcd-null mice died with LV contracture (EDV=0) and was not included in the assessments of new therapies, with less emphasis placed on indirect measures such as serum ferritin levels and liver iron.

GLP-1 Improves Myocardial Performance in Conscious Dogs With Pacing Induced Heart Failure

Robert M. Weiss, Donald C. Oren, Nadia L. Davison, Richard C. Horbro, Kevin P. Campbell. University of Iowa, Iowa City, IA; VA Medical Center, Iowa City, IA

Background: GLP-1 improves cardiac function in 5gcd-null mice as an age-dependent mechanism of development of overt cardiomyopathy. Methods: 8 untrained 5gcd-null mice, age 4-5 mo., and 6 wild-type controls (WT) were studied with high-speed 2D [13 MHz, 162 frames/sec] and Doppler echocardiography at rest and after staged treadmill Ex [3° incline, 6 meters/minstage). Ex was terminated when the mouse preferred a noxious stimulus [tail shock] to Ex. Left ventricular (LV) mass and volumes were measured using the area-length method, previously validated (Th5, 65% vs. 1.1 for L1 LV mass). Heart rate (HR) was measured by frame count analysis.

Results: Heart, LV mass, ejection fraction (EF), LV end-diastolic volume (EDV) and cardiac output (CO) were normal in rest in 5gcd-null mice (p>NS vs. WT), but Ex time was delayed/reduced (5.62 min vs 12.93 min in WT, p<0.05) (48% vs. 60% were immediately post-Ex (first image <15 sec) and 5gcd-null mice had no change in HR (58±4 vs 63±1 min 19 min 18; 0.05 or Ex 0.42±0.02 vs 0.32±0.07) but EDV fell (53±2 vs 48±4 ml m2) causing 15% fall in CO. LV function during treadmill heart rate range (21±4 vs 24±2 sec/min) but LV shortening efficiency (S1) (43±3 vs 26±2%) - indicating LV diastolic dysfunction - which explains the fall in EDV and CO. At 3 min post-Ex, 5gcd-null mice developed LV dilatation (PW 67±10 mm, p<0.01 vs immediate) and decreased EF (1.2±1.5); One 5gcd-null mice died with LV contracture (EDV=0) and was not included in the assessments of new therapies, with less emphasis placed on indirect measures such as serum ferritin levels and liver iron.

GLP-1 was associated with increased endothelial function, with less emphasis placed on indirect measures such as serum ferritin levels and liver iron.

GLP-1 improves myocardial performance in conscious dogs with pacing induced heart failure.

GLP-1 improves myocardial performance in conscious dogs with pacing induced heart failure.

Exercise-induced left ventricular dysfunction precees overt cardiomyopathy in Delta-sarcoglycan deficient mice

Robert M. Weiss, Donald C. Oren, Nadia L. Davison, Richard C. Horbro, Kevin P. Campbell. University of Iowa, Iowa City, IA; VA Medical Center, Iowa City, IA

Background: Mutation of the gene encoding delta-sarcoglycan, a cytoskeletal protein, causes adult-onset cardiomyopathy in mice (5gcd-null) and humans - purportedly via a process involving coronary microvascular dysfunction. Purpose: to evaluate the effects of submaximal exercise (Ex) on cardiac function in 5gcd-null mice as an age-dependent mechanism of development of overt cardiomyopathy. Methods: 8 untrained 5gcd-null mice, age 4-5 mo., and 6 wild-type controls (WT) were studied with high-speed 2D [13 MHz, 162 frames/sec] and Doppler echocardiography at rest and after staged treadmill Ex [3° incline, 6 meters/minstage). Ex was terminated when the mouse preferred a noxious stimulus [tail shock] to Ex. Left ventricular (LV) mass and volumes were measured using the area-length method, previously validated (Th5, 65% vs. 1.1 for L1 LV mass). Heart rate (HR) was measured by frame count analysis.

Results: Heart, LV mass, ejection fraction (EF), LV end-diastolic volume (EDV) and cardiac output (CO) were normal in rest in 5gcd-null mice (p>NS vs. WT), but Ex time was delayed/reduced (5.62 min vs 12.93 min in WT, p<0.05) (48% vs. 60% were immediately post-Ex (first image <15 sec) and 5gcd-null mice had no change in HR (58±4 vs 63±1 min 19 min 18; 0.05 or Ex 0.42±0.02 vs 0.32±0.07) but EDV fell (53±2 vs 48±4 ml m2) causing 15% fall in CO. LV function during treadmill heart rate range (21±4 vs 24±2 sec/min) but LV shortening efficiency (S1) (43±3 vs 26±2%) - indicating LV diastolic dysfunction - which explains the fall in EDV and CO. At 3 min post-Ex, 5gcd-null mice developed LV dilatation (PW 67±10 mm, p<0.01 vs immediate) and decreased EF (1.2±1.5); One 5gcd-null mice died with LV contracture (EDV=0) and was not included in the assessments of new therapies, with less emphasis placed on indirect measures such as serum ferritin levels and liver iron.

Conclusion: Thus, GLP-1 infusion causes a significant improvement in LV performance in moderate CHF, in association with increased FFA oxidation and improved endothelial function.
Background: Patients with heart failure (HF) are frequently discharged from the emergency room (ER) of Parkland Memorial Hospital, a facility serving predominantly indigent Dallas County residents. In performing a review of the medical literature, we were struck by the frequency of deaths that patients discharged from the ER with HF are not well known. Methods: In order to define the outcomes of this patient population and identify risk factors for adverse events, all patients discharged from the Parkland Memorial Hospital ER between 10/98 and 12/98 with a primary diagnosis of HF were identified by computerized search. Patients on dialysis (n = 14) and those with no clinical follow-up after the index ER visit (n = 16) or unverifiable medical records (n = 8) were excluded. A prespecified composite endpoint (failure of outpatient therapy) included recurrent HF visit, hospitalization for HF, or death at 3 months. The diagnosis of HF was verified by data abstraction in all cases. Results: The demographics of the study population (n = 112) included age 56 ± 14 years; gender: 56% females; ethnic distribution: 78% African American, 12% Caucasian, and 10% Hispanic. 48% of patients were Medicare or Medicaid recipients. Within 3 months of the index ER visit, 61% of subjects met the composite endpoint. The median time to endpoint was 32 days (25 percentile: 10 days, 75 percentile: 60 days). Univariate analysis of 24 clinical and demographic variables yielded only initial respiratory rate during the index visit as a predictor of failure of outpatient therapy (p < 0.03). In a multivariate model incorporating 8 prespecified variables, respiratory rate remained as the only predictor of death (odds ratio 1.6 for each increase of 3 breaths/minute; p < 0.03). Conclusion: Patients discharged with HF from an urban county hospital ER have an alarmingly high rate (61%) of failure of outpatient therapy within 3 months. Similar data need to be acquired in other patient populations to determine the extent of this problem. Research into risk factors and presentation to the ER is associated with an adverse outcome following ER discharge for HF.

Restoration and Maintenance of Sinus Rhythm in Patients With Left Ventricular Dysfunction and Atrial Fibrillation/Flutter is Associated With Improved Survival. A DIAMOND Substudy

Ole D. Pedersen, Department of Cardiology P. Gentofte University Hospital, Helleborn, Denmark

Purpose: Patients with left ventricular (LV) dysfunction commonly exhibit atrial fibrillation (AF) and flutter (AFR), which is associated with increased morbidity/mortality. Dofetilide, a new class III antiarrhythmic agent, is effective in restoring and maintaining sinus rhythm (SR). The effect of restoring SR on morbidity and mortality is unknown. This sub-study was designed to answer this question. Methods: The Danish Investigations of Arrhythmia and Mortality ON Dofetilide (DIAMOND) studies on conge
tive heart failure and myocardial infarction included 2029 patients with LV wall motion indices of 2 or less (n = 2029) at baseline. 1 month, 3 months, and 1 year, respectively. The acceleration of SR for 1 year was 79% for do
tetilde;ilde; with 42% for placebo (P < 0.001). Do
tetilde;ilde; had an overall neutral effect on mortality but a Cox multivariate analysis including restoration and maintenance of SR as a time-dependent variable, revealed that being in SR was associated with a signif
cant reduction of mortality (Hazard Ratio (HR) = 0.41 (0.30-0.54); P < 0.001). This effect was most pronounced in patients who received DC-cardioversion. In addition, relapse of AF/AFR was associated with a significant increase in mortality (HR = 2.71 (1.67-4.41); P < 0.001). Conclusions: This study demonstrates that restoration and main

Subjects in Heart Failure Trials Are Not the Same as Your Patients


Background: CHF guidelines and practices are based primarily on large clinical trials. However, this "evidence-based" approach assumes trial patients (Pts) are representative of the general CHF population. Objective: To evaluate to what extent this assumption is accurate, we compared CHF Pts in two clinical populations—a large staff-model HMO and an academic VA medical center—with Pts enrolled in several major CHF trials. Methods: Outpatients with a CHF diagnosis (ICD-9 codes 428.0-428.9) at 7/95-12/95 (VA sample) were evaluated, of whom a total of 778 Pts were included in this analysis after excluding individuals without Framingham CHF criteria, those lacking continuous follow-

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