were processed by a non linear anisotropic filter and LV edges were identified using an active contour algorithm, guided by image gradient. End-diastole and end-systole were identified based on R wave synchronization and cavity size, respectively. In both methods, LV volumes were calculated by the modified Simpson's rule. A commercially available automatic image analysis method was utilized for endocardial detection in MRI (Fast Cine, Leiden University version 4.0). Manual analysis showed a good correlation with MRI volumes (correlation coefficient r = 0.88); using this automatic approach the correlation was still good (r = 0.82); however, LV diastolic and systolic volumes were higher for MRI (206 ± 96ml. and 148 ± 105 ml) than for contrast echo assessed both manually (177 ± 88 ml. and 108 ± 73, p= <.001) and automatically (179 ± 104ml. and 107 ± 79 ml. , p=.<001). In conclusion, automatic endocardial border delineation is feasible on contrast enhanced images. Despite manual detection on contrast images showed a better correlation with MRI for LV contour analysis, preliminary results show that this method may represent a promising approach for automatic LV function assessment.

4:48 p.m.

1144MP-130 Quantitative Three-Dimensional Intravascular Ultrasound: Improvements Toward Semi-Automated Border Detection Including the Stent Border

Jouke Dijkstra, Gerhard Koning, Joan C. Tuinenburg, Pranobe V. Oemrawsingh, Johan H.C. Reiber, *Leiden University Medical Center, Leiden, The Netherlands.*

Background: IntraVascular UltraSound (IVUS) is a catheter-based technique, which provides real-time high-resolution images of the entire arterial wall. The technique is used often to monitor the stent placement or to visualize in-stent restenosis. Automation of the boundary detection of the stent, lumen, and vessel reduces the required analysis time and the subjectivity of the manual tracing procedure. The three-dimensional reconstruction permits an advanced assessment of the morphology.
Methods: The (semi-)automated approach is a combination of transversal and longitudinal contour detection techniques and is based on a model of the vessel and uses knowledge about the morphologic structures. The stent contour is detected based on the high intensity of the stent struts as compared to other structures and their expected location in the vessel wall based on an approximately circular model. The detection method itself is able to perform corrections based a continuously three-dimensional structure.
Results: In a set of 150 slices from different pullback series (acquired with Boston Scientific and EndoSonics equipment) the automatically detected stent boundaries were compared to manually drawn stent boundaries. The comparison of the cross-sectional stent areas for the manually traced and automatically detected boundaries resulted in an r-value of 0.99. In a set of 50 pullback runs (acquired with Endosonics equipment) the entire stented segment was analyzed automatically and the most distal and the most proximal slice in a continuous series of slices containing stent struts was selected to assess the stent length. The comparison of these distances with the original stent lengths resulted in an average overestimation of 0.35 +/- 1.42 mm by IVUS. The start and end point of a stent is not well defined because the catheter moves in and out the stent, due to cardiac motion.
Conclusion: Due to the flexible use of more than two longitudinal cutplanes and the advanced knowledge-guided contour detection approach, the new IVUS analysis system has proven to be suitable for clinical research studies. The inclusion of the stent boundary is very useful for stent studies e.g. to study the effect of drug coated stents.

YOUNG INVESTIGATORS AWARDS COMPETITION

411 Young Investigators Awards: Clinical Investigations

Monday, March 18, 2002, 4:00 p.m.-5:30 p.m.
Georgia World Congress Center, Room 257W

4:00 p.m.

411-1 A Prospective, Blinded Determination of the Natural History of Aspirin Resistance Among Stable Cardiac Patients

Patricia A. Gum, Kandice Kottke-Marchant, Eric J. Topol, *The Cleveland Clinic Foundation, Cleveland, Ohio.*

Background. Aspirin resistance, as defined by comprehensive, ex vivo platelet function testing as well as presumed clinical unresponsiveness to aspirin, has been previously reported by our group and others. However, little information exists linking the laboratory documentation of aspirin resistance and long-term clinical events.
Methods. We prospectively enrolled 326 stable cardiac patients from 1997 to 1999 on aspirin (325 mg/day for ≥ 7 days) and no other antiplatelet agents. We tested them for aspirin sensitivity by optical platelet aggregation using adenosine diphosphate (ADP) and arachidonic acid (AA) and followed them for clinical events. The primary outcome was the composite of death, myocardial infarction (MI), or cerebrovascular accident (CVA). Mean follow-up was 679 ± 185 days. Aspirin resistance was defined as a mean aggregation of ≥ 70% with 10 μ M ADP and ≥ 20% with 0.5 mg/ ml AA.
Results. Of the patients studied, 17 (5.2%) were aspirin resistant and 309 (94.8%) were not aspirin resistant. During long-term follow-up, aspirin resistance was associated with a significantly increased risk of death, MI, or CVA compared to patients who were aspirin sensitive (24% vs 10%, HR 3.12, 95% CI (1.10-8.90), p=0.03). Stratified multivariate analyses identified elevated platelet count, advancing age, history of congestive heart failure and aspirin resistance to be independently associated with major adverse long-term outcomes (HR for aspirin resistance 4.14, 95% CI (1.42-12.06), p=0.009).
Conclusion. This study is the first prospective determinant of the natural history of aspirin resistance, documenting a greater than 2-fold increase in the risk of major adverse events associated with aspirin resistance.

4:15 p.m.

411-2 Loss of Thrombomodulin Expression Impairs Vein Graft Thromboresistance

Antony Y. Kim, Kenneth Lee Baughman, Peter L. Walinsky, Frank D. Kolodgie, C. E. Bian, Jason Sperry, Clayton Deming, Eric Peck, Jay Shake, Gregory Ang, Charles Esmon, Renu Virmani, Jeffrey Rade, *Johns Hopkins School of Medicine, Baltimore, Maryland.*

Background: Thrombosis is the major cause of early vein graft failure. The aim of this study was to determine whether alterations in the expression of the anticoagulant proteins, thrombomodulin (TM) and the endothelial cell protein C receptor (EPCR), impair endothelial thromboresistance and contribute to vein graft failure. ***Methods and Results:*** Immunohistochemical analysis of autologous rabbit vein grafts revealed that the expression of TM, but not EPCR, was reduced by 98% 3 days after implantation, with gradual but incomplete recovery by 42 days. This resulted in up to a 95% reduction in the capacity of the grafts to activate protein C and was associated with increased bound thrombin activity, that peaked on day 7 at 28.7" 3.8 mU/cm^2 and persisted for over 14 days. Restoration of TM expression using adenovirus vector-mediated gene transfer significantly enhanced the capacity of grafts to activate protein C and resulted in a near 80% reduction in bound thrombin activity on day 7, to levels comparable to normal veins (5.7 " 0.4 vs. 5.2 " 1.1 mU/cm^2, respectively, p= 0.74). Surprisingly, neointima formation was not affected by this inhibition of local thrombin generation. ***Conclusions:*** These results suggest that early loss of TM expression enhances local thrombin generation that contributes to early vein graft failure due to thrombosis, but does not contribute significantly to late vein graft failure due to neointimal hyperplasia.

4:30 p.m.

411-3 Improvement in Diastolic Suction in Patients With Hypertrophic Obstructive Cardiomyopathy After Septal Ablation

Aleksandr Rovner, Marta Sitges, Rebecca Smith, Neil L. Greenberg, Irmien Vlassak, Takahiro Shiota, Murat E. Tuzcu, Nicholas Smedira, Harry M. Lever, James D. Thomas, Mario J. Garcia, *Department of Cardiovascular Medicine, The Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: Septal alcohol ablation (PTSA) is an effective treatment in hypertrophic obstructive cardiomyopathy (HOCM). Intraventricular pressure gradient (IVPG) is a novel method to evaluate diastolic function. Our aim was to analyze the IVPG and diastolic function in HOCM patients with PTSA.
Methods: 19 patients had an echocardiogram performed at baseline and after PTSA (mean follow up 5.6±1.2 months). Diastolic parameters were obtained using PW-Doppler through the mitral valve (E, A, DT), pulmonary venous flow (S, D), mitral annulus tissue Doppler imaging (Ea). Color M-mode was used to obtain the flow propagation velocity (Vp) through the mitral valve and to calculate IVPG off-line using custom written software. LV dimensions were obtained. LV outflow tract (LVOT) gradient was calculated.
Results: LVOT gradient decreased from 62±10 to 29±5 mmHg (p<0.001), severity of mitral regurgitation (MR) decreased from 2.1±0.2 to 1.3±0.2 (p<0.01). The septal size decreased from 2.3±0.09 to 1.9±0.05 mm (p<0.01). Diastolic results are shown in the Table.

	IVPG (mmHg)	Vp (cm/s)	E/A	DT (ms)	S/D	E/Vp	E/Ea
Pre	1.5±0.2	48±5	1.5±0.2	258±15	1.2±0.1	2.2±0.2	14.2±2.5
Post	2.6±0.3*	74±7*	0.9±0.1*	256±12	1.3±0.1	1.3±0.1*	11.3±1.3

*p<0.01 vs Pre.
The increase in IVPG correlated with the increase in Vp (r=0.5) and with the decrease in LVOT gradient (r=-0.6), E/Vp (r=-0.5), E/Ea (r=-0.7), (all p<0.05), and decrease in MR (r=-0.7, p<0.01). No correlation was found between the increase in IVPG and decrease in E/A, S/D and DT.
Conclusion: IVPG is a reliable indicator of diastolic function improvement in HOCM after PTSA as indicated by the increase in IVPG and change in other diastolic parameters.

4:45 p.m.

411-4 L-Arginine Protects Human Heart Cells From Simulated Anoxia and Reoxgenation

Subodh Verma, Noritsugu Shiono, Ren-Ke Li, Donald A. Mickle, Paul W. Fedak, Richard D. Weisel, *University of Toronto, Toronto, Ontario, Canada.*

The present study was conducted to evaluate the direct effects of L-arginine in a human ventricular heart cell model of simulated ischemia and reperfusion independent of alternate cell types such as endothelial cells, neutrophils, platelets or fibroblasts. Human ventricular heart cell cultures were subjected to 90 minutes of low volume ischemia and 30 minutes of reperfusion. L-arginine (0-5.0 mM) was administered during the pre-ischemic period or during the reperfusion phase. Nitric oxide synthase (NOS) activity, nitric oxide (NO) production, cGMP levels and cellular injury were assessed. To evaluate the effects of L-arginine on cell signaling, the effects of NOS antagonist (L-NAME), NO donor (SNAP), guanylate cyclase inhibitor (methylene blue), cGMP analogue (8-BrCGMP) and K_{ATP} antagonist (glibenclamide) were examined. Our data indicate, that ischemia and reperfusion increased NOS activity and facilitated the conversion of L-arginine to NO,

which provided protection against the effects of ischemia and reperfusion in a dose-dependent fashion. In addition, L-arginine cardioprotection was mediated by the activation of guanylate cyclase leading to increased cGMP levels in human heart cells. The final effector of NO/cGMP may be the opening of K_{ATP} channels.

5:00 p.m.

411-5 **L-Arginine for Partial Resynchronization of Abnormal Peripheral Vascular Reactivity in Heart Failure: A Prospective Randomized Double-Blind Study**

Mohammed Yousufuddin, Mohamed Amrani, Waqar Shamim, Faisal Al-Nasser, Fouad Amin, Nicholas R. Banner, Andrew J S. Coats, *National Heart and Lung Institute, London, United Kingdom.*

We investigated the effects of oral l-arginine (ARG) supplement on brachial artery (BA) reactivity in patient with CHF. Methods: Fifty-men (59±10 yr.) with stable CHF of NYHA grade I-III and ejection fraction <40% were randomized to oral ARG or matching placebo for 1-week. Twenty-healthy men (57±9yr) with no clinical evidence of disease served as parallel controls for baseline comparison. BA reactivity was measured as a) flow-mediated dilation (FMD) in response to hyperemia induced by 5-min of distal forearm occlusion by blood pressure cuff, b) exercise-induced constriction (EIC) immediately after treadmill exercise, and c) resting, hyperemic and post-exercise BA blood flow by high-resolution ultrasound technique using 8-11 MHz vascular probe connected to SONO 5500 (Agilant Tech, USA). FMD and EIC were measured as % change in diameter of the BA after increased flow and exercise respectively. Exercise was performed with modified Bruce protocol and peak oxygen consumption (VO_2) was measured (AMIS 2000, Denmark). Exhaled nitric oxide (NO) was measured by a chemiluminescence analyzer. Investigations were performed after overnight fast under identical condition. Inferential statistics were restricted to CHF patients. Results: ARG and placebo patient-groups and controls were similar in demographics. Baseline characteristics were comparable between ARG and placebo groups in patients. Controls and patients differ in their BA reactivity and exercise capacity with former showing higher FMD and VO_2 but lower EIC (all P<0.0001). At one-wk FMD (2.24±0.89 to2.6±1.1 Vs 2.3±0.32 to 2.3±1.07%;P=0.02) has increased while EIC (7.2±4.0 to 5.3±2.8 vs 5.9±3.2 to 5.8±3.1%;p=0.02) decreased with ARG supplementation compared to placebo in patients. Exhaled NO was increased, independent of changes in FMD or EIC in ARG arm compared to placebo (7.6±2.8 to 9.4±3.4; vs 8.9±2.5 to 9.4±3.4 parts per billion; P=0.01). Patients, who received ARG demonstrated a strong trend toward increase in exercise interval, VO_2, and hyperemic blood flow compared to placebo group. Conclusion: ARG, via an increase in NO bioavialability, partially resynchronizes brachial artery reactivity towards normal in patients with CHF.

ORAL CONTRIBUTIONS

849 Improving Quality of Care

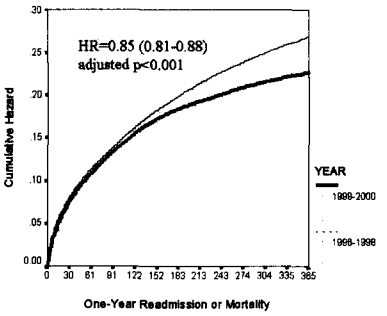
Tuesday, March 19, 2002, 8:30 a.m.-10:00 a.m.
Georgia World Congress Center, Room 367W

8:30 a.m.

849-1 **An Institutional Discharge Medication Program Reduces Future Cardiovascular Readmissions and Mortality: An Analysis of 43,841 Patients With Coronary Artery Disease**

Robert R. Pearson, Benjamin D. Horne, Chloe A. Allen Maycock, Donald L. Lappe', Susan Kralick-Goldberg, Tami L. Bair, Janette A. Orton, Diane S. Wallace, Haeli Hanseen, Dale G. Renlund, Joseph B. Muhlestein, *LDS Hospital, Salt Lake City, Utah.*

Background: Patients (pts) admitted with a diagnosis of coronary artery disease (CAD) carry a significant risk of re-hospitalization or death during the year after discharge. We have shown that successful implementation of a multi-faceted discharge medication program (DMP) increases the likelihood of CAD pts being discharged on appropriate medical therapy (ASA/Antiplatelet and a statin for all; Beta-Blockers post-MI). We hypothesized that this DMP would result in reduced cardiovascular readmissions and mortality.
Methods: We analyzed 43,841 pts discharged after a CAD-related hospitalization from 10 hospitals within an integrated health care system. Implementation of the DMP was initiated in 1/1999 and increased overall medication use from 65% to 95%. We compared one year cardiovascular readmission or death rates of pts discharged between 1/1996-12/1998 (n=25,185) (pre-DMP) to pts discharged between 1/1999-6/2000 (n=18,656) (post-DMP).
Results: Average pt age was 64±15 years; 62% were male; demographics did not differ between pre- and post-DMP groups. After controlling for age and gender in Cox regression, post-DMP one-year re-admission rates were reduced from 20.4% to 17.7% (hazard ratio [HR]=0.86, p<0.001) and one-year mortality was reduced from 4.5% to 3.5% (HR=0.79, p<0.001).
Conclusions: The successful implementation of an institutional cardiac DMP can significantly lower the rate at which pts with CAD are readmitted for cardiac complications and also will lower their mortality rates.



8:45 a.m.

849-2 **Quality of Care of Patients Admitted With Congestive Heart Failure: Influence of Physician Specialty and Hospital Type**

Jay K. Amin, Michael J. Lim, Yassar Almanaseer, Chih-Wen Pai, Gerriann Finnegan, Kim A. Eagle, Rajendra H. Mehta, *University of Michigan, Ann Arbor, Michigan, Michigan Peer Review Organization, Plymouth, Michigan.*

Background: Congestive heart failure (CHF) is a common admission diagnosis in elderly patients (pts) in the United States. Increased resource utilization by CHF pts has generated great interest in improving quality of care for these pts. The impact of physician specialty and hospital type on the quality of care has not been well studied.
Methods: We evaluated 5871 Medicare beneficiaries admitted to 31 acute care hospitals in Southeast Michigan with CHF (1/98-12/98). Patients were identified retrospectively using ICD-9 codes for CHF. Indicators were evaluated with respect to physician specialty (cardiologist vs. non-cardiologist) and hospital type (teaching, n=17 vs. non-teaching, n=14).
Results: Indicators are shown (Table). Patients treated by cardiologists had shorter length of stay (LOS, 5.5 vs. 6.0 days, p<.001) and similar 1-year mortality rates (37.9% vs. 35%, p=.06) compared to non-cardiologists. Patients treated in teaching hospitals had shorter LOS (5.6 vs. 6.1 days, p<.001) and lower 1-year mortality rates (34.7% vs. 37.4%, p=.04).
Conclusion: Quality of care for CHF pts tends to be less optimal in those treated by non-cardiologists and at non-teaching hospitals despite similar or higher mortality rates. This data supports the need for further educating non-cardiologists in the management of elderly pts admitted with CHF. In addition, it suggests that systemization of processes at non-teaching hospitals may improve the quality of care for CHF pts, thus leading to better long-term outcomes.

Quality Indicators	Teaching Hospital, n=3350	Non-teaching Hospital, n=2521	P Value	Cardiologist, n=1297	Non-cardiologist, n=3599	P Value
Discharge ACE-inhibitor/ARB (%)	81.6	73	<0.001	79.6	76.5	0.24
LVEF documented (%)	70.5	64.6	<0.001	65.3	68.3	0.05
Discharge smoking cessation counseling (%)	24.0	34.5	0.08	28.1	27.9	0.98
Discharge written instructions (%)	97.0	97.3	0.75	97.8	97	0.43
Weights measured, >50% hospital days (%)	68.4	61.6	0.006	77.7	62.6	<0.001
Discharge warfarin in CHF pts with atrial fibrillation (%)	48.7	41.7	0.16	56.5	39.1	<0.001

9:00 a.m.

849-3 **Regional Differences in Quality of Care for Heart Failure: The Role of Patient, Physician, and Hospital Characteristics**

Edward P. Havranek, Pam Wolfe, Frederick A. Masoudi, Harlan M. Krumholz, Saif S. Rathore, Beth Stevens, Diana L. Ordin, *Colorado Foundation for Medical Care, Aurora, Colorado.*

Background: Quality of care for elderly heart failure patients varies across the United States, but the extent to which patient, provider and hospital characteristics contribute to this variation is unknown. Methods: We used data from the National Heart Failure project, a Center for Medicare and Medicaid Services quality initiative that studied 37,500 Medicare patients hospitalized with heart failure, to evaluate the extent to which patient, physician and hospital characteristics explain regional variation in heart failure treatment. Small area variation for two quality indicators (QI)- documentation of ejection fraction (EF) and appropriate prescription of angiotensin converting enzyme inhibitor (ACEI)- was assessed by estimating the QI rates by Hospital Referral Regions (HRRs) in the United States using a non-linear mixed-effects model. To identify variables associated with performance on the quality indicators by census divisions we used the method of generalized estimating equations for a logistic model entering HRR as a random effect. We compared the distribution of the predictors across regions using a chi-square test for