

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 ( $206 \pm 96$  ml. and  $148 \pm 105$  ml.) than for contrast echo assessed both manually ( $177 \pm 88$  ml. and  $108 \pm 73$ ,  $p < .001$ ) and automatically ( $179 \pm 104$  ml. and  $107 \pm 79$  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. Tuinenbor, 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  $0.35 \pm 1.42$  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  $\geq 7$  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  $679 \pm 185$  days. Aspirin resistance was defined as a mean aggregation of  $\geq 70\%$  with  $10 \mu\text{M}$  ADP and  $\geq 20\%$  with  $0.5 \text{ mg/ml}$  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**

Anthony 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  $28.7 \pm 3.8 \text{ mU/cm}^2$  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 ( $5.7 \pm 0.4$  vs.  $5.2 \pm 1.1 \text{ mU/cm}^2$ , 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 Royner, 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  $5.6 \pm 1.2$  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  $62 \pm 10$  to  $29 \pm 5 \text{ mmHg}$  ( $p < 0.001$ ), severity of mitral regurgitation (MR) decreased from  $2.1 \pm 0.2$  to  $1.3 \pm 0.2$  ( $p < 0.01$ ). The septal size decreased from  $2.3 \pm 0.09$  to  $1.9 \pm 0.05 \text{ mm}$  ( $p < 0.01$ ). Diastolic results are shown in the Table.

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

\* $p < 0.01$  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 Reoxygenation**

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-Br-cGMP) and KATP antagonist (glibenclamide) were examined. Our data indicate, that ischemia and reperfusion increased NOS activity and facilitated the conversion of L-arginine to NO,