Elevated troponin in ACS confers a significantly high risk for death or MI, with death or MI occurring in 11.4% of patients with TnI (95% confidence interval [CI] 7.8% to 16.9%), 16.1% of patients with CRP (95% CI 11.4% to 22.5%), and 18.1% of patients with BNP (95% CI 13.5% to 23.3%) (all p < 0.001 vs. controls). The risk of death or MI increased progressively with rising levels of TnI (p < 0.0001), CRP (p < 0.0001), and BNP (p < 0.0001). Troponin correlated only weakly with the other markers (|r| < 0.1 for each). Other treatments associated with higher risk of death or MI included older age, hypertension, diabetes, prior CAD, and prior CHF (p < 0.05 for each). TnI levels correlated only weakly with troponin I (TnI), C-reactive protein (CRP), and B-type natriuretic peptide (BNP) (|r| = 0.1 for each). The risk of death, MI, Urg Revacs, Sev Isch, and the composite increased progressively with rising levels of TnI (Fig). After adjusting for baseline differences, including TnI, CRP, and BNP, patients with TnI levels above the median remained at significantly increased risk for the composite endpoint (hazard ratio 1.47, p = 0.001).

Conclusion: In patients with ACS, elevated levels of TnI at baseline are associated with an increased risk of death and ischemic complications. These data support the value of combining a marker of active thrombosis, such as TnI, with established biomarkers of necrosis, inflammation, and hemodynamic stress for risk assessment in ACS.

**Table 1**

<table>
<thead>
<tr>
<th>n (patients)</th>
<th>Stable</th>
<th>Unstable</th>
<th>Post MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TnI</td>
<td>19</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>High strain spots</td>
<td>0.7 ± 0.5</td>
<td>1.7 ± 0.4</td>
<td>2.0 ± 0.8</td>
</tr>
</tbody>
</table>

Conclusion: IP can be used to assess the number vulnerable plaques in humans. This pilot study revealed a clear association between clinical presentation and the amount of vulnerable plaques. Additional validation has to be performed to assess the predictive value of the technique to identify vulnerable patients.

**Impact of Troponin Status and Coronary Artery Disease by Angiography on Outcome in Acute Coronary Syndrome: A TACTICS TIMI-18 Substudy**

**Methods and Results**

To evaluate whether patients have false positives and if there is clinical significance of an elevated TnI, we evaluated the prognosis of ACS patients enrolled in TACTICS-TIMI-18 study according to the presence or absence of CAD on angiography and Tn status on admission. In this study, 1,372 patients underwent angiography. A subset of 465 patients were TnI negative, and of those, 362 (79.6%) had significant CAD (>50% stenosis in one or more vessels). Fifty-seven out of 917 patients (62.6%) with TnT or 1 did not have significant CAD. The mean value of TnT in patients with angiographic CAD was 0.603 ng/ml compared to 0.281 ng/ml in those without CAD (p = 0.01). The mean value of TnI was 9.39 ng/ml in patients with CAD compared to 3.32 ng/ml in patients without CAD (p = 0.005).

An outcome of death or readmission at 6 months is shown in table. There was a significant difference between the stable vs. unstable group (p < 0.001) and stable vs. post MI group (p = 0.0001). There was no difference between the unstable group and post MI group (p = 0.056).

**Enhanced External Counterpulsation Decreases Wave Reflection Amplitude and Reduces Left Ventricular Afterload and Systolic Stress in Patients With Refractory Angina**

**Background:** Myocardial ischemia is associated with increased arterial stiffness which causes early return of reflected pressure waves from the lower body and augments aortic systolic and pulse pressures and increases left ventricular afterload and myocardial oxygen demand. The aim of this study was to determine if arterial properties and wave reflection characteristics are altered after EECP treatment in patients with chronic stable angina resistant to anti-anginal medication. Methods: High-fidelity radial artery pressure waveforms were recorded non-invasively by applanation tonometry and ascending aortic pressure waveforms generated using a mathematical transfer function. Twenty patients (age 61 ± 7.3 years) with refractory angina taking two or more anti-anginal drugs were studied. Data were collected before and after 34 one-hour EECP sessions. Augmentation index (Ala, index of aortic stiffness) and amplitude and timing of the reflected pressure wave (index of myocardial oxygen demand) were calculated from the generated aortic pressure waveform. Results: EECP caused a significant decrease in Ala from 27.5 ± 10 to 19.9 ± 8% (p < 0.02) and a delay in reflected wave travel time from 68.8 ± 3 to 74.6 ± 8 msec (p < 0.01). These modifications in wave reflection characteristics were associated with a decline in reflected wave amplitude (from 120 ± 18 to 108 ± 18 mm Hg, p < 0.01) and duration (from 189 ± 34 to 174 ± 40 msec, p < 0.01) which caused a decrease in aortic stiffness (from 120 ± 18 to 108 ± 18 mm Hg, p < 0.01) and pulse (from 48 ± 15 to 41 ± 16 mm Hg, p < 0.01) pressure. The average number of anginal episodes per week decreased from 7.1 ± 6.0 to 1.1 ± 1.2 (p < 0.02) while heart rate, body weight and drug regimen did not change during the course of the study. Conclusions: EECP treatment delays return of the reflected pressure wave from the periphery to the heart, reduces its amplitude and, therefore, decreases aortic blood pressure and systolic stress in patients with refractory angina taking anti-anginal medication. These changes, which are likely due to decreased arterial stiffness and pulse wave velocity of the muscular arteries in the legs, reduce myocardial oxygen demand and decrease the number of anginal episodes.

**Incidence of Vulnerable Plaques in Humans: Assessment With 3-D Intravascular Palpography**

Johannes A. Schlag,1 Evelyn Regar,2 Francesco Saia,3 Chris L. de Korte,2 Frits Mastik,1 Evelyn Regar, Francesco Saia, Chris L. de Korte, Frits Mastik,1,2 Anton F. van der Steen,1 Patrick W. Serruyts,3 Erasmus Medical Center, Rotterdam, The Netherlands, Interuniversity Cardiology Institute of the Netherlands, Utrecht, The Netherlands

Intravascular palpography (IP) can detect deformable thin-cap fibroatheroma with a high sensitivity and specificity by measuring the strain of the plaque surface. These vulnerable plaques show a typical high strain pattern. We hypothesized that it is possible to detect vulnerable plaques in vivo in human coronary arteries by scanning the coronary artery for typical high strain patterns. Method: IP was performed in 56 patients by using standard 20 MHz intravascular ultrasound catheters (Avanar, JOMED inc). Analysis included the complete length of the vessel. The population was divided into 3 groups: Patients with [1] antecedent (≥24 h) myocardial infarction, [2] unstable angina (ST depression, TnI negative), [3] Stable angina (stable). Per patient one coronary artery was investigated. Results: IP was successful performed in all patients. The number of typical strain patterns reflecting the number of vulnerable plaques per coronary artery are given in the table. There was a significant difference between the stable vs. unstable group (p < 0.001) and stable vs. post MI group (p = 0.0001). No difference was seen between the unstable group and post MI group (p = 0.056).

**Enhanced Extracorporeal Counterpulsation: Mechanisms and Clinical Results**

Wednesday, March 10, 2004, 10:30 a.m.-Noon
Morial Convention Center, Room 257

**External Counterpulsation Therapy: Significant Clinical Improvement Without Electrophysiologic Remodeling**

Charles A. Henrikson,1 Nisha Chandra-Strobos,2 Johns Hopkins Medical Institutions, Baltimore, MD

Background: External counterpulsation therapy (ECP) non-invasively improves coronary flow, hemodynamics, and time to ischemia in patients with severe coronary artery disease (CAD). Other treatments with similar effects, e.g. left ventricular assist devices, promote electrophysiologic remodeling, with a narrowing of the QRS complex. Methods: We studied 28 patients, who completed a 7-week 36-hour session of ECP, to assess whether such therapy would also result in electrophysiologic remodeling, especially if associated with clinical improvement. All patients had class III-IV angina, imaging-proven ischemia, and severe CAD. Results: Of 28 patients, with mean age 62±13 years (mean ±SD), 78% were male, 46% diabetic, 82% hypertensive, 60% had undergone angioplasty, and 67% bypass surgery. The mean ejection fraction was 44% (range 25-60%). Following ECP, most patients (87%) had at least one full class improvement in their anginal pattern. In most patients, there was substantial baseline conduction system disease present: a mean QRS of 116±19 msec. Of note, there was no significant change in heart rate, PR, QRS, or QTc intervals before and after ECP in either clinical responders or non-responders. When
Enhanced External Counterpulsation Improves Functional Capacity and Quality of Life in Women With Chronic Angina

Georgiana C. Linemeyer, Elizabeth D. Kennard, Ozlem Soran, Sheryl F. Kelsey, University of Pittsburgh, Pittsburgh, PA

Background: Within the population of the United States, 36% of women aged 55-64 years are disabled by clinical manifestations of coronary heart disease, with disability rates of 55% for women over 75 years of age. We examined the therapeutic efficacy of EECP on functional status and quality of life in women with chronic angina as assessed by the Duke Activity Status Index (DASI), a standardized assessment that correlates well with peak oxygen uptake (Spearman correlation coefficient, 0.58).

Methods: Demographic and clinical outcome data were analyzed on all patients enrolled in the International EECP Patient Registry-2 who had baseline and post-treatment DASI scores (N=524). Linear regression model analyses were used to examine independent predictors of DASI scores.

Results: Baseline characteristics of the study group were: mean age-68 years, female-27%, duration of CHD-12 years, prior myocardial infarction-71%, history of diabetes-42%, and history of congestive heart failure (CHF)-32%. Angina was classified as Canadian Cardiovascular Society class 3 or 4 in 90% of patients. Patients experienced a mean of 11 episodes of angina/week despite optimal medical management and previous cardiac revascularization. Pre-treatment, the mean DASI score was 12 (a possible score range 5-20); with females scoring 8.7 and males scoring 13.7 (p<0.001). Post-treatment, the mean DASI score was 17.9. Females scored 15.4 and males scored 18.8 (p<0.01). Linear regression analysis demonstrated that female gender, history of CHF, prior coronary artery bypass surgery, and class III/IV angina were independent predictors of low DASI scores pre-treatment. Age, diabetes and history of CHF were associated with a lower post-treatment score. Female gender was not independently associated with a lower score post-treatment.

Conclusion: This study demonstrates that, even with adjustment for comorbidities, there is more functional disability among female patients with chronic angina than with male patients. EECP improves functional capacity and quality of life as assessed by the DASI questionnaire with no gender disparity.

The Effects of Enhanced External Counterpulsation on Myocardial Perfusion in Patients With Stable Angina: A Single-Blind Multicenter Pilot Study

Andrew D. Michaels, Ajit Raisinghani, Ozlem Soran, Paul-Andre de Lame, Michele L. Lemaire, Paul Kligfield, Denny D. Watson, George Bolger, University of California, San Francisco, San Francisco, CA, University of Virginia, Charlottesville, VA

Introduction: Enhanced external counterpulsation (EECP) has been shown to reduce angina and improve exercise tolerance and quality of life (QOL) in patients with angina. However, the mechanism of these effects is unclear. We sought to determine whether EECP improves exercise-induced myocardial perfusion. Methods: Patients with class II-IV angina and exercise-induced provokable ischemia were enrolled from 5 US centers. QOL was assessed using SF-36 and Seattle Angina Questionnaires prior to and after EECP therapy. Exercise testing with sestamibi SPECT exercise perfusion imaging was performed prior to and 1-month post-EECP. Statistical analysis was performed with the student t test; significance level p<0.05. Reversibility (rest-stress) was 10.3±6.8 vs 9.4±8.1 (p=0.51). Average thickening fractions in target segments were 28.8±11.1 vs 26.9±13.3 (p=0.32). Conclusions: We confirm previous work that EECP reduces angina, improves exercise capacity, and improves QOL. A training effect with peripheral changes occurred after EECP. There were no significant changes in mean defect magnitude, amount of reversibility, and thickening fractions measured using myocardial quantitative SPECT imaging when compared at identical pre- and post-EECP heart rates. These data do not preclude balanced changes in global myocardial perfusion.

The long-term clinical outcomes and QOL of EECP patients are as follows:

- **Improvement in functional capacity and quality of life.**
- **Reduction in angina frequency and severity.**
- **Increase in exercise tolerance.**
- **Improvement in cardiovascular risk factors.**
- **Stabilization or regression of coronary artery disease.**
- **Enhancement of cardiac muscle function.**
- **Reduction in cardiac arrhythmias.**
- **Improved sleep quality.**
- **Enhancement of emotional well-being.**

Enhanced external counterpulsation (EECP) relieves angina in most patients (pts). However, angina may not respond or may reoccur necessitating repeat EECP.

Purpose: To investigate EECP retreatment frequency, pt characteristics, retreatment course and response.

Methods: Sequential refractory angina pts. enrolled in the International EECP Registry-2, from 1 year follow up post initial EECP therapy were examined. A Cox Proportional Hazards model was used to determine independent predictors of return for treatment within one year.

Results: Of 2,255 IEPR pts, 233 (10%) repeated EECP within 14 months. Mean age was 66.5±10.9 years, 93.7% white, 73.4% male. By history, 68.8% had prior Ml and 32.8% CHF. Risk factors included: DM 40.7%, HBP 70.7%, hyperlipidemia 82.3%, smoking 71.3%. The mean EF was 47.0±14.4 %. 18.5% had an EF < 35%. Only 14.8% were PCI or CABG candidates. At baseline, 85.9% had CCS class II/IV angina. Pts received 33.5±9.3 hrs of EECP; 83.7% completed therapy. Post EECP 74% improved angina by 1 or more CCS classes; 28.7% remained CCS III/IV. Of the returning pts, 215 had full data available. Mean time to return was 168±129 days. Retreatment reasons included: angina increase (27.8%), persistent angina (34.2%), completing an incomplete initial course (38.1%). At retreatment 78.3% had CCS class III/IV angina. Treatment averaged 26.4±12.6 hrs; 77.1% completed therapy. Post retreatment angina was reduced by one or more classes in 71.4%; 30.8% had class III/IV angina. In pts completing their initial course, major retreatment predictors of: prior CABG (RR 1.63; CI 1.07-2.49), prior PCI (RR 1.96; CI 1.13-3.32), HBP (RR 1.43; CI 1.09-1.84). In pts with an incomplete initial treatment, lack of anginal reduction predicted return (RR 2.19; CI 1.28-3.75).

Conclusions: Retreatment occurred in 6.2% of pts for persistent or worsening angina and in 3.8% for an incomplete initial course. EECP was similarly effective as initial and subsequent therapy. Return was predicted by prior revascularization and HBP in pts completing the initial course of EECP and by lack of angina reduction in pts with an incomplete initial course.

Long-Term Improvement in Microvascular Angina Patients Treated With Enhanced External Counterpulsation

Kenneth D. Kronhaus, William E. Lawson, Lake Cardiology, Mount Dora, FL, SUNY Stony Brook, Stony Brook, NY

Background: Angina in patients without significant angiographic epicardial disease can be a medically refractory cause of chronic disability. For these microvascular angina patients Enhanced External Counterpulsation (EECP) may prove uniquely beneficial. Patent epicardial arteries facilitate transmission of the increased flow and pressure generated by EECP to the microcirculation and may promote angiogenesis, normalize endothelial function and improve myocardial perfusion and anginal symptoms. The benefit and durability of EECP therapy in these patients was studied.

Methods: Patients with typical angina refractory to medical therapy and evidence of microvascular angina (a pharmacologic or exercise stress test with radionuclide or echocardiographic imaging [ST] showing regional ischemia together with a cardiac perfusion defect demonstrating significant coronary disease) were treated with EECP. Angina, assessed by the Canadian Cardiovascular Society class (CCS), and stress tests were evaluated at baseline and after completing EECP treatment. Major cardiovascular events (cardiac hospitalization, death, infarction) were tracked for the duration of follow-up. Statistical analysis was performed with the student t test; significance level p<0.05.

Results: Twenty one pts, 14 women and 7 men with a mean age of 68.5 years, received an average of 36.4 hours of EECP; CCS improved in all patients; the average baseline CCS class III of IV improved to an early follow-up of I of II (p<0.001). ST obtained a mean of 5.0 months post EECP showed complete resolution of defects in 16/17 cases (p<0.05). There was a durable reduction in angina in 20/21 patients at a mean 12.9 months of follow-up. With up to 19 months of follow-up only 1 patient had an adverse event [heart failure requiring admission] and increasing angina (treated with EECP).

Conclusions: Microvascular angina is effectively treated with EECP. There is a reduction in angina and provokable ischemia. The effect is durable with a low incidence of recurrent angina one year post treatment and few adverse cardiovascular events.

308A ABSTRACTS - Myocardial Ischemia and Infarction JACC March 3, 2004