



SUPPLEMENT TO

JACC

MARCH 6, 2007
VOLUME 49, No. 9
(SUPPLEMENT A)

JOURNAL of the AMERICAN COLLEGE of CARDIOLOGY



56th Annual Scientific Session
March 24 - 27, 2007, New Orleans

For Online Planning, Go to www.acc07.acc.org

3 Abstracts on
EECP

Abstracts of Original Contributions

Presented at
American College
of Cardiology
56th Annual
Scientific Session



The Cardiovascular World Comes to New Orleans

ELSEVIER

ISSN 0735-1097

www.onlinejacc.org

841-7

A Prospective Study Comparing Two Different Algorithms for Predicting Cardiovascular Events in Renal Transplant Candidates: In Whom Should Cardiac Scintigraphy Be Performed?

Luis Henrique W. Gowdak, Rodolfo L. Arantes, Flavio J. de Paula, Marcos Rienzo, Luiz Antonio M. Cesar, Luiz Estevan Ianhez, Elias David Neto, Eduardo M. Krüger, Jose Antonio F. Ramires, Jose J.G. de Lima, Heart Institute (InCor), University of São Paulo Medical School, São Paulo, Brazil, Renal Transplant Unit, University of São Paulo Medical School, São Paulo, Brazil

Background: Patients (pt) with end-stage renal disease (ESRD) routinely undergo cardiovascular assessment for their increased risk of cardiovascular disease (CVD) and major adverse cardiovascular events (MACE). No prospective study compared the value of two different clinical risk stratification algorithms in predicting the occurrence of MACE, and in selecting pt in which additional workup might be needed.

Methods: 663 pt (65% men, 55±10 years-old) with CKD on dialysis were stratified according to either the American Society of Transplantation (AST) (*high-risk [HR]*: age ≥ 50 years, or diabetes [+], or CVD [+]; *low-risk [LR]*: none of the above) or the European Renal Association (ERA) (*HR*: CVD [+]; *intermediate-risk [IR]*: diabetes [-] or age ≥ 50 years; *LR*: none of the above). All pt were further stratified by cardiac scintigraphy (SPECT-Sestamibi-dipyridamole), irrespectively of symptoms, and followed-up for 60 months (median, 24). The risk for the primary endpoint (the composite incidence of fatal/non-fatal MACE) was determined using the Cox proportional hazards model.

Results: There were 120 fatal/non-fatal MACE. HR-pt (n=537) by the AST criteria had twice the risk for MACE compared to LR-pt (n=96) (RR=2.00 [1.29-3.61]; P=0.0006). When SPECT results were included in the analysis, HR-pt with abnormal scans (n=167) had the lowest survival free of events (RR=1.36 [1.11-1.67]; P=0.002). In LR-pt, an abnormal scan (n=12) did not influence long-term prognosis (RR=0.72 [0.12-1.31]; P=.12). Using the ERA criteria, HR-pt (n=244) also had a significant increase in the risk for MACE compared to IR-pt (n=294) (RR=2.6 [1.85-3.99]; P<.0001), whereas LR-pt (n=95) had the lowest risk (RR=0.42 [0.19-0.75]; P<.0001). Adding the SPECT results to the analysis, only IR-pt with abnormal scans had an increased risk for MACE (RR=1.54 [1.11-2.16]; P=.01). Pt with abnormal scans at HR (RR=1.04 [0.81-1.36]; P=.74) or LR (RR=0.66 [0.18-1.47]; P=.1) had no increase in the risk for MACE.

Conclusions: Pt with CKD on dialysis should be first risk-stratified by current clinical algorithms. Further stratification by SPECT should be reserved to HR-pt (AST) or IR-pt (ERA), affording a more rational use of resources.

12:15 p.m.

841-8

Prognostic Value of Stress Gated SPECT Imaging in Diabetics: Contribution of Perfusion and Function for Prediction of Adverse Cardiac Outcome

Alexey V. Sorokin, Gerassimos Stavens, Alan W. Ahlberg, Gary V. Heller, Hartford Hospital, Hartford, CT

Background: Diabetes is considered a coronary disease equivalent. There are limited prognostic data using gated SPECT (GS) in this population. This study examined the prognostic contribution of perfusion and function from GS among diabetics.

Methods: Consecutive diabetic patients were identified from a prospective database. Images were interpreted in blinded fashion by 3 readers using a 17-segment model. Abnormal summed stress score (SSS), summed difference score (SDS) and ejection fraction (EF), respectively, were defined as: 4-13, 2-7 and 30-49% (mildly to moderately abnormal); >13, >7 and <30% (severely abnormal). Follow-up was 92.5% over 2.7 ± 1.9 years. Patients revascularized ≤60 days after GS were excluded. Endpoints were cardiac death (CD) or non-fatal myocardial infarction (MI). Cox regression modeling (I. pre-scan, perfusion, function; II. pre-scan, function, perfusion) was applied to identify predictors of adverse outcome.

ted
the
102;
ced

ide
y in

risk stratification (figure).

Conclusions: Among diabetics, perfusion and function data from gated SPECT provide independent and incremental prognostic information and should be utilized routinely in risk stratification.

JACC March 6, 2007

ABSTRACTS - Diagnostic Testing 111A

Exercise Testing

Tuesday, March 27, 2007, 11:00 a.m.-12:30 p.m.

Room 271-273

11:00 a.m.

842-3

Improved Detection of Stress-Induced Ischemia Using Analysis of High-Frequency ECG Components

Eran Toledo, Nechi Almog, Jonathan A. Lipton, Stafford G. Warren, Michael Broce, Donald R. Lilly, Dan B. Lucas, Galen S. Wagner, Duke University, Durham, NC, Charleston Area Medical Center, Charleston, WV

ECG detection of ischemia is based on identifying changes in the repolarization phase. Investigation of mid-QRS potentials, related to depolarization, using analysis of high frequency QRS (HFQRS) components was recently reported to better identify ischemia. Our aims were to validate (i) this technique in patients undergoing exercise myocardial perfusion SPECT (MPS) and (ii) compare its performance with conventional ECG.

Methods: Exercise MPS was performed in 133 consecutive pts (63±12 yo, 100 men) and used as the gold standard for ischemia. Pts with BBB (n=19) or inconclusive MPS (n=5) were excluded. Conventional ECG was combined with high resolution ECG acquisition that was digitized and analyzed using the HyperQ™ System (BSP, Tel Aviv, Israel). The relative HFQRS intensity change during exercise was used as an index of ischemia.

Results: HFQRS analysis was possible in 105 pts of whom 22 exhibited MPS ischemia (4 pts excluded due technical reasons). The HFQRS index of ischemia was found more sensitive than the conventional ST analysis (77% vs 43%, p<0.05, see table) with comparable specificity (66% vs 57%, p=NS). In women, HFQRS analysis resulted in improved specificity relative to conventional ECG (70% vs 33%, p<0.05). In pts with inconclusive ST changes, HFQRS analysis correctly identified 17/21 pts.

Conclusions: HFQRS analysis was more sensitive in detecting stress-induced ischemia and exhibited improved specificity in women. Thus, it may aid in the non-invasive diagnosis of ischemic heart disease.

	Number of subjects	HFQRS Sensitivity	ST Sensitivity	HFQRS Specificity	ST Specificity
All patients	105	77% * (17/22)	43% (9/21)	66% (55/83)	57% (37/65)
Women	29	83% (5/6)	75% (3/4)	70% * (16/23)	33% (5/15)
Inconclusive ECG	21	100% (2/2)	NA	79% (15/19)	NA

11:15 a.m.

842-4

Enhanced External Counterpulsation Decreases Arterial Stiffness and Myocardial Oxygen Demand in Patients With Refractory Angina

Darren P. Casey, C. Richard Conti, Wilmer W. Nichols, Matheen A. Khuddus, Calvin Y. Choi, Randy W. Braith, Center for Exercise Science, Department of Applied Physiology and Kinesiology, University of Florida, Gainesville, FL, Department of Cardiovascular Medicine, University of Florida, Gainesville, FL

Background: Enhanced external counterpulsation (EECP) is a non-invasive modality

for treatment of symptomatic coronary disease (CAD) in patients not amenable to revascularization procedures. However, the mechanism(s) underlying the benefits of EECP remain unknown. We hypothesized that extra-cardiac factors, such as peripheral arterial stiffness and elevated myocardial oxygen demand are the therapeutic target for EECP.

Methods: We randomly assigned 20 symptomatic patients with CAD to 35 1-hr sessions of EECP (n=12) or 35 1-hr sessions of sham-EECP (n=8). Radial artery pressure waveforms were recorded by applanation tonometry and aortic pressure waveforms were generated using a mathematical transfer function. Augmentation index (AI₀) and timing of the reflected pressure wave (Δt_r) were calculated from the generated aortic pressure waveform. Aortic pulse wave velocity (PWV; m/sec) between the carotid and femoral arteries (CFPWV) was calculated by determining the delay between the appearance of the pressure waveform foot at each site. Exercise duration, anginal threshold, and peak oxygen consumption (VO_{2peak}) were measured by a graded treadmill test.

Results: EECP decreased AI₀ and increased Δt_r (24 ± 1.9% vs. 18 ± 2.0%, P < 0.01; 135 ± 3.3 vs. 142 ± 2.9 msec, P < 0.01, respectively) but did not change in sham (22 ± 3.7% vs. 21 ± 3.7%; 134 ± 4.7 vs. 132 ± 4.8 msec, P > 0.05, respectively). Left ventricular wasted energy, a measure of myocardial oxygen demand, decreased after EECP (6149 ± 924 vs. 3704 ± 595 dynes/sec/cm², P < 0.01) but did not change in sham (5471 ± 706 vs. 5105 ± 635 dynes/sec/cm²; P > 0.05). EECP decreased CFPWV (11.9 ± 0.8 vs. 10.4 ± 0.6 m/s, P < 0.01) but did not change in sham (11.3 ± 0.8 vs. 11.4 ± 0.5 m/s, P > 0.05). EECP increased exercise duration, time to angina, and VO_{2peak} (595 ± 52 vs. 762 ± 73 sec, P < 0.01; 377 ± 50 vs. 598 ± 50 sec, P < 0.01; 17.3 ± 1.5 vs. 19.9 ± 1.6 ml/kg/min P < 0.01, respectively) but did not change in sham (601 ± 56 vs. 625 ± 57; 376 ± 26 vs. 400 ± 21; 17.0 ± 1.1 vs. 17.9 ± 1.3 ml/kg/min, P > 0.05, respectively).

Conclusions: EECP therapy reduces central arterial stiffness, reduces myocardial oxygen demand, and improves exercise tolerance and anginal threshold in symptomatic patients with CAD.

10:00 a.m.

10:00 a.m.

1001-73 Manganese Superoxide Dismutase Polymorphism is Associated with Acute Coronary Syndrome

Hajime Fujimoto, Ryozo Nagai, Minoru Ohno, Toranomon Hospital, Tokyo, Japan, University of Tokyo, Tokyo, Japan

Background: Oxidative stress plays an important role in atherogenesis. Manganese superoxide dismutase (MnSOD) is an antioxidant enzyme localized in the mitochondria, where it catalyzes the conversion of superoxide radicals. There are two genetic variants of MnSOD arising from a valine-to-alanine substitution in the signal peptide. We previously reported that the alanine variant of MnSOD increases the mitochondrial MnSOD activity, and protects macrophage against the oxidized low density lipoprotein (oxLDL)-induced apoptosis. So, we hypothesized that MnSOD polymorphism may affect the vulnerability of the plaque and occurrence of acute coronary syndrome (ACS). In this study, we investigated the association between MnSOD genotype and ACS.

Methods: Blood samples were collected from 641 healthy subjects who did not have any symptoms and evidence suggesting coronary artery disease and 87 ACS patients. ACS patients underwent coronary angiography (CAG) and diagnosed to be non-ST elevated myocardial infarction (NSTEMI) or ST elevated myocardial infarction (STEMI) from CAG, ECG, and laboratory findings. MnSOD genotype of each subject was analyzed by real-time polymerase chain reaction.

Results: Among the 87 ACS patients, 44 were NSTEMI, and 43 were STEMI. The valine allele frequency was higher in the ACS patients (0.929) than in the healthy subjects (0.835) (odds ratio [OR] = 2.56, P = 0.0016 by chi-square analysis). MnSOD genotype distribution in healthy subjects was as follows; alanine/alanine 2.2%, alanine/valine 28.5%, and valine/valine 69.3%, and was compatible with Hardy-Weinberg equilibrium. In ACS patients the genotype distribution was: alanine/alanine 0.0%, alanine/valine 13.8%, and valine/valine 86.2% (ACS patients, P = 0.0037 by chi-square analysis). Multivariate logistic regression analysis revealed the valine/valine homozygosity to be a genetic risk factor for ACS independent of other coronary risk factors (OR = 2.73, 95% CI (1.38, 5.41); P = 0.0041). **Conclusion:** The alanine variant of MnSOD signal peptide reduces the risk of ACS. This may be related to the fact that alanine variant increases the tolerance of macrophages against oxLDL-induced apoptosis.

10:00 a.m.

1001-74 Transradial Approach in Percutaneous Coronary Intervention Following Pre-hospital Fibrinolysis Reduce Vascular Access Site Complication: Data From The French National OPTIMAL Study

Christophe LOUBEYRE, Loic BELLE, Dominique SAVARY, Meyer ELBAZ, Sandrine CHARPENTIER, Yves COTTIN, Louis SOULAT, Vanina BONGARD, Darko MILJKOVIC, Philippe Gabriel STEG, Jacques PUEL, On behalf of the OPTIMAL Study Group, University Hospital, Toulouse, France, Boehringer Ingelheim France, Reims, France

Trans Radial Approach in Percutaneous Coronary Intervention Following Pre-Hospital Fibrinolysis Reduces Bleeding Compared to the Femoral Route: Data from the French National OPTIMAL study.

Background: Early post lysis angiography and percutaneous coronary intervention (PCI) is largely used in ST elevation myocardial infarction (STEMI). Bleeding, particularly at the access site is a major concern and the impact of radial route as not been assessed.

Methods: From Nov 2004 to Nov 2005 a prospective study was conducted in France with STEMI patients treated by PHT and who underwent coronary angiography within 6 hours after lysis. The vascular access site was left to the operator's discretion.

Results: Data were available for analysis in 948 patients. 937 underwent early PCI. Mean age was 60.3 years, 82% were males. Arterial access was radial in 39% of cases. Baseline characteristics were similar in the two groups, except for cardiogenic shock more common in the femoral group (9.1 vs 1.6%, p<0.001). Radial access was associated with more frequent use of GP IIb/IIIa inhibitors (18.9 vs 13.7%, p=0.04). The rate of early discharge (<3 days) was 44% after trans-radial PCI vs 34 % after transfemoral PCI (p=0.004).

	Femoral (%)	Radial (%)	OR	95% CI	p
Any bleeding	9.44	4.38	2.28	[1.16:4.49]	0.020
Minor bleeding	7.28	3.32	2.29	[1.05:4.97]	0.035
Major bleeding	2.27	1.11	2.06	[0.54:7.84]	0.365
ICH and Stroke	1.78	2.20	0.80	[0.28:2.31]	0.788
Hospital Death:	7.43	2.43	3.22	[1.46:7.10]	0.002

Major bleeding includes transfusion and/or surgery

Conclusion: Radial approach in early PCI post lysis is associated with a low bleeding risk as compared to the femoral route. The radial approach may reduce hospitalization stay duration and enables the adjunctive use of a GP IIb/IIIa inhibitors when necessary.

1001-75 Direct Collagen Injection To Thicken The Infarct Scar: Collagen Density Determines Angiogenesis

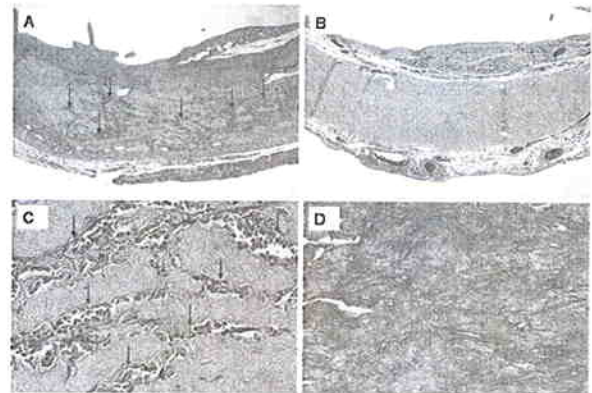
Wangde Dai, Gregory L. Kay, Aarne J. Jyrala, Robert A. Kloner, Heart Institute in the Good Samaritan Hospital, Los Angeles, CA

Background: We have reported that implantation of dense collagen (Col) thickened the scar of myocardial infarcts in rats, but no angiogenesis developed within the Col implant (Col-I). We determined whether the Col density could affect angiogenesis within the Col-I.

Methods: Low density (LD, 35mg/ml) and high density (HD, 65mg/ml) Col were used. Col or saline (100 µl) was injected into the scar of 1-week-old myocardial infarcts in rats (n=3 LD Col; n=11 HD Col; n=13 Saline). Rats were euthanized at 1 week (n=3 LD Col; n=2 saline) or 6 weeks (n=11 HD Col; n=11 saline), and hearts processed for histology.

Results: Compared with hearts that received saline, Col-I was easily identified histologically as homogeneous bright red staining by picrosirius red. H&E staining demonstrated capillary-like tubular structures containing erythrocytes within the Col-I in 3/3 hearts that received LD Col at 1 week (Fig A:40x and C:400x; black arrows; 435±78 blood vessels/mm² within the Col-I). The capillary-like tubular structures were not observed within the Col-I in 11/11 hearts that received HD Col at 6 weeks (Fig B:40x and D:400x). LD and HD Col were associated with thicker scars, but only LD Col reduced LV volume (31±5mm²) compared to saline (47±0.2mm², p=0.03)

Conclusions: Blood vessels developed within LD Col-I at 1 week and were associated with less LV remodeling, but did not appear within HD Col-I even at 6 weeks. The results suggest that the density of Col significantly affects the development of angiogenesis and remodeling.



10:00 a.m.

1001-90 Enhanced External Counterpulsation Inhibits Intimal Hyperplasia by Downregulating Proliferative Signaling Proteins

Yan Zhang, Hong Ma, Gui-Fu Wu, Xiao-Hong He, Xiao-Lin Chen, Dong-Hong Liu, Zhi-Min Du, Yu-Gan Dong, Ya-Fei Jin, Dian-Qiu Fang, Jin-Yun Luo, Yan Xiong, Kui-Jian Wang, William E. Lawson, John CK Hui, Zhen-Sheng Zheng, The Key Laboratory on Assisted Circulation, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, People's Republic of China, Cardiology Division, State University of New York at Stony Brook, Stony Brook, NY

Background: Hypercholesterolemia promotes intimal hyperplasia (IH). Enhanced external counterpulsation (EECP) increases shear stress, improves endothelial function. This study hypothesizes that EECP reduces IH by downregulating the VSMCs proliferative signaling pathway, altering atherogenesis due to hypercholesterolemia.

Methods: 48 male pigs were randomly assigned to usual diet (N; n=7), high cholesterol diet (Chol; n=18), or Chol+EECP (34 hrs of EECP last 7 wks, n=23) for 15 wks. Blood lipids, viscosity, hemodynamic parameters were measured. Animals were sacrificed at 15 wks and their LAD stained with hematoxylin/eosin to assess IH by intima-to-media area ratio (IMR) and wall-to-lumen ratio (WLR). VSMCs proliferation index was measured by the Elivision immunohistochemical technique incubated with mouse anti-proliferating cell nuclear antigen (PCNA) Ab. Proliferative signaling protein expression were monitored by incubating LAD cross sections with rabbit polyclonal phospho-AKT Ab and by indirect immunofluorescence using rabbit polyclonal NF-κBp65 Ab. Statistical analysis was by Kruskal-Wallis and Mann-Whitney tests.

Results: Cholesterol of CHOL and CHOL+EECP groups were higher than N (9.2±2.8 and 8.5±3.6 vs 1.9±0.3 mmol/L, p<0.001). Doppler diastolic peak flow in the brachial artery increased with EECP (59.5±13.6 vs 24.6±4.7 cm/sec, p<0.001), increasing arterial wall shear stress > 2X (54.4±12.5 vs 23.9±7.3 dynes/cm², p<0.001). EECP decreased IMR and WLR (N: 19.7±9.0, 18.0±8.2; CHOL: 36.4±16.6, 24.0±4.4; CHOL+EECP: 21.3±10.0, 17.6±4.7%, p<0.001), a finding supported by reduction of VSMCs proliferation index (N: 0.4±0.2, CHOL: 0.7±0.2, CHOL+EECP: 0.5±0.1; p<0.05), with suppression of protein kinase AKT (N: 1.0±0.2, CHOL: 14.6±9.5, CHOL+EECP: 1.6±0.5, p<0.05) and transcription factor NF-κB (3,893±116, 19,448±3,071, 7,153±1,469, p<0.05) by EECP.

Conclusions: EECP increased shear stress, suppressed activity of VSMC proliferation signaling proteins, and decreased intimal hyperplasia due to hypercholesterolemia. This paradigm suggests that EECP offers a novel modality for prevention and treatment of cardiovascular disease.

and ideal levels (LDL <70 with HDL ≥60 mg/dL) in only 1.4% (Table). Prior to admission, only 21.1% of pts were receiving LRx (LDL 94.3 ± 36.4, HDL 39.6 ± 12.6 mg/dL). Predictors for higher LDL included younger age, no diabetes, higher BMI, Hx hyperlipidemia and no prior LRx. Lower HDL was associated with younger age, prior MI, male, higher BMI, and diabetes. Both LDL and HDL levels declined over time (P<0.0001).

Conclusions: In a large cohort of hospitalized CAD patients, almost half have admission LDL levels < 100 mg/dL and less than 10% have HDL levels above 60 mg/dL. These findings provide further support for recent guideline revisions with even lower LDL goals and for developing effective treatments to raise HDL.

HDL (mg/dL)	LDL (mg/dL)					Total (n=103,632)
	<70 (n=18,191)	70-100 (n=33,111)	100-130 (n=28,429)	130-160 (n=15,385)	≥160 (n=8,516)	
<40 (n=56,587)	10.8%	17.8%	14.7%	7.6%	3.8%	54.6%
40-60 (n=38,883)	5.3%	11.7%	10.6%	6.2%	3.7%	37.5%
≥60 (n=8,162)	1.4%	2.5%	2.1%	1.1%	0.7%	7.8%
Total (n=103,632)	17.6%	32.0%	27.4%	14.9%	8.2%	

Noon

1206-276

The Effect of External Counterpulsation Therapy on Circulating Endothelial Progenitor Cells in Patients With Angina Pectoris

Alon Barsheshet, Hanoch Hod, Michael Shechter, Orna Sharabani-Yosef, Eti Rosenthal, Israel M. Barbash, Shlomi Matetzky, Reshef Tal, Ariel G. Bentancur, Ben-Ami Sela, Arnon Nagler, Jonathan Leor, Neufeld Cardiac Research Institute, Heart Institute, Sheba Medical Center, Ramat Gan, Israel, The Division of Hematology and Bone Marrow Transplantation, Sheba Medical Center, Ramat Gan, Israel

Background: External counter pulsation therapy (ECPT) offers symptomatic relief and improves ischemia in patients with refractory angina pectoris. Its mechanism of action, however, remains unclear. Our objective was to test the hypothesis that ECPT improves the number and function of circulating endothelial progenitor cells (EPCs).

Methods: We prospectively studied 25 consecutive patients with angina pectoris treated with ECPT (n=15) or standard care (n=10). The number of EPCs positive for CD34 and kinase insert domain receptor (KDR) was determined by flow cytometry and function was assessed by the number of colony forming units (CFUs) in a 7-day culture, prior to intervention and after 2 months.

Results: Anginal score was improved by ECPT from 3.0 to 2.0 (p<0.001). The number and function of circulating EPCs were significantly improved in patients treated by ECPT: EPC numbers increased from 10.2 to 17.8/10⁵ mononuclear cells (p<0.05), and CFUs from 3.5 to 11.0 (p=0.01). Flow mediated dilatation (FMD) was improved by ECPT (from 7.4 to 12.2, p<0.001) and was correlated with an increase in EPC-CFUs (r=0.461, p=0.027). The levels of asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide synthase were reduced by ECPT (from 0.70 to 0.60 μmol/L, p<0.01). Conversely, these variables remained unchanged in the control group, before and after 2-month follow-up.

Conclusions: Our preliminary findings show, for the first time, that ECPT increases the number and function of circulating EPCs and proposes a new mechanism whereby ECPT relieves symptoms in patients with angina

Noon

1206-277

Higher Resting Heart Rate Is Associated With Metabolic Syndrome and Lower Ejection Fraction in Patients With Diabetes and Known Coronary Artery Disease in Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Trial

Jamal S. Bana, Regina M. Hardison, Rodica Pop-Busul, Maria M. Brooks, Teresa Jones, Richard W. Nesto, Martial G. Bourassa, University of Pittsburgh, Pittsburgh, PA

Background: Neuroadrenergic status affects key regulatory mechanisms of cardiovascular as well as metabolic function. Both Metabolic Syndrome (Met S) and the presence of a high resting heart rate have been shown to be associated with increased cardiovascular events. However, the relation between Met S and resting heart rate is unknown.

Methods: We evaluated 2252 patients in Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial. All patients had Type 2 Diabetes and coronary artery disease (CAD) and were randomized to early revascularization and aggressive medical therapy versus aggressive medical therapy alone for CAD and to insulin-sensitizing versus insulin-providing treatments for diabetes. The ATP III definition of Met S was used. Linear regression model adjusted for age, sex, use of beta blockers, exercise and LDL levels was used to evaluate the relation of Met S and its risk factors (RF) to resting heart rate as measured on the 12 lead ECG. The relationship between heart rate and ventricular function was also evaluated.

Results: In BARI 2D, 90.8% of the participants had the Met S. The mean heart rate was 68.3±12.5 beats per minute. The heart rate was higher (p < 0.001 for trend) with increasing number of risk factors for Met S. Multiple linear regression analyses demonstrated that as compared to individuals without Met S, the heart rate was significantly higher in participants with Met S (regression coefficient: 2.0, p=0.001). Participants with 2 RFs had adjusted regression coefficient of 1.5 (p=0.13), presence of 3 RF regression coefficient of 3.0 (p=0.002) and participants with all 4 RF had a regression coefficient of 4.1 (p 50%), the heart rate was significantly higher in participants with EF 60% participants with EF < 35% had adjusted regression coefficient of 5.5 (<0.001).

Conclusion: Higher heart rate is associated with Metabolic Syndrome and ventricular dysfunction. Autonomic dysfunction manifests as sympathetic overactivity and consequently may be one way by which Met S imparts higher risk for cardiovascular disease. Higher resting heart rate in diabetic patients with CAD identifies a subgroup in whom additional secondary preventive strategies may be necessary.

Noon

1206-278

Statin-Like, Dose-Dependent Reductions in LDL-C and Apolipoprotein B With ISIS 301012, an Antisense Inhibitor of Apolipoprotein B, in Subjects With Polygenic Hypercholesterolemia

Evan Stein, JoAnn Bradley, Emil Chuang, Mark Wedel, John Su, Richard Geary, Rosie Yu, John Kastelein, Metabolic & Atherosclerosis Research Center, Cincinnati, OH, Isis Pharmaceuticals, Inc., Carlsbad, CA

Background: ISIS 301012 selectively inhibits apoB protein synthesis in the liver. Previously, we have shown an LDL-C reduction up to 70% in healthy volunteers in Phase I dose ranging studies with short term dosing. The safety and efficacy profile allowed for longer treatment duration (13 weeks), less frequent dosing (every other week), and a target population of polygenic hypercholesterolemic failing to meet target with diet and exercise alone.

Methods: Subjects (n=10 per group) with elevated LDL-C > 130mg/dL were enrolled into 1 of 5 groups. The first 2 groups received four 200 mg doses of ISIS 301012 in the first 11 days (Days 1, 4, 8, and 11; "Load") followed by 100 mg qow (avg 50 mg/week), or 200 mg qow (avg 100 mg/week). The last 3 groups received 200, 300, or 400 mg every week without a load. Treatment to placebo was 4:1 in each cohort. Study drug was administered subcutaneously.

Results: The study is ongoing. A 12, 22, and 42% median reduction in LDL-C and a 22, 23, and 47% median reduction in apoB were observed in the 50, 100, and 200 mg/week dose groups, respectively, with negligible changes in the pooled placebo group. Preliminary results in the 300 mg/wk cohort showed a 42 and 41% reduction in LDL-C and apoB, respectively following the first 7 weeks of 13 weeks treatment. The most common adverse event has been mild, painless erythema at injection sites. No serious adverse events occurred. The drug was well tolerated. One subject displayed an isolated ALT >3x ULN 45 days after last dose.

Conclusions: The initial results show that ISIS 301012 achieves statin-like LDL-C reductions via a complementary mechanism. Furthermore, achieving such LDL-C reductions with a dosing interval of every other week is feasible. Dose escalation to the 400 mg/wk dose group is underway. Final data from the study will be presented at the meeting.

ACC.POSTER SESSION

1008

Vascular Disease, Hypertension and Prevention

Sunday, March 25, 2007, 1:30 p.m.-5:00 p.m.
Hall H

3:30 p.m.

1008-1

Rapid True Aneurysm Formation after Healing of Thrombosed Aortic Dissection

Rieko Ishimura, Akiko Maehara, Tomotaka Dohi, Jun Masuda, Hajime Fujimoto, Yo Fujimoto, Haruo Mitani, Sugao Ishiwata, Minoru Ohno, Cardiovascular center, Toranomon Hospital, Tokyo, Japan

Background: Aortic dissection (AD) of DeBakey IIIb type with thrombosed false lumen has a good short-term prognosis. However, the long-term prognosis has not been well evaluated.

Methods and Results: From 1996 to 2006, 96 consecutive patients (age 65 ± 13 yo, 70 males) were admitted to our institution for acute AD. AD was evaluated with computed tomography (CT). CT scans were performed every year. There were 20 patients with type IIIb AD with thrombosed false lumen. Among these, 8 patients (38%) showed rapid aortic dilatation as a true aneurysm in the follow-up period. During the acute phase, the first measured maximum dissected segment diameter in the dilated group (N = 8) tended to be larger than that of non-dilated group (N = 12) (max dissected segment; 44.7±7.0mm vs. 37.0±8.5mm, p=0.06), although the adjacent reference diameter between two groups were similar. The expanded diameter per year tended to be larger than that of the true thoracic aortic aneurysm (TAA) group (N = 14) as control (5.6±6.5 vs. 2.0 ± 3.2mm, p = 0.12), although the first measured maximum dilated segment diameter in each group was similar.

Conclusions: One third of thrombosed aortic dissections of DeBakey IIIb type with the larger maximum dissected diameter may undergo rapid dilatation that may develop into a true thoracic aneurysm in the healed dissected segment.

