Myocardial Ischemia/Infarction—Basic

Sunday, March 29, 2009, 9:30 a.m.-12:30 p.m.
Orange County Convention Center, West Hall D

1014 Myocardial Ischemia/Infarction—Basic

ACC POSTER CONTRIBUTIONS

1014

Myocardial Ischemia/Infarction—Basic

Three-Dimensional RGD-Modified Alginate Scaffold Designed to Enhance Efficacy of Cell Transplantation to Infarcted Myocardium

Hugo P. Sonderegger, Fiona See, Tetsunori Seki, Silviu Itescu, Columbia University, New York, NY

Background: Cell transplantation strategies for cardiac repair are currently limited by poor survival of transplanted cells. Three-dimensional (3D) scaffolds improve cell transplants survival after delivery to infarcted myocardium. We aimed to design a biocompatible porous 3D scaffold using custom purified alginate that augments cell viability. Two-dimensional surfaces coated with cyclic RGDfK peptides have been shown to improve cell viability. We hypothesized that a three-dimensional alginate scaffold covalently modified with cyclic RGDfK peptides would improve cell viability and could be used to transplant cells to infarcted myocardium following myocardial infarction (MI).

Methods: Cyclic RGDfK peptide modified porous alginate scaffolds were seeded with 3x10^6 neonatal rat cardiomyocytes (nCM), 3x10^6 neonatal rat cardiac fibroblasts (nCF), or 3x10^6 human mesenchymal stem cells (hMSCs), followed by culture for one week. Cell viability was determined by trypan blue exclusion and WST-1. Circular scaffolds (16mm x 0.75mm) without hMSCs (n=4), 1x10^6 hMSCs (low dose, n=13) or 3x10^6 hMSCs (high dose, n=6) were applied to the epicardial surface of nude rat hearts 48 hours after MI. Intramyocardial saline injected animals served as controls. 1 week later, cardiac function was determined by echocardiography.

Results: At 1 week, nCM viability inside scaffolds increased from 3.3±1.2% (0 mg/g cRGDfK) to 12.3±0.1% (10 mg/g cRGDfK) + gelatin (p=0.06). Clusters of beating myocytes could be detected. nCF viability increased from 48.2±21% (0 mg/g cRGDfK) to 77.2±3.2% (10 mg/g cRGDfK) (p=0.005). Human MSC viability increased from 15.3±0.7% (0 mg/g cRGDfK) to 59.5±2.2% (20 mg/g cRGDfK) (p=0.01). Fractional shortening (FS) decreased by 15.2±2.5% in saline controls. Following epicardial scaffold application, FS decreased by 1.4±0.3% (without hMSCs) and 12.3±0.1% (10 mg/g cRGDfK) to 28.9±7.3% (10 mg/g cRGDfK + gelatin) (p=0.05).

Conclusion: 3D alginate scaffolds modified with cRGDfK peptide promote cell viability in vitro. Epicardial application of 3D modified alginate scaffolds seeded with low dose hMSCs improves cardiac function following MI.

9:30 a.m.

Human Fetal Mesenchymal Stem Cells Exert More Powerful Cytoprotective Paracrine Effects Than Bone Marrow-Derived Mesenchymal Stem Cell

Elisabetta Cerri, Patricia Danieli, Chiara Ciufrredda, Andrea Di Marco, Roberto Bassani, Marianna Rocco, Gianluca Viarengo, Peter J. Schwartz, Massimiliano Gneckchi, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, Università di Pavia, Pavia, Italy

Background: We and others have shown that adult mesenchymal stem cells (MSC) repair experimental infarcted hearts mainly through paracrine mechanisms. In particular, MSC produce and release anti-apoptotic factors (AAF) that lead to cytoprotection. However, the production of AAF may be negatively influenced by donor age. We hypothesized that MSC of fetal origin may exert more powerful cytoprotective effects compared with adult MSC.

Methods: MSC were isolated from amniotic membranes (A-MSC) of human term placenta or from the bone marrow (BM-MSC) of healthy donors. The immunophenotype was determined by FACs analysis. The ability of MSC to turn into terminally differentiated cell types was also tested. The production of several known AAF was measured by RT-PCR. Rat neonatal cardiomyocytes (H9c2 cells) were used to test the anti-apoptotic effects exerted by the MSC. H9c2 cells were exposed for 24 h to hypoxia in presence of control medium (CTRL-M) or conditioned medium (CM) from either A-MSC or BM-MSC. The amount of apoptosis was quantified by TUNEL staining. Cleaved Caspase 3 in HM Hc2 cells was evaluated by flow cytometry and Western blotting.

Results: MSC were successfully isolated from 15 amniotic membranes and 10 BM aspirates (donor age: 59.2 ± 3.8 years). At passage two, all cells from the amniotic and the BM displayed the antigen profile typical of MSC and efficiently differentiated into osteocytes, adipocytes and chondrocytes. Compared with BM-MSC, A-MSC expressed significantly higher levels of PDGf B (+6.6 fold), EPO (+4.8), IGF-1 (+2.1), BMP2 (+1.7), FGF2 (+1.4) and VEGF (+1.3). A-MSC-CM reduced the number of TUNEL positive H9c2 cells by 70% compared with CTRL-M (p<0.05) and by 60% compared with BM-MSC-CM (p<0.05). Fluorimetric assay showed reduced levels of cleaved Caspase 3 in the presence of A-MSC-CM (-33% vs CTRL-M, p<0.05; -25% vs BM-MSC-CM, p<0.05). Western blotting confirmed the reduction of Caspase 3 in the presence of A-MSC-CM (+27% vs BM-MSC-CM).

Conclusions: A-MSC produce high amount of AAF and exert remarkable cytoprotective effects on hypoxic cardiomyocytes. A-MSC may represent a novel and powerful approach to cardioprotective therapy for ischemic heart disease.

9:45 a.m.

1014-127 Targeted Delivery of Immunoliposomes Containing Vascular Endothelial Growth Factor to Post Myocardial Infarction Tissue Improves Cardiac Function and Microvascular Perfusion

Jenna M. Rosario, Robert C. Scott, Zharina Ivanov, Bin Wang, Parkinson Lee-Gau Chong, Deborah L. Crabb, Mohammad F. Kiani, Temple University, Philadelphia, PA

Background: Stem cell therapies have yielded inconsistent improvements in cardiac function. One potential reason is the lack of a supporting vascular microenvironment. Selective targeting of vascular endothelial growth factor (VEGF) to post-myocardial infarction (MI) tissue may improve microvascular perfusion and cardiac function.

Methods: Seventeen Sprague-Dawley rats underwent coronary ligation to create a large MI. Animals were randomly selected to receive either a dose of 0.1 ml anti-P-selectin conjugated immunoliposomes containing VEGF (0.12 ug/kg, n=8) or blank immunoliposomes (n=5) injected via tail vein immediately post-MI. Untreated MIs were followed for comparison (n=4). Immunohistochemical staining with CD31, and DIOCs was used to quantify the number of anatomical and perfused vessels in the border zone respectively. Animals were followed for 4 weeks with serial echocardiograms to measure LV internal dimensions and function.

Results: Data are expressed as mean ± SEM. ANOVA was used to determine differences between experimental groups. Values of p<0.05 were considered statistically significant.

Conclusions: Targeted delivery of low doses of VEGF to post-MI tissue results in significant improvements in microvascular structure and LV function.

9:30 a.m.

1014-128 The Role of Uncoupling Protein (UCP3) in Myocardial Necrosis and Cardiomyocyte Energetics During Ischemia-Reperfusion Injury

Cevher Ozcan, Monica Palmeri, Raymond R. Russell, III, Section of Cardiovascular Medicine, Yale University School of Medicine, New Haven, CT

Background: Recently, we have demonstrated that hearts lacking endogenous uncoupling protein 3 (UCP3) are vulnerable to ischemia-reperfusion (IR) injury. However it is not clear whether this sensitivity is associated with myocardial necrosis during oxidative stress. We hypothesize that UCP3 may prevent myocardial necrosis during IR by maintaining cardiomyocyte energetics through preserving mitochondrial function and structure.

Methods: This study examined the role of UCP3 in myocardial necrosis. UCP3-deficient and wild type mouse hearts (8-10 week-old male) were subjected to 20-min of in vivo ischemia and reperfusion. Serum troponin I levels were measured as an indicator of myocardial necrosis by ELISA in both groups with IR injury and compared to sham operated animals. In addition, myocardial nucleotide profile, as a marker of cellular energy status, was measured by HPLC.

Results: Following IR injury, the serum troponin I level was significantly higher in UCP3−/− mice (347±57 ng/ml versus 124.5±17 ng/ml, p=0.009). However both groups had similar troponin I level in control state with no IR injury (0.63±0.45 ng/ml versus 0.43±0.08 ng/ml, p>0.05). The AMP/ATP ratio, a marker of metabolic stress, increased with IR in wild type from (0.45±0.1 to 0.90±0.03, p=0.03) and UCP3−/− mouse hearts (from 0.43±0.03 to 1.05±0.2, p=0.02). The amount of ATP in UCP3−/− mice hearts decreased significantly with IR injury (from 3.59±0.2 to 1.48±0.14 nmol/mg protein, p=0.001) as well as in wild type mouse hearts (from 3.82±0.4 to 2.3±0.01 nmol/mg, p=0.02). However, wild type mice had significantly higher levels of ATP after IR injury.
**Erythromycin Attenuates Myocardial Ischemia Reperfusion Injury in Rats via Inhibition of Microcirculatory Disturbance and Inflammatory Response**

Yuji Kita, Toshihisa Aruzai, Koji Ueno, Takashii Koho, Kotaro Naito, Yui Nagatomo, Yuichiro Maekawa, Toshikui Takahashi, Tsutomu Yoshikawa, Satoshi Ogawa, Division of Cardiology, Department of Medicine, Keio University School of Medicine, Tokyo, Japan

**Background:** Myocardial ischemia-reperfusion (I/R) injury is associated with systemic inflammatory response, in which neutrophils and inflammatory cytokines play critical roles. Macrophages have been widely used in patients with chronic obstructive pulmonary disease based on their inhibitory effects against inflammatory changes in the bronchial epithelium. However, the effect of macrolides on I/R injury has not been clarified. The aim of this study is to determine the effect of erythromycin on I/R injury.

**Methods:** Eleven week-old rats were divided into 2 groups and given intravenous administration of erythromycin (25 mg/kg, EM) or saline as control group (CON/IR), 30-minute prior to myocardial ischemia. Rats underwent 30-minute occlusion of the left coronary artery, followed by reperfusion. Myocardial contrast echocardiography was performed in order to assess microcirculatory impairment in the area at risk 24 hours after I/R.

**Results:** Contrast echocardiography revealed that EM had greater collateral intensity in the area at risk compared with CON (P<0.003). Hemodynamic study 24 hours after I/R revealed that LV end-diastolic pressure in EM was lower with LV+dp/dt in EM was higher than those in CON/IR (3±v.5±2 mmHg, P<0.01, 848±1906 vs. 598±1258 mmHg/sec, P<0.01, respectively). LV ejection fraction by echocardiography was significantly greater in EM/IR than that in CON/IR (79±3 vs. 67±9 %, P<0.0001). Myocardial fibrosis as assessed by Masson's trichrome stain remained unaffected (from 8.09±1.53% to 6.08±1.02%; p=NS). By contrast, muscles containing skeletal fibers remained unaffected (from 14.0±1.5% to 16.5±2.2%; p<0.05). The number of inflammatory cells in the interstitial space was significantly lower in the treatment group (62±14 vs. 251±37; p<0.001).

**Conclusion:** Administration of t-PA (1 mg/kg, 20 min), 10 animals received CLOP 10 mg/kg IV bolus for 5 min. 10 received ADZ140 initiated with a 1 min bolus (75 μg/kg/min) followed by continuous infusion (10 μg/kg/min) for 2 h, and 10 received IV saline for 2 h. All received a
heparin 80 U/kg bolus followed by continuous infusion of 17 U/kg/hr. Results. Reoxygenation rate, cyclic flow variation, and infarct size were significantly decreased with AZD6140 (P<0.05). ADP-induced (20 μmol/L) platelet aggregation was decreased by AZD6140 (1.9 mm x ±0.7%) compared to control (26.3 mm x ±2.5%). P<0.05) at the end of adjunctive therapy. Bleeding time increases were significantly greater with CLOP vs AZD6140 (8.24±2.61 vs 5.16±2.17 min, P<0.01). Compared to their own baseline, contrast echocardiography showed complete recovery of myocardial perfusion in the AZD6140 group (73% recovery, P=0.231) compared to CLOP (50% recovery, P=0.051) and saline group (62% recovery, P=0.060). Conclusion. Administration of AZD6140 in combination with a PA in a dog coronary thrombosis model blocks ADP-induced platelet activation, aggregation and recruitment, and prevents platelet-mediated thrombosis, suggesting that AZD6140 has a better antiplatelet effect than clopidogrel.

### 9:30 a.m.

**1014-134** Dose-Dependent Contribution of Adult Human Stem Cells in Post-Infarct Myocardial Recovery

**Methods:** Mesenchymal stem cells (MSCs) were derived from sternal of 46 patients. MSCs were differentiated into cardiomycocyte-like cells (CLCs) using cardiomycogenic induction medium. One week after ligating left anterior descending artery of Wistar rats, Vibrant DiI-labeled low dose MSCs (1x 10^6, n=15) were injected into the peri-infarcted regions of myocardium. Left ventricular (LV) function was analyzed 6 weeks post transplantation by Millar's 2-F Micro-tip pressure-volume (PV) catheter.

### 9:30 a.m.

**1014-136** Ischemic Preconditioning Selectively Protects Subsarcomeral Mitochondrial Repolarization Against Ischemic Injury

**Results:** High dose cell therapy significantly improved post-infarct remodeling by infarcted regions of myocardium. Left ventricular (LV) function was analyzed 6 weeks post infarct.

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**End Ischemia**

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**1014-137** Acute Systemic and Local Neutrophil and Monocyte Depletion Prior to Primary Percutaneous Coronary Intervention in ST Elevation Myocardial Infarction

**Results:** Acute depletion of neutrophils and monocytes is shown below. 64% of STEMI patients had TIMI 0-1 flow at time of coronary artery sampling. 24 hours post PCI, neutrophil and monocyte MPO stores were similar in both groups.

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**Conclusions:** Acute neutrophil and monocyte degranulation in STEM to prior to restoration of epicardial flow suggests a possible role for neutrophil activation in the pathophysiology of occlusive plaque rupture.
An Insertion/Deletion Polyporphism in α2B-Adrenergic Receptor Gene is a Genetic Risk Factor for Sudden Cardiac Death

Jari A. Laukkanen, Timo Matikallio, Jussi Kauhanen, Sudhir Kurli, Lapland Central Hospital, Rovaniemi, Finland, Research Institute of Public Health, University of Kuopio, Kuopio, Finland

Background: A variant of the human α2B-adrenergic receptor gene that encodes a D of three residues in an intracellular acidic motif has been shown to confer decreased receptor desensitization. This receptor variant could, therefore, be involved in cardiovascular diseases (CVDs) associated with enhanced vasoconstriction. Our aim was to study whether an insertion/deletion (I/D) polymorphism in the α2B-adrenergic receptor gene is associated with the risk for sudden cardiac death.

Methods: This study was part of a prospective population-based study investigating risk factors for CVDs in a cohort of middle-aged men from eastern Finland. The study sample is based on 1606 men 42 to 60 years of age followed for an average time of 17 years.

Results: In this study population, 338 men (21%) had the D/O genotype; 467 (29%) had the I/I genotype, and 801 (50%) had a heterozygous genotype. There were 117 coronary heart disease deaths, of which 76 were due to sudden cardiac deaths within 24 hours from symptoms. In a Cox model adjusting for other coronary risk factors (age, systolic blood pressure, smoking, diabetes, serum LDL and HDL cholesterol, body mass index and exercise-induced myocardial ischemia), men with the D/O or I/D genotype had a 1.95-fold (95% confidence interval, 1.07 to 3.55, P = 0.029) risk of sudden cardiac death and a 1.71-fold (95% confidence interval, 1.08 to 2.73, P = 0.023) risk of coronary heart disease death as compared with men carrying the I/I genotype. The α2B-adrenergic receptor genotype D/D or I/D were associated with the risk of sudden cardiac death (relative hazard 3.47, 95% confidence interval, 1.36 to 8.87, <0.009) among those with previously diagnosed cardiovascular disease CVD but not among those without previous CVD.

Conclusions: The D/O and I/D genotypes of the α2B-adrenergic receptor are novel genetic risk predictors for unexpected sudden cardiac death and coronary heart disease mortality.

Ischemic Preconditioning Robustly Reduces In Vivo Myocardial Infarction in Both Male and Female Mice with Short or Long Infarct Periods and This Protection Is Lost in the Absence of Endothelial Nitric Oxide Synthase

Fuchun Yang, M.A. Hassan Talukder, Jay L. Zweier, Davis Heart and Lung Institute, The Cleveland Clinic, Cleveland, Ohio

Ischemic preconditioning (IPC) is a powerful phenomenon that provides robust cardioprotection with reduced myocardial infarction. While it occurs in mammalian hearts (including both ischemia and post-ischemic) and in human clinical trials, it is unclear whether IPC is present in mice and can protect them from myocardial infarction (MI). IPC is considered a paradigm for myocardial protection and a model of MI.

Methods: In this study, IPC was induced in male and female mice expressing the long form of the murine eNOS gene, the α2B-adrenergic receptor gene, or both. IPC was induced in male and female mice expressing the long form of the murine eNOS gene, the α2B-adrenergic receptor gene, or both.

Results: In the group of mice expressing the long form of the murine eNOS gene, IPC significantly reduced the size of infarction in both male and female mice. In mice expressing the α2B-adrenergic receptor gene, IPC significantly reduced the size of infarction in both male and female mice. However, in mice expressing both the eNOS and α2B-adrenergic receptor genes, IPC did not significantly reduce the size of infarction in either male or female mice.

Conclusions: These results demonstrate that IPC is a robust mechanism for myocardial protection in both male and female mice and that it is not dependent on the expression of both eNOS and α2B-adrenergic receptor genes.

Stabilization of Cardiac Electrophysiology in Ischemic Myocardium by Granulocyte Colony Stimulating Factor

Natichka Kanlop, Wasanrut Rutjanaprom, Punate Weerateerangkul, Nipon Chattipakorn, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Background: Granulocyte colony-stimulating factor (G-CSF) has been shown to have cardio-protective effects during ischemia/reperfusion (IR) period in vitro. However, its effects on cardiac electrophysiology in vivo is unclear. We tested the hypothesis that G-CSF can stabilize cardiac electrophysiology during IR injury by prolonging the effective refractory period (ERP), preventing the reduction of ventricular fibrillation threshold (VFT) and preserving the defibrillation threshold (DFT).

Methods: 17 pigs were divided into 3 groups. G-CSF (0.333 g/kg/min, n=6, Group 1) and saline (n=4, Group 2) were administered for 30 minutes prior to a 45-minute left anterior descending artery occlusion and at the time of reperfusion. The pacing threshold (DFT), ERP, VFT, DFT, QTc and GRD duration were determined in each pig before and during IR injury. In group 3 (n=7), G-CSF was infused without artery occlusion.

Results: During ischemic period, G-CSF (group 1) significantly increased the DFT, ERP and VFT without altering the DFT (see table). The QT interval and QRS duration were not altered for the entire study periods. Vehicle (saline) did not change the ERP, VFT or DFT. In group 3, G-CSF increased only the DFT (0.7±0.2 vs. 0.3±0.1 mA, p<0.05) without altering other parameters.

Conclusions: G-CSF increases the ERP, DFT and VFT, thus stabilizing the cardiac electrophysiology and may prevent fatal arrhythmia in ischemic myocardium. However, G-CSF does not improve defibrillation efficacy during IR injury.

Myocardial Regeneration With Autologous Mesenchymal Stem Cells in a Porcine Model of Myocardial Infarction.

Montserrat Rajo, Nuria Solanes, Jordi Farré, Mercé Roqué, Laura Novésa, Antonio Bernuex, Neus Bellera, Santiago Roura, David Tamborero, Cristina Prat, Montserrat Balle, Marta Sílges, José Ramirez, Josep Brugada, Antoni Bayses-Génis, Magda Horas, Hospital Clinic, IDIBAPS, Barcelona, Spain, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Background: Stem cell therapy offers a promising approach to reduce the short-term mortality rate associated with heart failure after a myocardial infarction (MI). We analyzed the regenerative capacity of mesenchymal stem cells (MSCs) and compared two types of administration pathways to deliver MSCs in a porcine model of MI.

Methods: Autologous MSCs were cultured from subcutaneous fat of 27 pigs, and labelled by transfection. MI was induced by balloon occlusion (90 min) of the mid-left anterior descending artery. Ten days later, animals that survived the MI induction (19 received: Group 1: intracoronary (ic) culture media (n=4); Group 2: ic MSCs (n=5); Group 3: transcendocardial culture media (n=4); and Group 4: transcendocardial MSCs (n=6). Cardiac function was tested before and 10 days after the MI using intracardiac echocardiography and again 3 weeks after MSCs administration. Then the percentage of left ventricular MI of the harvested hearts was measured by planimetry. Histological sections are being processed for the study of implantation and differentiation.

Results: See table. Macroscopic infarcts were observed in all hearts and there were no significant differences in the percentage of left ventricular MI between different groups (group 1: 19,3±5,2%; group 2: 24±0,6%; group 3: 22,2±6%; group 4: 21,7±2%).

Conclusions: This study demonstrates that neither cardiac function nor infarct size were significantly modified by the administration of ic or transcendocardial MSCs in our porcine model of MI.
Increased Beta-Catenin Pathway Expression by a Remote Ischaemic Preconditioning Stimulus: First Evidence in Humans


Background: Remote ischemic preconditioning (rIPC) induced by transient limb ischemia, protects central organs against ischemia-reperfusion (IR), and is effective in reducing myocardial injury in children and in adults during cardiac surgery. The PI3AKT/GSK-3β-pathway cell survival pathway has been proposed as being key in animal models. We tested the hypothesis that the same pathway is activated in human rIPC.

Methods: During a double blind, randomised, sham controlled trial of rIPC in patients undergoing on-pump coronary artery bypass grafting, left ventricular apical biopsy was taken 10 minutes after aortic cross-clamp release. Immunoblots were performed and quantified by densitometry (normalised to β-actin). Comparisons between control (n=6) and rIPC (n=7) was by unpaired t-testing.

Results: p-AKT and pan-AKT were increased in rIPC (p<0.05 and p=0.004 respectively). Total GSK-3β was increased by rIPC (p=0.0007) but there was no change in p-GSK-3β (p=0.98). β-catenin was significantly increased by rIPC (p<0.003)(see Figure 1).

Conclusions: We demonstrate for the first time, that rIPC increases myocardial expression of the β-catenin pathway. As well as yielding insights into the cell biology of cardioprotection, this observation may contribute to the development of clinically viable therapeutic strategies for reducing IR injury.

Figure 1: Relative expression of β-catenin pathway constituents in control and rIPC subjects. A=p-AKT, B=pan-AKT, C=p-GSK-3β, D=GSK-3β, E=β-catenin

Ejection fraction measured by intracardiac echocardiography

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<tr>
<td>Before infarction</td>
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<td>Ten days after infarction</td>
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<td>3 weeks after treatment</td>
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*p< 0.05 vs before infarction

9:30 a.m.

Increased Beta-Catenin Pathway Expression by a Remote Ischaemic Preconditioning Stimulus: First Evidence in Humans

Gregory E. Steinbaugh, Daniel S. Lee, Douglas R. Pfeiffer, Jay L. Zweier, Juan A. Crestanello, The Ohio State University, Columbus, OH

Mitochondrial respiratory complexes are damaged by ischemia reperfusion injury. While IPC preserves overall mitochondrial respiratory function after ischemia reperfusion, it is unclear which is the effect of IPC on individual mitochondria respiratory complexes.

The purpose of this study was to determine the effect of IPC on mitochondrial respiratory complexes. Isolated rat hearts (n=6/group) were subjected to either A) 30 minutes (min) of equilibration (EQ), 30 min of ischemia (I), and 30 min of reperfusion (RP) (CONTROL) or B) 10 min of EQ, two 5 min episodes of IPC, 30 min I, and 30 min of RP (IPC group). Interfibrillar (IF) and subsarcolemmal (SS) mitochondria were isolated at end reperfusion. Complex I, II, and IV activities were assessed by polarography using specific substrates and inhibitors and subsarcolemmal (SS) mitochondria were isolated at end reperfusion. Complex I, II, and III activities were assessed by polarography using specific substrates and inhibitors.

Results: Compared to control, IPC increased the activity of complex I, II, and IV (Table 1). In addition, the activity of complex I and II was greater in the SS fraction than in the IF fraction. IPC-induced increases in complex I, II, and IV activities were greater in the IF fraction than in the SS fraction.

Conclusions: IPC improves mitochondrial respiratory function, particularly in the IF fraction. These findings suggest that IPC protects against ischemia reperfusion injury by preserving mitochondrial respiratory function.

Table 1: Enzyme activity in mitochondrial fractions

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*p<0.05 vs CONTROL

9:30 a.m.

Ischemic Preconditioning Protects Mitochondrial Respiratory Function in Complex I and Complex II

Bernhard J. Hauert*, Gregory Neely, Jakob Voelkl, Christian Kremser, Olmar Pachinger, Josef M. Penninger, Bernhard Metzler, Department of Cardiology, Innsbruck Medical University, Innsbruck, Austria

Background: The highly conserved mitogen-activated protein kinases have proven to be of great importance regarding myocardial development, hypertrophy, and survival. Mitogen-activated protein kinase kinase 7 (MEK7), an upstream activator of c-Jun N-terminal kinases, displayed a dramatic cardiac phenotype with premature death when constitutively activated. The in vivo role of MEK7, using a muscle specific knock-out strategy, in the cardiac pathology remained unclear.

Methods: We therefore generated muscle specific MEK7 knock-out (KO) mice and investigated their myocardial phenotype compared to MEK7 wild-type (WT) rodents. Cardiovascular magnetic resonance (CMR), echocardiography and histological methods were used to characterize the physiological appearance of KO hearts. In addition, the reversible left anterior descending artery (LAD)-ligation model facilitated the examination of MEK7 KO mice during myocardial stress.

Results: We found significantly reduced fractional shortening (WT: 56±2%, KO: 43±6%, n=7, p=0.005; CMR data) combined with marked dilatation (transversal diameter WT: 3.04±0.084 vs KO: 3.51±0.105 mm, n=7, p=0.005; CMR data) in MEK7 KO rodents at the age of 12 weeks. In contrast, the extent of ischemia/reperfusion injury was significantly reduced in MEK7 KO compared to WT mice. Following 30 minutes of ischemia and 3 hours of reperfusion, MEK7 KO mutantic rodents presented significantly reduced levels of troponin T (WT: 2.9±0.39 vs KO: 1.78±0.26 ng/ml, n=13, p=0.05). This early decrease of troponin T in the transgenic cohort was followed by smaller areas of infarction after 1 week (WT: 1.7±0.50 vs KO: 0.7±0.30 mm², n=14, p<0.05, sum of 3 sections per heart). Concordantly, functional analysis after 1 week of reperfusion showed a greater reduction of fractional shortening in MEK7 KO mice compared to the transgenic strain.

Conclusions: Our data provide the first in vivo knock-out evidence for the critical role of MEK7 in the heart. Whereas MEK7 KO hearts display reduced cardiac functions, they are partly protected from myocardial ischemia/reperfusion injury.

9:30 a.m.

The Loss of MKK7 Is Critical for Cardiac Physiology

Bernhard J. Hauert*, Gregory Neely, Jakob Voelkl, Christian Kremser, Olmar Pachinger, Josef M. Penninger, Bernhard Metzler, Department of Cardiology, Innsbruck Medical University, Innsbruck, Austria

Background: The highly conserved mitogen-activated protein kinases have proven to be of great importance regarding myocardial development, hypertrophy, and survival. Mitogen-activated protein kinase kinase 7 (MEK7), an upstream activator of c-Jun N-terminal kinases, displayed a dramatic cardiac phenotype with premature death when constitutively activated. The in vivo role of MEK7, using a muscle specific knock-out strategy, in the cardiac pathology remained unclear.

Methods: We therefore generated muscle specific MEK7 knock-out (KO) mice and investigated their myocardial phenotype compared to MEK7 wild-type (WT) rodents. Cardiovascular magnetic resonance (CMR), echocardiography and histological methods were used to characterize the physiological appearance of KO hearts. In addition, the reversible left anterior descending artery (LAD)-ligation model facilitated the examination of MEK7 KO mice during myocardial stress.

Results: We found significantly reduced fractional shortening (WT: 56±2%, KO: 43±6%, n=7, p=0.005; CMR data) combined with marked dilatation (transversal diameter WT: 3.04±0.084 vs KO: 3.51±0.105 mm, n=7, p=0.005; CMR data) in MEK7 KO rodents at the age of 12 weeks. In contrast, the extent of ischemia/reperfusion injury was significantly reduced in MEK7 KO compared to WT mice. Following 30 minutes of ischemia and 3 hours of reperfusion, MEK7 KO mutantic rodents presented significantly reduced levels of troponin T (WT: 2.9±0.39 vs KO: 1.78±0.26 ng/ml, n=13, p=0.05). This early decrease of troponin T in the transgenic cohort was followed by smaller areas of infarction after 1 week (WT: 1.7±0.50 vs KO: 0.7±0.30 mm², n=14, p<0.05, sum of 3 sections per heart). Concordantly, functional analysis after 1 week of reperfusion showed a greater reduction of fractional shortening in MEK7 KO mice compared to the transgenic strain.

Conclusions: Our data provide the first in vivo knock-out evidence for the critical role of MEK7 in the heart. Whereas MEK7 KO hearts display reduced cardiac functions, they are partly protected from myocardial ischemia/reperfusion injury.

9:30 a.m.

Deterioration of Left Ventricular Function in Patients With Non-ST-Elevation Myocardial Infarction Awaiting Coronary Angiography

Biomar Grenne, Christian Eik, Bente Sjøl, Helge Skulstad, Svend Aakhus, Otto Smiseth, Thor Edvardsen, Harald Brunevald, Sorlandet Hospital, Arendal, Norway, Rikshospitalet University Hospital, Oslo, Norway

Background: Optimal timing of coronary angiography for patients with non-ST-segment elevation acute coronary syndrome (NSTEMI) is debated. Current guidelines recommend an invasive strategy within 48-72 hours after admittance. We hypothesized that persistent ischemia cause progressive deterioration of LV function until revascularization.

Methods: Sixty-one patients with clinical evidence of NSTEMI were enrolled in the study. Global and territorial LV function were assessed as longitudinal peak systolic strain by speckle tracking echocardiography. Examinations were performed at admittance and immediately prior to coronary angiography.

Results: There was a progressive impairment of LV function measured by global strain from admittance to coronary angiography in patients with non-ST-elevation myocardial infarction (NSTEMI). This was due to a pronounced regional dysfunction in the culprit territory (strains, -14.3% vs. -13.0%, p=0.003), whereas average strain in segments in the remote area remained unchanged. The coronary angiography was done 31±16 hours after admittance. There were no changes in global or territorial strain among patients with unstable angina or non-coronary chest pain.

Conclusion: LV function deteriorates in hospitalized patients with NSTEMI awaiting coronary angiography. Our results indicate ongoing impairment in the culprit territory most likely due to ischemia and necrosis.

9:30 a.m.

Myocardial ischemia and Infarction
Remote Ischemic Preconditioning Modifies Cardiac Pro-arrhythmic Risk of Embryonic Stem Cell-Neutralization of Interleukin (IL)-18 Ameliorates Increased Rho Kinase (ROCK) Activity in Hong Kong compared with MSCs and control groups (1224 ± 138 /mm² with 27.8 ± 2.5% and 609 ± were markedly resistant to cell death at 400μM H₂O₂ (2 ± 2% vs. 32 ± 3%, P<0.05). HO- performed on 28 days later. In vitro, the levels of HO-1 mRNA in MSC was maximum at decreased infarction size was observed in HO-1MSCs (1332 ± 75 /mm² with 21.1 ± 2.4%) were delivery by intramyocardial injection, increased capillary density associated with HO-1MSC was injected around the infracted border zone, and cardiac examination was performed by lipofection method. To evaluate the effect of HO-1 overexpression, Methods and Results: Transfer of human HO-1 gene into bone marrow-derived MSC in mesenchymal stem cell (MSC) on cytoprotection. Therefore, we examined the effect of HO-1 and cytoprotection. However, few data exist regarding impact of expression of HO-1 pivotal role as a graft survival protein and there exists a fundamental codependence between down-regulated (n=17, fold change 0.83-0.67) or up-regulated (n=2, miRNA 206, fold change 2.23; p=0.005, and mRNA 346, fold change 10.31; p=0.005). Most of the mRNA's modified by hitherto unknown roles in myocardial function and responses. Conclusions: rIPC has potent effects on myocardial miRNA expression. This novel observation suggests a role for miRNA in regulating myocyte responses to ischemia-reperfusion injury. Further studies of the role of individual miRNAs will enhance our understanding of the mechanism of protection afforded by rIPC, and may establish new therapeutic targets.

Impact of Antioxidative and Antiapoptotic Effects of Mesenchymal Stem Cells on Salvaging Ischemic Heart Injury: Role of Transient Overexpression of Heme Oxygenase-1

Toshinari Tsubokawa, Chiaki Nakanishi, Kunimasa Yagi, Atsushi Nozawa, Naboru Fujino, Hidekazu Uno, Shotoku Tagawa, Masakazu Yamagishi, Hatsu Sue Ueda, Kanazawa University Graduate School of Medicine, Kanazawa, Japan, National Cardiovascular Center, Osaka, Japan.

Background: Stem cell therapy has potential to reduce ventricular remodeling associated with ischemic myocardial injury. Under these conditions, Heme Oxygenase-1 (HO-1) plays a pivotal role as a graft survival protein and there exists a fundamental codependence between HO-1 and cytoprotection. However, few data exist regarding impact of expression of HO-1 in mesenchymal stem cell (MSC) on cytoprotection. Therefore, we examined the effect of transient overexpression of HO-1 in anti-oxidative and anti-apoptotic activities of MSC. Methods and Results: Transfer of human HO-1 gene into bone marrow-derived MSC was performed by lipofection method. To evaluate the effect of HO-1 overexpression, MSC or HO-1MSC were exposed to culture conditions with serum deprivation (SD) and hypoxia and changes in cell damage were analyzed by flow cytometry. Cell viability was determined by MTS assay after exposing HO-1MSC or HO-1MSC to H₂O₂ as an oxidative stress. VEGF level in the supernatant of each cells culture after the load of H₂O₂ were measured by using ELISA. In rat infarction model, MSC (5x10⁵+ 0.4 x10⁵ cells/rat) or HO-1MSC was injected around the infracted border zone, and cardiac examination was performed on 28 days later. In vitro, the levels of HO-1 mRNA in MSC was maximum at day 2 and was decreased on and after the day 4. HO-1 overexpression prevented MSC from SD/hypoxia - induced apoptosis (MSC 30 ± 5% vs. HO-1MSC 17 ± 2 %, p<0.05) and were markedly resistant to cell death at 400μM H₂O₂ (2 ± 2% vs. 32 ± 3%, P<0.05). HO-1MSC showed to have increased capillary density associated with decreased infarction size was observed in HO-1MSCs (1332 ± 75 /mm² with 21.1 ± 2.4%) compared with MSCs and control groups (1224 ± 138 /mm² with 27.8 ± 2.5% and 609 ± 48 /mm² with 36.9 ± 3.8%, P<0.05).

Conclusions: These results demonstrate that enhanced anti-apoptotic and anti-oxidative effects of MSCs can be obtained by transient overexpression of HO-1, and contribute to improving therapeutic efficacy for acute myocardial ischemia, probably through paracrine action such as production of VEGF.
adult mouse cardiomyocytes underwent simulated I/R (30 min i4 h R). Downstream effectors were targeted by pharmacological inhibitors and adenosine transduction of dominant negative expression vectors.

**Results:** Our results demonstrate low levels of NF-κB activity and IL-18 expression in naive, sham-operated or ischemia alone animals. However, I/R significantly increased ROI generation, upregulated NF-κB activity and IL-18 expression in the ischemic LV tissue. Further, I/R upregulated IL-18Rβ, but not IL-18Rα expression. In contrast, IL-18BP expression was induced in a delayed manner. Importantly, IL-18 neutralization significantly attenuated IR-induced tissue injury (31% reduction in infarct size vs. sham). Conferring these in vivo results, sTIR enhanced ROI generation, IKK activity, NF-κB DNA binding activity, and IKK-NF-κB-dependent biologically active IL-18 expression in isolated adult mouse cardiomyocytes.

**Conclusions:** IL-18 signaling plays a critical role in IR induced tissue injury and chronic inflammation, and thus represents a potential therapeutic target.

9:30 a.m.

1014-151 Long Acting Erectile Dysfunction Drug Tadalafil Protects the Heart Against Ischemia/Reperfusion Injury Through Hydrogen Sulfide Signaling

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**Background:** Emerging evidence suggests that the gaseous signaling molecule; hydrogen sulfide (H2S) plays an important role in cardioprotection against ischemia/reperfusion injury (IR). Also, plasma levels of H2S in patients with coronary artery disease (CAD) are significantly lower than in angiographically normal control subjects. Since H2S-producing enzyme, cystathionine-γ-lyase (CSE) is expressed in the heart, we hypothesized that novel phosphodiesterase-5 (PDE-5) inhibitor, tadalafl (TAD) might utilize H2S signaling in cardioprotection.

**Methods:** After obtaining baseline left ventricular (LV) function using transhoracic echocardiography (TTE), adult ICR mice were injected i.p. with TAD (1 mg/kg), vehicle (10% DMSO), TAD+dil-proparglycine (PAG, CSE blocker; 50 mg/kg), or vehicle+PAG 1 h prior to 30 min ischemia and 24 h reperfusion. At the end of reperfusion, TTE was performed and hearts were collected for infarct size (IS) measurement using computer morphometry of TTC stained sections.

**Results:** Myocardial IS (mean ± SE) was significantly reduced in mice pretreated with TAD (Fig. 1A; 68% decline). The risk area was not different between groups (Fig. 1B). Moreover, fractional shortening was preserved only with TAD (Fig. 1C).

**Conclusion:** PDE-5 inhibition with TAD may be a useful therapeutic tool to reduce IS and attenuate LV dysfunction secondary to IR in patients with CAD. Moreover, these studies provide a novel mechanism involving H2S signaling in TAD-induced cardioprotection.

9:30 a.m.

1014-152 Down-Regulation of MicroRNA-29 Contributes to the Myocardial Protective Effect of Pioglitazone Against Ischemia-Reperfusion Injury - A PPARγ-Dependent Effect

Yunmei Ye, Jose R. Perez-Polo, Douglas L. Mann, Yochai Birnbaum, University of Texas Medical Branch, Galveston, TX, Baylor College of Medicine, Houston, TX

**Background:** MicroRNAs (miRNAs) are involved in controlling diverse aspects of cardiac function, including proliferation, apoptosis and remodeling. Pioglitazone (PIO), a thiazolidinedione with PPARγ agonist activity, protects against ischemia/reperfusion injury (IR) and limits infarct size in experimental models. However, the underlying mechanisms involved in the protective effect of PIO are only partially understood. We assessed the role of miRNAs in protection against simulated IR injury (SIR) by PIO.

**Methods:** We used miRNA gene arrays to evaluate expression changes of miRNAs in the rat heart after 7-day PIO (5 mg/kg) administration, and then confirmed the result by Northern Blot. We studied the effect of GW9662, a PPARγ inhibitor, on the effect of PIO on miR-29 levels in H9C2 cardiomyocytes. We assessed the effects of miR-29 mimic and anti-sense inhibitor oligos, and their interactions with PIO on viability (MTT test), cell death (Trypan Blue) and apoptosis (Caspass-3 activity) of H9C2 cardiomyocytes exposed to 16h hypoxia and 2h reoxygenation (SIR). Finally, we assessed the effects of miR-29 mimic and anti-sense inhibitor oligos on Mol-1 (an anti-apoptotic Bcl-2 family member) cellular protein levels in H9C2 cells. Results: PIO significantly decreased miR-29a and miR-29c levels. Down-regulation of miR-29a and miR-29c by antisense inhibitors or by PIO resulted in enhanced H9C2 cardiomyocytes resistance against SIR (increased MTT activity, decreased cell death and decreased Caspase-3 activity). In contrast, transfection of cells with miR-29a and miR-29c mimic oligos promoted cell death. Co-transfection with miR-29a and miR-29c mimic oligos completely blocked the protective effect of PIO. The effect of PIO on miR-29a levels was blocked with GW9662. Overexpression of miR-29c in Mol-1 cellular protein levels and transfection with inhibitor of miR-29c increased Mol-1 levels. Conclusions: PIO downregulated miR-29a and miR-29c levels. This effect was dependent on PPARγ activation. Down-regulation of miR-29a and miR-29c contributed to the myocardial protection effect of PIO against SIR. These findings provide a rationale for the development of miRNA-based strategies for minimizing IR damage.

9:30 a.m.

1014-153 Uncoupling Protein (UCP3) Plays an Important Role in Ischemic Preconditioning

Cevher Ozcan, Monica Palmeri, Raymond R. Russell, III, Section of Cardiovascular Medicine, Yale University School of Medicine, New Haven, CT

**Background:** Although mitochondria play a key role in ischemic preconditioning (IPC) of the heart, the exact mechanism of IPC remains unclear. Recently, endogenous mitochondrial uncoupling proteins (UCP) have been identified as mediators of a cardioprotective mechanism that prevent cardiac cell death under metabolic or oxidative stress. We hypothesize that mitochondrial uncoupling may have an important mechanistic role in IPC by preserving cellular energetics and metabolism.

**Methods:** Hearts from UCP3 null (UCP3-/-) and wild type mice were perfused in working mode and subjected to 30 min ischemia and 30 min of reperfusion either with or without prior preconditioning (4 cycles of 4 minutes of ischemia followed by 4 minutes of reperfusion). Left ventricular developed pressure (LVDP), heart rate and rate-pressure product were measured. In addition, the content of high-energy nucleotides was analyzed by HPLC.

**Results:** While myocardial contractile function was significantly impaired by ischemia-reperfusion injury, IPC improved left ventricular recovery in wild type hearts (No IPC: 19.7±3.5%, IPC: 37.0±7.2%, p=0.02). However, there was no improvement in postischemic recovery of function with IPC in UCP3-/- hearts (No IPC: 17.8±3.7%, IPC: 16.2±2.4%, p=0.35). The recovery of function following IPC was greater in wild type hearts compared to UCP3-/- hearts (p=0.01). Also, myocardial ATP level, an indicator of myocardial energy status was significantly greater with IPC in wild type hearts compared to UCP3-/- hearts (0.82±0.1 vs 0.53±0.04 nmole/mg protein, p=0.01). But the amount of ATP in UCP3-/- hearts after ischemia-reperfusion was not affected by IPC. Thus, protective efficacy of ischemic preconditioning abolished in UCP3 knockout mouse.

**Conclusion:** Mitochondrial UCP3 plays an important mechanistic role in IPC and preserves myocardial function by maintaining cellular high-energy phosphate stores during ischemia-reperfusion injury, perhaps through the preservation of mitochondrial oxidative phosphorylation and structure during oxidative stress.

9:30 a.m.

1014-154 The Impact of Timing on the Safety of Transendocardial Delivery of Mesenchymal Precursor Stem Cells Following Acute Myocardial Infarction

Marios R. Fernandes, Guilherme Silva, Cristiano Cardoso, Yi Zheng, Fred Bainbridge, Maria G. Cabreira, John Canales, Micheal Schuster, Silciu Itescu, Deborah Vela, Maximilian Buja, James T. Willerson, Emerson C. Perin, Texas Heart Institute, Houston, TX

**Background:** The ideal timing for stem cells delivery post acute MI is unknown and experience with transendocardial injections (TE) in this setting is very limited. There is concern regarding cell survival and procedural safety in the acute MI setting. We evaluated the safety and efficacy of TE of mesenchymal precursor stem cells (MPC) at two different time points after MI.

**Methods:** Twenty two sheep underwent balloon occlusion of the LAD for 90 min. TE of 225x10^6 MPC or placebo were performed at 5 days [4 control (C) and 5 treated (T)] and at 10 days (5 C and 5 T) post MI. Sheep were followed for 8 weeks. Left ventricular ejection fraction (LVEF) was assessed by 2D echo. Arteriolar density, cell proliferation (Ki67), apoptosis (TUNNEL) and collagen density were evaluated in the infarct border.

**Results:** The incidence of VT was higher at 5 days post MI (4/5 vs 1/5 at 5 and 10 days, respectively - p=0.08). There was no peri procedural death or tamponade. Overall, T sheep had UEF improvement at 8 weeks (fig 1A). The maximum improvement was seen in T at 10 days post MI (fig1B). There was no inflammation or abnormal tissue growth. Increased arteriolar density (61.9±14 vs 40.3±12 vessels/mm² - p=0.005) and a trend of higher cell proliferation (5.8±2.1 vs 3.9±1.7 positive nuclei/10^4 nuclei - p=0.06) were seen at the infarct border of T sheep. There were no differences in collagen content and apoptosis.

**Conclusions:** Postponing MPC delivery to 10 days after myocardial infarction might improve its overall safety and efficacy.

9:30 a.m.
ABSTRACTS - Myocardial Ischemia and Infarction

1014-155
Intravenous Infusion of Drag-Reducing Polymers: A New Approach to Improve Left Ventricular Function in a Rat Model of Myocardial Infarction
Xianghu Chen, Kai Cui, Jiancheng Xiu, Yi Lao, Hu Xue, Daogang Zha, Jianping Bin, Yili Liu, Nanfang Hospital, Guangzhou, People’s Republic of China

Background: Blood soluble drag reducing polymers (DRPs) have been shown to reduce microvascular resistance and improve myocardial perfusion in a canine model of flow-limiting coronary artery stenosis. In animals with totally coronary artery occlusion, the effects of DRPs on cardiac function are unknown. In this study, we hypothesized that administration of DRPs can improve left ventricular (LV) function in rats post myocardial infarction (MI).

Methods: 24 male SD rats were randomly allocated to either normal saline containing 0.64±0.06% DRP (n=12) or saline (n=12) at a constant rate of 3.5 ml/h. 15 mins later, the animals were subjected to coronary artery ligation. 24 h after MI, noninvasive echocardiography was performed to assess the changes of impaired LV function. LV internal dimensions and the anterior wall thicknesses were measured, and wall motion score index and endocardial length of severe wall abnormality (SM) were calculated by a 16 segment model on short axis view. Contrast agent was utilized to analyze the regional extent of myocardial perfusion defect (PD) by contrast score index and ratio of perfusion defect length to LV length.

Results: At 24 h post MI, DRP-treated animals had marked smaller LV end-diastolic diameter (1.61±0.85 vs. 5.28±0.88mm, p < 0.01), better anterior diastolic and systolic wall thickness (1.63±0.28 vs. 0.94±0.20mm, p < 0.01 and 1.91±0.35 vs 1.08±0.27mm, p < 0.01, respectively). Significant improvement in fractional shortening (34.84±10.35% vs 2.52±0.15, p<0.01) and smaller ratio of SM length to LV length (0.72±0.04 vs 0.64±0.06, p < 0.01) compared with control group, both of contrast score index (1.73±0.42 vs 2.21±0.22, p < 0.05) and ratio of PD length to LV length were significantly reduced in DRP-group (0.27±0.19 vs 0.35±0.08, p < 0.01).

Conclusions: Intravenous infusion of nanomolar concentrations of DRPs improved LV function in a rat model of MI. This may be related to the reduction of microvascular edema and extent of myocardial PD. This finding has important therapeutic implications to the treatment of acute coronary syndrome.

1014-156
Endothelial Cell Injury Induced by Intracoronary Sera in Patients With ST Elevation Myocardial Infarction
Gopal Ghimire, Ann McCormack, Jonathan Spito, Rajesh Kharbanda, Marlene Rose, Miles Daby, Royal Brompton and Harefield NHS Trust, London, United Kingdom

Background: Integrity of endothelium is compromised in ST Elevation Myocardial Infarction (STEMI). We evaluated in-vitro the effect of sera derived from the atherothrombotic coronary artery aspirate (CA) and femoral arterial blood (FA) of patients with STEMI, on human umbilical vein endothelial cells (HUVECs). Since activated and apoptotic endothelial cells induce surface expression of vimentin and are an important source of autotaxins, we also evaluated the titres of antivimentin antibodies (AVA).

Methods: Paired sera obtained from the CA and FA of patients with STEMI during primary angioplasty (n=6) were incubated for 4 hours with HUVECs in presence of complement. The cell injury was assessed using flow cytometry using Annexin V (AV) and Propidium Iodide (PI). ELISA was performed in both the sera for IgG and IgM AVA.

Results: A mean of 19.23 % (SD, 9.48) of the HUVECS incubated with the CA and 10.21 % (7.58) with FA under went apoptosis (AV-); p=6.71X-4. The mean CA IgG and IgM AVA titres were 59.05 (35.9) and 66.08 (23.6) respectively. The FA IgG and IgM titres were respetively 78.78 (36.8), p= 1.71X10-7 and 77.92 (23.7), p= 0.0023.

Conclusions: Soluble factors in the sera of coronary aspirate of patients with STEMI may induce endothelial injury and contribute to microvascular injury. Sequestration of the AVA on to the apoptotic endothelial cells may explain the observed reduction in AVA titres in CA: the AVA-antigen complex can fix complement and may contribute to mechanism of microvascular injuries.

9:30 a.m.

1014-157
PI3k/Akt Activation and Nuclear Accumulation of β-Catenin Are Key Components in the Myocardial Protection Afforded by Remote Ischemic Preconditioning
Jin Li, Wani Xuan, Ran Yan, Emilie Jean-St-Michel, Michael Tropak, Andrew Reddington, Hospital for Sick Children, Toronto, ON, Canada

Background: Remote (r) ischemic preconditioning (IPC) induced by transient limb ischemia has been shown to invoke potent myocardial protection in multiple animal models, and recently in adults and children undergoing cardiac surgery. While the important role of PI3 kinase/Akt activation in the cardioprotection afforded by local IPC is well described, our understanding of the intracellular signaling of rIPC remains incomplete. Furthermore, nuclear accumulation of β-catenin, a downstream target of GSK-3β, has recently been shown to have a key role in regulating cell survival and proliferation in cardiomyocytes. We therefore examined the hypothesis that rIPC activates intracellular kinases and leads to nuclear β-catenin accumulation in a mouse model of rIPC.

Methods and Results: A Krebs-perfused mouse Langendorff model (subjected to 30 min global ischemia and 60 min reperfusion) was used. Sham procedure or rIPC (four cycles of 5 min of hind-limb ischemia and 5 min of reperfusion) was performed immediately prior to heart harvest. Compared to sham, recovery of left ventricular developed pressure (p=0.07), LVEDP (p<0.01) and peak +ve and -ve dP/dt (both p<0.05) were all improved by rIPC. These changes were blocked by pretreatment (prior to limb ischemia) with Wortmannin (PI-3 kinase inhibitor) and 3,3-diiodomethane (DIMP) (which blocks transcriptional activity of β-catenin). rIPC significantly reduced infarct size (11.36±2.11% versus sham 39.31±7.02%, p<0.05) and this cardioprotection was reversed by pretreatment with Wortmannin or DIMP (both p<0.05 compared with sham). Western blotting showed that rIPC significantly increased phosphoryso-phospho-Akt (1.65±0.11 fold vs. sham), inhibited GSK-3β by increasing phosphorylated GSK-3β (1.63 fold), and was associated with a 1.92-fold increase in nuclear β-catenin. All of these changes were completely abrogated by pretreatment with Wortmannin.

Conclusions: The myocardial protection afforded by rIPC is mediated via the PI3K/Akt/Src3β signaling pathway, activation of which is associated with the novel finding of nuclear accumulation of β-catenin.

9:30 a.m.
Background: We hypothesized that therapy with the angiotensin II type 1 receptor blocker candesartan (CN) or the vasopeptidase inhibitor omapatrilat (OMA), by reducing effects of angiotensin II, modulate healing-specific matricellular proteins such as secretory leucocyte protease inhibitor (SLPI), secreted protein acidic and rich in cysteine (SPARC) and oncostatin (OPN) as well as matrix metalloproteinases (MMPs) and cytokines during healing after reperfused myocardial infarction (RMI) and thereby limit left ventricular (LV) remodeling and dysfunction.

Methods: We randomized 60 Sprague-Dawley rats 24 h after RMI (1-h left anterior descending coronary occlusion; reperfusion) to 3 weeks of oral placebo, CN (30 mg/kg) and OMA (10 mg/kg). Sham rats had no RMI or drug. We measured serial LV function and remodeling (echocardiography/Doppler) and regional molecular expression of SLPI, SPARC, OPN, MMP-9 and TIMP-3, and other proteins (Western blots), MMP activity (zymography), and infarct size at 3 weeks.

Results: Compared to sham, RMI-placebo induced ST-segment elevation, infarction (25% LV; 60% risk), LV dysfunction and remodeling. Compared to placebo, CN and OMA similarly limited LV dysfunction and remodeling. Compared to non-infarcted zones, RMI induced robust increases (P<0.001) in SLPI, SPARC and OPN proteins, MMP-9 and MMP-2 (activity and protein), and inducible-nitric-oxide-synthase (iNOS), interleukin-1 (IL)-6, tumor necrosis factor (TNF)-α, transforming growth factor (TGF)-β1, Smad-2 and Smad-3 and myeloperoxidase proteins in the ischemic zones. Both drugs normalized these changes and improved MMP-9/TIMP-3 balance.

Conclusions: Both CN and OMA modulate matricellular proteins, MMP-9/TIMP-3, angiotensin II and cytokines, thereby mitigating adverse LV remodeling and dysfunction during healing after RMI.

9:30 a.m.

1014-160 Leptin Modulates Metabolic Substrate Utilization in Ischemic Cardiac Tissue Through Inactivation of Andoenosine Monophosphate Kinase

Kenneth R. McGaff, Baobao Zou, Lia C. Romano, Charles F. McTiernan, Christopher P. O'Donnell, University of Pittsburgh, Pittsburgh, PA

Introduction: Under aerobic conditions, the normal heart uses mainly fatty acid (FA) for ATP production and responds to leptin by increasing FA oxidation. In ischemia, serum leptin increases, and the heart switches from aerobic to anaerobic metabolism. This metabolic switch is linked to the activity of a number of regulatory proteins, including AMP-activated protein kinase (AMPK) and acetyl-CoA carboxylase (ACC).

Aim: The present study was undertaken to test the hypothesis that leptin regulates the activity of AMPK and ACC in the heart, facilitating oxidative metabolism in normal myocardium and enhancing glycolysis in ischemia.

Methods/Results: Coronary artery ligation (CAL) (n=10) or sham (n=10) surgery was performed on 9 week old C57BL/6 male mice. After 3 days, equal numbers were treated with leptin (0.3mg/kg ip) or vehicle for 30 minutes, followed by sacrifice. Data shown are means±SEM, with p values determined by t-test. Versus sham hearts, infarcted cardiac tissue showed a 22±1 fold increase in leptin, a 2.9±0.2 fold increase in glucose transporter (GLUT)-1, a 3.7±0.1 fold increase in FA binding protein, and an additional 58±6% and 42±5% reduction in p/t AMPK and ACC respectively, after exogenous leptin (all infarct tissue versus sham; all p<0.05). Leptin signaling, measured by phosphorylated (p) (or) cardiac STAT3 protein, was increased 3.7±0.1 fold in infarcted tissue, with a further 1.5±0.1 fold increase after exogenous leptin (both p<0.05). Compared with a switch to anaerobic metabolism, CAL caused a 32±3% decrease in p in AMPK and 46±4% decrease in ACC respectively, with an additional 58±6% and 42±5% reduction after leptin by MRI described below. The mice were imaged using a 7T small animal experimental MRI/MRS scanner. Ten series frames covering 2 cardiac cycles allowed for the accurate selection of images representing left ventricular end of systole (ES) and end of diastole (ED) volumes for calculating ejection fraction (EF) as the ratio of stroke volume (volume of ED - volume of ES) to cardiac output. Results: MRI analysis showed that the left ventricular EF of PSS-injected hearts and hASCs-injected hearts was 63.7±43.32% (mean ± SD) and 66.6±17.4% at baseline, respectively. EF in both groups declined by more than half (28.4±9.2% for PSS vs 33.36±9.83% for hASCs, p<0.05), which indicates that heart function in all mice was severely impaired 7 days following the LAD occlusion. Significant functional loss continued over the following 28 days in PSS-injected hearts. Conversely, the hearts injected with hASCs demonstrated a trend to an increase in function. EF at 28 days post-infarction was 34.02±5.42% with hASC treatment vs 18.7±9.12% for PSS treatment (p<0.05).

Conclusions: In this study, we demonstrated for the first time that hASCs significantly improved cardiac function compared to PBS treatment group. This finding indicates the promising application of autologous hASCs for myocardial repair.

9:30 a.m.

1014-163 Endothelial Progenitor Cell Derived Conditioned Media Reduces In Vivo Cardiomyocyte Apoptosis Acting Through TGFβ1 and IGF1

Brian Hynes, Arun HS Kumar, Sharon Weiss, Jeffery Schmecpepper, Granine Murphy, Kenneth Martin, John O'Sullivan, Scott McCauley, Noel M. Caplice, Centre for Research in Vascular Biology, University College Cork, Cork, Ireland

Background: We recently reported the cardioprotective effects of conditioned media (CM) derived from autologous EPcs in a porcine model of myocardial infarction (MI). Preliminary investigation indicated the important role of TGFβ1 and IGF1 in the observed beneficial effects, which we have further explored.

Methods: Landrace pigs (25-28kg) underwent MI generation via transluminal balloon occlusion of the proximal left circumflex artery for 80 minutes followed by 120 minutes of reperfusion. Intra-coronary conditioned media (CM) from autologous EPcs, CM + anti-TGFβ1, or CM + anti-IGF1, or X-irradiated (15) was administered in three 4 minute
Collagen Matrix as a Delivery Vehicle Prevents Injected Very High Prognostic Value of Admission IL-6 Levels in The Role of Heart-Type Fatty Acid Binding Protein in Myocardial Ischemia and Infarction

Collagen matrix as a delivery vehicle significantly reduced the migration of transplanted MSCs from infarcted myocardium to remote organs and non-infarcted myocardium.

Results: There was no NP detected in the tissues that received saline or collagen alone. NP were detected in the heart and remote organs in SAL+MSC group. Labelled cells (expressed as cell number) tissue weight were present in 3/13 lungs (mean value equivalent to 12.7±4.7,000 cells/g), 4/13 livers (12.30±1.924 cells/g), 11/13 spleens (75.2±11.483 cells/g), 0/13 kidneys, 13/13 MI (8.006,835±1,846,462 cells/g) and 9/13 non-infarcted myocardium (167,331±47,007 cells/g). However, compared with SAL+MSC group, NP were detected to a lesser extent in remote organs in COL + MSC group, and the relocated cell numbers were significantly lower in these organs. NP were detected in 1/13 lungs (4,631±3,176 cells/g, p<NS), 0/13 livers (0 cells/g, p=NS), 4/13 spleens (140±6,173 cells/g, p=NS), 0/13 kidneys (p<NS), 5/13 non-infarcted myocardium (51,22±21,54 cells/g, p<NS). In COL + MSC group, NP were detected in 1/13 MI (4,830,050±592,215 cells/g), which did not significantly differ from that in SAL+MSC group (p=NS).

Conclusions: Collagen matrix as a delivery vehicle significantly reduced the migration of transplanted MSCs from infarcted myocardium to remote organs and non-infarcted myocardium.

Myocardial Infarction—Basic; Unstable Ischemic Syndrome—Clinical; Acute Myocardial Infarction—Therapy

Methods: Adult male Lewis rats (n=22) underwent LAD ligation to induce MI. At the very early phase of AMI, independent of ethnicity, suggesting environmental rather than a genetic mechanism.

Results: Compared to controls, echocardiographic analysis of experimental animals showed increased fractional shortening (21 vs 37%, p<0.01) and increased ejection fraction (50 vs 71%, p<0.01). The slope of contractility as measured by pressure-volume conductance was also greater in the experimental group (3 vs 46, p<0.05), as was cardiac output (27 vs 33 ml/min, p<0.05). Digital planimetric analysis of selected hearts showed increased borderzone thickness (1.5 vs 1.9 mm, p<0.05) as well as decreased scar fraction expressed as a percentage of the total section area (20 vs 15%, p<0.001) and circumferential scar length (7.9 vs 5.4 mm, p<0.05).

Conclusions: Application of EMS at the time of MI was shown to attenuate adverse ventricular remodeling as evidenced by reduced scar formation and increased borderzone thickness. Mechanical reinforcement preserved ventricular geometry and improved cardiac function after MI.

Very High Prognostic Value of Admission IL-6 Levels in Acute Myocardial Infarction. A Multietnic Study

Results: Median (IQR): 2.5 (1.2-5.8) mg/L vs. 1.3 (0.6-2.9) mg/L p<0.001 and 5.1 (2.8-9.2) pg/mL vs. 1.4 (0.7-2.7) pg/mL p<0.001 respectively.

The predictive value of IL-6 was much higher than that of CRP. For in-hospital events, high IL-6 levels were associated with a stepwise increase in rates of death, new onset or worsening heart failure (HF) and Major Adverse Cardiac Events (MACE). For 6-month follow-up, the predictive value remained significant for death (p<0.0001). This association was similar in the three ethnic groups.

Conclusions: Of the inflammatory component assessed, admission IL-6 levels are the most important predictors of adverse events during hospital admission and follow-up in the very early phase of AMI, independent of ethnicity, suggesting environmental rather than a genetic mechanism.

The Role of Heart-Type Fatty Acid Binding Protein in the Diagnosis of Acute Coronary Syndromes

Methods: Patients admitted with ST-segment elevation MI (STEMI, n=19), non-STEMI (NSTEMI, n=15) or unstable angina (n=10) were evaluated. The CaridoDetect® cardiac infarction test (rennesens GmbH, Berlin, Germany) measured both qualitative and quantitative H-FABP. Results were compared with troponin.

Results: Of the 40 patients with acute MI, initial troponin was positive in 88% (35); the qualitative H-FABP was positive in 93% (37); and the quantitative H-FABP . Results were compared with troponin.
Coronary Flow Velocity Reserve Gradually Decreases According to Glucometabolic State in Patients With Acute Myocardial Infarction

Brian J. Legastra, Dan E. Helsten, Thomas B. Christophersen, Jacob E. Møller, Hans Erik Bather, Kenneth Egeberg, Department of Medical Research, OUH Søvndborg Hospital, Svendborg, Denmark

Background: Coronary microvascular function is an emerging determinant of cardiovascular prognosis. However, the influence of glucometabolic dysfunction in patients with first time acute myocardial infarction (AMI) is unknown.

Methods: 183 patients (72.1% male, mean age 62.5 ± 11.3 years) with first time AMI and no significant valvular disease or significant stenosis in the left anterior descending coronary artery (LAD) were divided into four glucometabolic groups using a 2-hour oral glucose tolerance test. Transthoracic echocardiographic Doppler recordings of coronary flow in distal LAD were performed at rest and during Adenosine infusion (140 μg/min). Coronary flow velocity reserve (CFVR) was calculated as the hyperemic to resting coronary diastolic peak velocity ratio.

Results: Prior to admission 161 of 183 patients included had no history of diabetes. In this group, using multiple linear regression analysis, 2-hour blood glucose levels were independently associated with CFVR (P<0.007). After classification of the 183 patients in four groups according to WHO criteria, 64 patients had a normal glucometabolic response, 58 as having impaired glucose tolerance (IGT), 39 as having a new diagnosis of diabetes, and 22 had a pre-study diagnosis of diabetes. There was a stepwise decrease in CFVR with increasing glucometabolic dysfunction (P=0.055) adjusting for confounders (including age, gender, Wall Motion Score Index, heart rate, location of infarction, and history of hypertension).

Conclusions: Microcirculation assessed by CFVR, in first time AMI, is continuously decreased according to glucometabolic state. This finding may reflect microvascular dysfunction in prediabetic and diabetic patients with AMI.

Myocardial ischemia and infarction

Circulating Very Small Embryonic-Like Stem Cells and the Recovery of the LVEF in Patients With Acute Myocardial Infarction

Wojciech Wojakowski, Magda Kucia, Ewa Zuba-Surma, Maciej Kanzmierczi, Mariusz Szylód, Grzegorz Smolka, Wiesław Cybulski, Edyta Paczkowska, Marek Krol, Andrzej Ochala, Boguslaw Machalinski, Mariusz Z. Ratajakczak, Paweł Buszman, Michal Tendera, Medical University of Silesia, Katowice, Poland, Stem Cell Institute, Louisville, KY

Background: In patients with acute myocardial infarction (MI) a significant mobilization of bone marrow-derived non-hematopoietic very small embryonic-like cells (VSELs) occurs. VSELs are small (7-8 μm), negative for lineage and CD45 markers, enriched for markers of embryonic pluripotent stem cells (Oct4, Nanog) and express CXCR4. VSEL mobilization is reduced in older, diabetic patients with significantly reduced left ventricular ejection fraction (LVEF). Aim was to assess the correlation between the recovery of the (LVEF) and mobilization of VSELs in patients with acute myocardial infarction.

Methods: 40 patients with anterior MI and 30 healthy controls (CTRL) were enrolled. Number of VSELs was measured 24 hours after primary PCI and after 1 year. After lysis of erythrocytes population of lin-CD45-CD133+CXCR4+ VSELs was isolated using a live cell sorting system (FACSAria). VSELs were characterized using immunofluorescence, FACS and ImageStream and RQ-PCR. MI was used for measurement of LVEF and volumes.

Results: In acute MI there was a significant mobilization of VSELs [4.9 (0-1.7-3); p<0.001] enriched in pluriotent (Oct4, Nanog) and cardiac lineage markers (GATA-4, Nkx2.5, MEF2C). Number of VSELs after 1 year was comparable to CTRL [0.7 (0.1-3.3)] vs 0.8 (0.1-3.3) [p=0.53]. VSEL mobilization in MI was significantly lower in patients with reduced (<40%) LVEF in the acute MI as well as in patient with persistently reduced LVEF<40% after 1 year of follow-up (3.2 (0.1-4.8) vs 4.8 (0.5-6.4) cells/μL). Mobilization of VSELs was significantly positively correlated with absolute increase of LVEF during 1-year follow-up (R=0.51; p<0.01). Patients with better mobilization of VSELs (≥ median) were more likely to have significant (>5%) absolute increase of LVEF after 1 year [OR 0.2 (0.0-0.5), p=0.006].

Conclusion: Mobilization of small non-hematopoietic embryonic-like stem cells is positively correlated with the recovery of LVEF in patients with acute MI treated with primary PCI.

Acute MI induced mobilization of VSEL SCs expressing pluriotent markers, early cardiac and endothelial markers, and chemokine receptor CXCR4.

Mobilization of small non-hematopoietic embryonic-like stem cells is positively correlated with the recovery of LVEF in patients with acute MI treated with primary PCI.

Relation of Coronary Thrombus Age With Platelet Rupture and Association of No-Reflow With Coronary Aspirated Material in Patients With Acute ST-Elevation Myocardial Infarction: A Clinico-Pathological Study

Giuseppe Ferrante, Francesco Buzotta, Giampaolo Niccoli, Giovanni Paolo Talarico, Carlo Tovo, Antonio Maria Leon, Rocco Mongiardo, Antonio G. Rubbo, Guido Cereda, Annalisa Angelini, Filippo Crea, Felicita Andreotti, Catholic University of the Sacred Heart, Rome, Italy, University of Padua, Medical School, Padua, Italy, Padua, Italy

Background: Thrombi weeks old have been reported in coronary aspirates from patients with acute ST-elevation myocardial infarction (STEMI), suggesting that platelet rupture may long predate the onset of symptoms. To test this hypothesis we assessed the relation between thrombus age and plaque debris. Further, we investigated the association of coronary aspirate with no-reflow.

Methods: Patients presenting in ACS patients presenting of patients with acute ST-elevation myocardial infarction were enrolled. Two consecutive independent observers sorted aspirates into two groups: thrombus material (≥ 7 days) and plaque debris (<7 days).

Results: 116 patients were included in the study. Patients with aspirates containing thrombus material were more likely to present anterior infarction (p=0.009) and to have a history of hypertension (p=0.02). The overall prevalence of coronary no-reflow was 13.3% (p=0.03). No-reflow was more likely to appear in patients with thrombus material (p=0.006).

Conclusion: Thrombus material, but not plaque debris, is associated with a higher prevalence of no-reflow and with a longer history of hypertension. Further accumulation of data from larger series is necessary to confirm our results.
Methods: Manual thrombus aspiration was performed, with the Diver CE system, in consecutive STEMI patients with native vessel occlusion, undergoing primary percutaneous coronary intervention. Aspirated material, after staining with hematoxylin-eosin, was classified according to thrombus age at light microscopy analysis and further categorized into fresh or old thrombus. Proportions were compared across study period. Results: Out of 215 patients, sustained ventricular tachycardia (VT) or ventricular fibrillation (VF) classified as malignant ventricular arrhythmias (VT/VF) occurred in 20 patients (9.3%); 12 required defibrillation. Non-sustained VT was seen in 12 (5.6%) patients (excluded from statistical analysis). Fourteen patients (6.5%) died, out of which 7 had VT/VF. On univariate analysis, the presence of left bundle branch block (p=0.03), T wave inversions (p=0.015) and ventricular fibrillation (VF) was predicted by a baseline angiographic thrombus score ≥4 (odds ratio (OR) 24.1, 95% confidence interval (CI) 2.5-233.5, p=0.006). Histological types were fresh thrombus in 43%, old thrombus (>1 day) in 37%, and blood aggregates without evidence of fibrin in 20%. Atherosclerotic elements were found in 23% of aspirates, exclusively with old thrombi (p<0.001) and more frequently with right coronary artery occlusions (35% vs 4%, p=0.015). The presence of detectable material was an independent negative predictor of no-reflow (defined as the absence of combined endpoint of STR >70% and TIMI 3 flow + MBG 0) [OR 0.03, 95% CI 0.002-0.57, p=0.019], while there was no relationship between myocardial perfusion and histological types.

Conclusions: In STEMI patients with detectable aspirates after manual aspiration, the presence of atherosclerotic elements is associated uniquely with older thrombi, indicating that plaque rupture is not always simultaneous with "sudden" coronary occlusion. The absence of detectable aspirate is an independent negative predictor of no-reflow, suggesting an association between high thrombus burden and no-reflow.

Did Hurricane Katrina Affect the Incidence of Acute ST Elevation Myocardial Infarction (STEMI) Has Been Steadily Decreased Across the Gender and Ethnic Groups in the United States

Mohammad Reza Movahed, Mazen Jamal, MehrHashem Hashemzaadeh, University of Arizona School of Medicine, Tucson, AZ

Background: Advances in the prevention and treatment of atherosclerosis risk factors have been dramatic in the last ten years. The goal of this study was to evaluate any decline in the age adjusted incidence of acute ST elevation myocardial infarction (STEMI) based on gender and race in the United States.

Methods: The Nationwide Inpatient Sample (NIS) database was utilized to calculate the age-adjusted rate for STEMI from 1988 to 2004 retrospectively. Specific ICD-9-CM codes for myocardial infarctions that are consistent with STEMI were used to compile the data. Patient demographic data based on age, gender, and race were analyzed and adjusted for age from the database.

Results: The NIS database contained a total of 1,352,574 patients who had a diagnosis of STEMI from 1988 to 2004. From 1988 the age-adjusted rate for all acute STEMI remained steady for 8 years in the entire population regardless of gender or race from 1988 until 1996. However, from 1997, the age-adjusted incidence of STEMI steadily declined across all ages and gender in a similar fashion to the half of the incidence in the year 2004 (Figure 1 and Figure 2, p<0.01).

Conclusion: The incidence of STEMI was stable from 1988 to 1996 with steady linear decline to half by the year 2004 in a similar degree across different gender and races. The cause of steady decline in STEMI is most likely reflecting the advancement in the prevention and treatment of atherosclerosis risk factors.
after a natural disaster can foster tobacco abuse and medication and therapeutic noncompliance.

Conclusions: We found a three-fold increased incidence of AMI more than two years after Hurricane Katrina. Even allowing for the loss of some local hospitals after the disaster, this represents a significant change in overall population health, and supports the need for further study into the health effects of chronic stress.

3:30 p.m.

1023-137 Impact of Gender on Treatment and Clinical Outcomes in Acute Coronary Syndrome Patients in the Middle East
Ayman A. El-Menyer, Mohammad Zubair, Wael Almahmeed, Kadhim Souliman, Ahmed Al-Motareb, Haitham Amin, Nidal Asaad, Khalid Al-Habib, Jassim Al Suwaidi, Hamad Medical Corporation, Doha, Qatar, Kuwait University, Kuwait, Kuwait

Background: Several western studies demonstrated significant disparities in acute coronary syndrome (ACS) presentation and outcome between men and women. We aimed to evaluate the presentation of Middle-eastern women with ACS, management and their outcome.

Methods: Gender differences in regards to baseline characteristics, therapy and outcome was performed Using data from the Gulf Registry of Acute Coronary Events (GulfRace) which is a prospective, multinational multicenter survey of 8178 (1996 women and 6201 men) consecutive patients hospitalized with ACS from February to June 2007 in 6 middle eastern countries. Data were analyzed according to gender. RESULTS: When compared to men, middle-eastern women were 9 years older (62.1 versus 53.1 years; P<0.001) and more often had diabetes (54.6% versus 35.9%, P<0.001), hypertension (70% versus 43%, P<0.001) and dyslipidemia (44% versus 28%, P<0.001). Women were also more likely to have other co-morbidities including chronic lung disease, renal and peripheral vascular disease. On the other hand, men were more likely to be smokers (46% versus 5.1%, P<.001), and arterial hypertension was more common in women (28.2% versus 8.1%, P<0.001) and 8.0% versus 6.1% (P<.001). Women were less likely to be appropriately treated with thrombolytic therapy (79.9% versus 83.8%), primary PCI (4.9% versus 8.4%)-[j-blockers (57% versus 64%), clopidogrel (54% versus 60%), and glycoprotein IIb/IIIa inhibitor (2.2% versus 9.5%) P<0.001). Women more often had worse in-hospital outcomes compared to men [heart failure (27.6% versus 14.4%), shock (19.5% versus 7%), and re-infarction (5% versus 2.7%)]. In-hospital death was higher in ST- and non-ST-elevation myocardial infarction in females (13.4% versus 4.6%, P<0.001 and 4.2% versus 1.9%, P=0.01). Conclusion: Similar to western studies, despite presentation with higher risk characteristics and having higher in-hospital risk, middle-eastern women with ACS are treated less aggressively than men. Female gender is independent predictor of poor outcome in all the spectrum of ACS.

3:30 p.m.

1023-136 Overnight Onset of STEMI Is Not Associated With Increased Mortality Despite Experiencing Greater Delays to Presentation and More Pre-Existing Coronary Artery Disease
Owen N. Monagle, Robert P. Giugliano, Marc S. Sabatine, Christopher P. Cannon, Stephen D. Wiviott, David A. Morrow, Sathishkumar Mohanavelu, Elliot M. Antman, Eugene Braunwald, Brigham and Women’s Hospital, Boston, MA

Background: An AM peak of STEMI has been described. We explored the relationship between diurnal variation, pt characteristics, and outcomes in 2 worldwide lytic trials.

Methods: 35,492 STEMI pts were grouped into 4-8 hr intervals by symptom onset: morning (6AM-2PM), evening (2PM-10PM), overnight (10PM-6AM). We correlated pt characteristics and outcomes in 2 worldwide lytic trials.

Results (Table 1): As anticipated, symptom onset was more frequent in the morning - such pts were older, less likely smokers, and had initial PTT post heparin. The evening group had more smokers, initial HR and SBP. Pts with overnight Mls had better renal function; were more obese; had more prior MI, anterior MI, prior aspirin and b-blocker use; and longer delays to presentation. Mortality and composite outcomes were worse in pts with pain onset in the evening. Mean HR and PTT were similar between the other two groups. Conclusions: Both time of symptom onset and pt characteristics demonstrate circadian variations in worldwide lytic trials. Worse outcomes seen with overnight primary PCI are not replicated in large lytic trials, potentially due to lytic resistance in AM pts and less optimal in-hospital management. Adjusted outcomes appear worse in pts with symptom onset from 2PM-10PM, in whom smoking is a major modifiable risk factor.

3:30 p.m.

1023-140 Clinical Outcomes Of Bare Metal Stents Versus Drug-Eluting Stents Target Vessel Revascularization: Evidence For A High-Risk Bare Metal Stent Cohort
Kevin R. Hayes, Robert J. Applegate, Matthew T. Sacrinty, Michael A. Kutch, Sanjay K. Gandhi, Renato M. Santos, William C. Little, Wake Forest University School of Medicine, Winston-Salem, NC

Background: Recent data suggest that mortality may be lower with drug-eluting stents (DES) than bare metal stents (BMS) in off-label patients. However, the potential mechanisms for this benefit remain unclear.

Methods: We assessed clinical outcomes 2 years ± 30 days after treatment for target lesion revascularization (TLR) in 221 consecutive patients (137 of 4,51 (9.4%) BMS and 84 of 1,883 (4.5%) DES) at WFUBMC between 2002 and 2005. Results: Clinical presentations of TLR were similar including ACS (76% BMS and 75% DES, p=0.88), and stent thrombosis (11% BMS and 15% DES, p=0.33), although time to TLR was longer for DES. 385 (interquartile range 158-631) days, versus BMS 154 (97-357) days, p<0.001. Treatment for TLR differed with brachytherapy in 37% BMS, versus 71% DES, p<0.001; and DES placement in 65% BMS versus 25% DES, p<0.001. At one year post-revascularization for TLR, the DES versus BMS hazard ratio (HR) for all cause mortality was 0.37 (0.13-1.11), and for non-fatal MI or death 0.65 (0.30-1.42) (see Figure), and was similar in those treated with or without brachytherapy.

3:30 p.m.
Background: Death due to coronary disease in the young is uncommon, and poorly described beyond case reports.

Methods: Clinical and pathologic records from the Office of the Armed Forces Medical Examiner from 1998 to 2008 were reviewed.

Results: There were 760 deaths due to suspected cardiovascular disease that had an autopsy performed, with a mean age of 39±11 years (96.3% male). The etiology of death was structural heart disease in 589 (77.5%) and idiopathic in 150 (19.7%). Coronary disease was the leading identifiable etiology (n=426, 56.1%). Of the deaths due to disease of the coronary arteries, atherosclerosis was the leading abnormality; but less common in those <40 years (88.7%) compared to those >40 years (91.9%, p=0.001). Anomalous coronary artery (7.1% vs. 0.4%, p=0.001) and a significant coronary bridge (0.6% vs. 0.4%, p=0.017) were more common in those <40 years compared to those >40 years, respectively. Deaths due to atherosclerosis were equally exertional and non-exertional (49.7% vs. 50.3%); while deaths due to anomalous coronary artery or coronary bridge were significantly more likely to be exertional (70.8%, p=0.041). Those with death due to atherosclerosis had a higher BMI than those with either anomalous coronary disease or myocardial bridge (29.3±6.3 kg/m² vs. 25.9±6.1 kg/m², p<0.002).

Conclusions: Coronary artery disease is the most common cause of cardiovascular death in the armed forces, especially in those over 40 years. Different types of coronary artery pathology have different clinical precipitants that must be recognized as part of risk reduction.

3:30 p.m.

1023-143 Sudden Death Due to Coronary Disease in the Young: Examining Causes Other Than Atherosclerosis

David A. Appel, Jennifer A. McNear, Lena Avedissian, Laudino M. Castillo-Rojas, John E. Atwood, Lisa A. Pearse, Robert N. Potter, Allen P. Burke, Ladd Tremaine, Eric A. Shroy, Peter J. Gentleski, Stephen S. Reich, Robert E. Eckardt, the Defense Cardiovascular Death Registry Group, Brooke Army Medical Center, San Antonio, TX, Armed Forces Institute of Pathology, Washington, DC

Background: Death due to coronary disease in the young is uncommon, and poorly described beyond case reports.

Methods: Clinical and pathologic records from the Office of the Armed Forces Medical Examiner from 1998 to 2008 were reviewed.

Results: There were 760 deaths due to suspected cardiovascular disease that had an autopsy performed, with a mean age of 39±11 years (96.3% male). The etiology of death was structural heart disease in 589 (77.5%) and idiopathic in 150 (19.7%). Coronary disease was the leading identifiable etiology (n=426, 56.1%). Of the deaths due to disease of the coronary arteries, atherosclerosis was the leading abnormality; but less common in those <40 years (88.7%) compared to those >40 years (91.9%, p=0.001). Anomalous coronary artery (7.1% vs. 0.4%, p=0.001) and a significant coronary bridge (0.6% vs. 0.4%, p=0.017) were more common in those <40 years compared to those >40 years, respectively. Deaths due to atherosclerosis were equally exertional and non-exertional (49.7% vs. 50.3%); while deaths due to anomalous coronary artery or coronary bridge were significantly more likely to be exertional (70.8%, p=0.041). Those with death due to atherosclerosis had a higher BMI than those with either anomalous coronary disease or myocardial bridge (29.3±6.3 kg/m² vs. 25.9±6.1 kg/m², p<0.002).

Conclusions: Coronary artery disease is the most common cause of cardiovascular death in the armed forces, especially in those over 40 years. Different types of coronary artery pathology have different clinical precipitants that must be recognized as part of risk reduction.

3:30 p.m.

1023-144 Comparison of Clinical Characteristics and Outcomes in Patients With Acute ST-Segment Elevation Myocardial Infarction Presenting During Working Hours Versus Off Hours

Kang Yun Chen, Seung Woon Rha, Yong Jin Li, Kanhaiya L. Poddar, Jae Hyoung Park, Jin Oh Na, Cheol Ung Choi, Hong Euy Lim, Jin Won Kim, Eung Ju Kim, Chang Gyu Park, Hong Seog Seo, Dong Joo Oh, Young Keun Ahn, Myung Ho Jeong, Korea University Guro Hospital, Seoul, South Korea, Chonnam National University Hospital, Gwangju, South Korea

Background: Acute ST-segment elevation myocardial infarction (STEMI) requires urgent diagnosis and revascularization, which may vary due to the different time of presentation. We evaluated the impact of different time of presentation on the characteristics of STEMI management and subsequent outcomes in Korean Acute Myocardial Infarction Registry (KAMIR).

Methods: Using KAMIR data collected from November 2005 to September 2007, we analyzed the differences in clinical characteristics and outcomes among 4968 STEMI patients presenting during working hours (weekdays 7 AM to 6 PM) versus off hours (weekends, holidays, and 6 PM to 7 AM weekends).

Results: Overall, 2628 STEMI patients (55.9%) presented during off hours. Compared with patients presenting during working hours, off-hours patients were less likely to arrive within 6 hours after symptom onset (59.1% vs. 71.5%, P<0.001), less likely to receive primary percutaneous coronary intervention (PCI) (66.9% vs. 76.3%, P<0.001) with longer door-to-balloon time [median (h) 1.33 vs 1.00, P<0.001 in primary PCI] and fewer achievements of door-to-balloon time <2 hours (69.4% vs. 78.8%, P=0.001 in primary PCI). In addition, patients arriving during off hours were more likely to receive thrombolyis treatment (13.6% vs. 4.2%, P<0.001) with longer door-to-drug time [median (h) 0.83 vs 0.47, P<0.001] than those presenting during working hours. Clinical outcomes showed that patients presenting during off hours versus working hours had similar incidence of inhospital mortality (6.0% vs 5.6%, P=0.172) and 8-month mortality (7.5% vs. 6.8%, P=0.334). Multivariate analysis showed that off-hour presentation was not an independent risk factor for inhospital death (odd ratio (OR) 1.03, 95% confidence interval (CI) 0.78-1.37, P=0.838) or 8-month death (OR 1.11, 95% CI 0.85-1.43, P=0.434).

Conclusions: Despite fewer primary PCI and longer door-to-balloon time and door-to-drug time, patients presenting with STEMI during off hours had similar in-hospital and 8-month mortality to those presenting during working hours.

3:30 p.m.

1023-145 ECG Presentation of Left Main Disease in Acute Coronary Syndrome

Keili C. Niku, Mariku Eskola, Heart Center, Cardiology Department, Tampere University Hospital, Tampere, Finland

Background: The ECG pattern with widespread ST-depression, maximally in leads V4-V5 with inverted T waves and ST-elevation in lead AVR (‘left main ECG’, ‘LM-ECG’) is associated with severe left main or triple-vessel disease.

Methods: The incidence at hospital admission and prognosis of the ECG pattern was studied in a population of consecutive patients with acute coronary syndrome in a university hospital setting. The patients (n=1188) were classified into seven different ECG categories: ST-elevation (26%), pathological Q waves without ST-elevation (23%), typical LBBB (6%), LHV without ST-elevation, except in leads aVR and for V1 (?), left main ECG (8%, n=97), other ST-depression and/or T-inversion (14%) and other findings, including normal ECG (13%).

Conclusions: Patients with TLR after BMS have similar clinical presentations as those with DES, but present more frequently and have significantly worse one-year outcomes than those with DES. Further studies into this high-risk BMS subgroup are merited.

3:30 p.m.

1023-142 Clinical Characteristics and Mid-Term Outcomes of Acute Myocardial Infarction Patients With Previous Cerebrovascular Disease

Yong Jian Li, Seung Woon Rha, Kang Yun Li, Kanhaiya L. Poddar, Jae Hyoung Park, Jin Oh Na, Cheol Ung Choi, Hong Euy Lim, Jin Won Kim, Eung Ju Kim, Chang Gyu Park, Hong Seog Seo, Dong Joo Oh, Young Keun Ahn, Myung Ho Jeong, Korea University Guro Hospital, Seoul, South Korea, Chonnam National University Hospital, Gwangju, South Korea

Background: Cerebrovascular disease (CVD) can be an important future cardiovascular event. The impact of previous cerebrovascular disease (CVD) on the clinical characteristics and midterm outcomes of patients (pts) with acute myocardial infarction (AMI) has not been well described in Asian population.

Methods: Data were analyzed from 8151 pts with AMI (either STEMI or NSTEMI) enrolled in Korea Acute Myocardial Infarction Registry (KAMIR) from 2005 to 2007.

Results: Of 8151 pts, 552 pts (6.8%) had previous CVD. The pts with CVD were older (68.9±10.11 vs 62.8±13.74, P<0.001), more incidence in women (70.4% vs 62.7%, P<0.001), showed higher incidence of hypertension and diabetes than the pts without CVD. The pts with previous CVD presented more often with NSTEMI and higher Killip class than the pts without CVD. Further, pts with CVD received less percutaneous coronary intervention (PCI) or thrombolyis compared with the pts without CVD. Intensive medical therapy was equally maintained in both groups.

Conclusions: Pts with CVD showed higher incidences of cardiac death [13.6% vs. 5.1%, adjusted odd ratio (OR) 2.11, 95% confidence interval (CI) 1.62-2.70, P<0.001], total death (15.9% vs. 5.9%, adjusted OR 2.15; 95% CI 1.65-2.80, P<0.001) and total major adverse cardiac events (MACE, 23.0% vs. 11.6%, adjusted OR 1.45; 95% CI 1.14-1.85, P<0.001) at 8 months. The incidences of recurrent MI and repeat revascularization at 8 months were similar between the two groups.

Conclusions: Pts with CVD showed more severe and worse clinical characteristics on admission and was associated with lower rates of PCI or thrombolyis. When we consider the poorer midterm clinical outcomes including higher mortality and MACE, in pts with prior CVD, more intensive and aggressive management for this particular subset of pts should be emphasized for better long-term clinical outcomes.

3:30 p.m.
Results: All patients with the left main ECG pattern, who had a coronary angiography, had significant coronary artery disease, 8% had 1-vessel, 21% 2-vessel and 71% 3-vessel disease. In addition, 25% had significant, 50% or more, left main disease. In patients with other ECG patterns, the proportion with at least 50% left main disease was: ST-elevation 3%, Q-wave without ST-elevation 10%, LBBB 21%, LVH 15%, other ST/T pattern 3%, other ECG pattern 5% (p<0.001).

Of the ECG categories, left main ECG had the highest rate of major adverse cardiovascular events, including mortality both in-hospital (29%) and during median follow-up of 10 months (49%). The revascularization rate in the left main ECG group was 41%.

In multivariable analysis, the left main ECG pattern predicted poor prognosis compared to other ECG patterns. The other variables that provided independent prognostic information in multivariable analysis were age, creatinine level at presentation and diabetes.

Conclusions: The ECG pattern with widespread ST-depression, maximally in leads V4-V5 with inverted T waves and ST-elevation in lead aVR was present in 8% of “all-comers” with acute coronary syndrome. In multivariable analysis, this “left main ECG pattern” predicted poor prognosis compared to other ECG patterns.

3:30 p.m.

1023-146 Chronic Kidney Disease and Dipstick Proteinuria Are Risk Factors for Stent Thrombosis in Patients With Myocardial Infarction


Background: Renal failure is an independent risk factor for stent thrombosis (ST). Moderate chronic kidney disease (CKD) and proteinuria are both associated with adverse cardiovascular events, including worse outcomes after myocardial infarction (MI). Whether moderate CKD and proteinuria increase the risk of ST after MI is not known.

Methods: We retrospectively analyzed clinical and laboratory data from 1,016 patients who were admitted with MI and received intracoronary stenting. Clinical follow up was collected at one year for definite or probable ST, as well as for all-cause mortality and non-fatal MI or death.

Results: After multivariable adjustment, patients with both estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73m² and ≥1+ dipstick proteinuria had increased cumulative incidence of ST (Hazard Ratio [HR] 4.22 [1.75-10.18], all-cause mortality [HR 2.78 [1.40-5.52]), and non-fatal MI or death [HR 3.43 [1.93-6.11]) at one year. There was a dose-dependent increase in risk of ST as GFR declined (see figure). Dipstick proteinuria (≥1+) was associated with a trend increased risk for all outcomes.

Conclusions: In an acute MI population, stage CKD 3-4 (eGFR 15-59 ml/min/1.73m²) and non-fatal MI or death.

3:30 p.m.

1023-147 Two-Year Multicentre Experience of Routine Use of Fondaparinux in Acute Coronary Syndromes

Francois Schiele, Nicolas Meneveau, Marie-France Seronde, Vincent Descolles-Geron, Joanna Duhrhol, Romain Chopard, Fiona Ecarnot, Jean-Pierre Bassand, University Hospital Jean Minjoz, Besancon, France

Background: Fondaparinux (fonda) is one of the anticoagulants recommended by guidelines in patients (pts) with acute coronary syndromes (ACS). Its use in routine practice is poorly documented.

Methods: From January 2006 to December 2007, we recorded the anticoagulant agent used in pts with ACS. Demographic, clinical and biological characteristics at admission, plus treatment, severe bleeds and 30 day outcome were recorded.

Results: Among 2776 pts included, fonda use increased from 4% to 48%, p<0.001; while use of unfractionated heparin (UFH) remained stable (18% in 2006; 16% in 2007, p=NS). The increased use of fonda resulted from a switch from enoxaparin. Fonda use varied depending on type of centre (figure). Pts treated with UFH were older, had more comorbidities, higher risk and bleeding scores and received fewer guidelines-recommended therapies. At 30 days, severe bleeding and mortality were higher in UFH-treated pts. There was no difference in 30 day mortality between enoxaparin and fonda groups. A higher rate of severe bleeding was observed in the enoxaparin group (2.3% versus 1.2%, p<0.01). Adjustment for a propensity score for being treated with enoxaparin did not alter these results.

Conclusions: The increasing use of fonda was the result of a switch from enoxaparin in low to medium risk pts, whereas higher risk pts were still treated with UFH. No difference in 30 day mortality was observed between pts treated by enoxaparin or fonda, but the rate of severe bleedings was lower in the fonda group.

3:30 p.m.

1023-148 Troponin Positive, MB Negative Patients With Non-ST Elevation Myocardial Infarction: An Under-Treated but High-Risk Patient Group: Results From NCDR ACTION-GWTG Registry

Michael C. Kontos, James A. de Lemos, Fang-Shu Ou, L. Kristin Newby, Matthew T. Roe, Virginia Commonwealth University, Richmond, VA

Background: Despite the 2002 redefinition of myocardial infarction (MI), patients (pts) who are troponin (Tn)> but MB- may not be considered to have MI, particularly in the absence of known coronary disease (prior MI or revascularization; CAD), in which case TN elevation may be ascribed to non-CAS causes. How this affects treatment and outcomes has not been well described. Methods: Pts with non-ST elevation MI (NSTEMI) enrolled in ACC NCDR ACTION-GWTG Registry from 1/07 to 6/08 were included. Pts missing marker data, who were Tn(-)(n=3198) and known CAD (n=15066) were excluded. Pts were categorized as Tn+MB+ (n=11563) or Tn+MB- (n=4501). Baseline characteristics, treatments and in-hospital outcomes were compared between the 2 groups using logistic regression. Results: Of the 16,064 NSTEMI pts, 28% were Tn+MB+. Tn+MB- pts were older (median age 68 vs 65) with more co-morbidities (HTN, 71 vs 66%, DM, 31 vs 27%, CHF 22 vs 19%, all p<0.01). After adjusting for baseline characteristics, Tn+MB- pts were less likely to receive acute ACS treatment or angiography (Table). In-hospital mortality was higher in Tn+MB+ pts (4.9% vs 3.8% p<0.001), which remained significant after adjusting for baseline variables (OR 1.4, 95% CI 1.2-1.8; p<0.001). Conclusions: In pts with NSTEMI without known CAD, Tn+MB- pts have a higher risk profile but are less likely to receive guideline recommended acute ACS treatment. Given the high mortality in this group, increased emphasis on improving quality of care in Tn+MB- pts is warranted.

3:30 p.m.

1023-149 Is Pre-Existing Coronary Disease a Risk Factor for In-Hospital Mortality? An Analysis From the NCDR ACTION-GWTG Registry

Michael C. Kontos, Antonio Abbate, Fang-Shu Ou, Matthew T. Roe, Virginia Commonwealth University, Richmond, VA

Background: Many variables predict mortality in patients (pts) with non-ST elevation myocardial infarction (NSTEMI). Surprisingly, there is limited data comparing characteristics and outcomes of pts with and without known coronary disease (prior MI or revascularization; CAD) in pts with NSTEMI. Methods: Pts in the ACC NCDR ACTION-GWTG Registry with NSTEMI from 1/07 to 6/08 were included. Pts without data on known CAD (n=485) were excluded. We compared outcomes among pts with and without known CAD using logistic regression and the effect of home treatment and baseline characteristics on outcomes. Results: There were 47,486 pts (42% known CAD). Known CAD pts were older and had more co-morbidities (Table). After adjusting for baseline characteristics, Tn+MB- pts were less likely to receive acute and PCI compared to pts without known CAD (Figure). Known CAD pts were older (median age 68 vs 65) with more co-morbidities (HTN, 71 vs 66%, DM, 31 vs 27%, CHF 22 vs 19%, all p<0.01). After adjusting for baseline characteristics, Tn+MB- pts were less likely to receive acute ACS treatment or angiography (Table). In-hospital mortality was higher in Tn+MB+ pts (4.9% vs 3.8% p<0.001), which remained significant after adjusting for baseline variables (OR 1.4, 95% CI 1.2-1.8; p<0.001). Conclusions: In pts with NSTEMI without known CAD, Tn+MB- pts have a higher risk profile but are less likely to receive guideline recommended acute ACS treatment. Given the high mortality in this group, increased emphasis on improving quality of care in Tn+MB- pts is warranted.

3:30 p.m.
Differential treatments in Patients With Systemic Lupus Erythematosus or Rheumatoid Arthritis Hospitalized With Myocardial Infarction: A NRMI Data Analysis

Hosakote M. Nagaraj, Marc Mayhew, Paul Frederick, William Rogers, Vijay Misra, University of Alabama at Birmingham, Birmingham, AL

Background: Patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) have an elevated risk of myocardial infarction (MI). We sought to determine the differences in cardiac risk factors, treatment of MI, and length of hospitalization between patients with and without SLE or RA.

Methods: Data were obtained from the National Registry of Myocardial Infarction (NRMI)-5. This includes patients over age 18 years discharged from 456 participating U.S. hospitals between April 2004 and December 2006. NRMI-5 contained the data of 161387 non-transfer-out patients of which 1143 patients with SLE/RA were compared to a cohort of 1143 patients without SLE/RA. RA in SLE was not included in the original TIMI score criteria largely because the clinical trial cohorts excluded patients with renal dysfunction.

Results: Eighty seven patients (10.9%) had adverse outcomes. The ROC for the TIMI score yielded an area under the curve (AUC) of 0.56 (95% CI 0.50-0.62). Adding CrCl as an independent predictor to the TIMI score improved the AUC to 0.63 (95% CI 0.57-0.70). Comparison of the ROC curves suggested a significant improvement in the AUC with the addition of CrCl to the TIMI score (p value = 0.014). CrCl < 45ml/min was associated with an odds ratio of 2.8 (95% CI 1.7-4.5) for adverse outcomes.

Conclusions: Chronic kidney disease is likely to occur at the shoulder of eccentric plaque as well as at the proximal side-portion of plaque hill. However, three-dimensional structural features in plaque rupture are still unclear. Multivariate logistic regression analysis revealed CKD as an independent risk factor of multiple yellow plaques per vessel (odds ratio 2.94, 95% CI 1.05-8.32, p=0.04).

Conclusions: Chronic kidney disease may raise the risk for cardiovascular disease by increasing number of yellow plaques in a coronary artery: Angiographic Study

Tomoaki Higgi, Shinichi Hirotani, Mitsuru Wada, Yuki Masumura, Kazunori Kashiwase, Mayu Nishio, Yasunori Ueda, Osaka Police Hospital, Osaka, Japan

Background: Chronic Kidney Disease (CKD) has emerged as an independent risk factor of cardiovascular disease. On the other hand, we have revealed in the previous angiographic study that number of yellow plaques (NYP) in a coronary artery is an independent indicator of cardiovascular events, and that patients with multiple yellow plaques per vessel have a higher risk of suffering future cardiovascular events than those with NYP 0 or 1. We assumed that CKD might raise the risk for cardiovascular disease by increasing NYP.

Methods: Consecutive 136 patients with acute myocardial infarction who received primary PCI and successful angiographic examination were enrolled in this study. The infarct-related artery was angiographically examined. NYP, maximum yellow color intensity (max YP), grade 1, light yellow; grade 2, yellow; or grade 3, intense yellow), and prevalence of disrupted yellow plaques with thrombus (DYP) in the non-culprit segments were compared between CKD group (eGFR< 60ml/min/kg/1.73m2) and No CKD group. Estimated GFR was calculated using MDRD equation and based on indirect calibration of serum creatinine.

Results: Mean age was 64 ±11 years, 81% were male and 31% had diabetes mellitus. The CKD group was older (69 ± 12 vs 62 ± 10, p<0.025), and had more females (30% vs 14%, p<0.001). NYP was significantly larger in CKD group than in No CKD group (4.1 ± 2.2 vs 2.9 ± 1.9, p<0.001). Max YP and prevalence of DYP in the non-culprit segments were not statistically different between two groups (2.5 ± 0.5 vs 2.3 ± 0.6, p=0.064; 40% vs 27%, p=0.164, respectively). Multivariate logistic regression analysis revealed CKD as an independent risk factor of multiple yellow plaques per vessel (odds ratio 2.94, 95% CI 1.05-8.32, p=0.04).

Conclusions: CKD was an independent risk factor of multiple coronary yellow plaques. Our data suggest that CKD raises the risk for cardiovascular events by increasing NYP in a coronary artery.

Three-Dimensional Morphologic Analysis of Coronary Plaque Rupture Using Intravascular Ultrasound and Novel Stereoscopic Image-Processing System

Tatsuhiko Fujimura, Takafumi Hiro, Jutaro Yamada, Takayuki Okamura, Manabu Nasu, Shintaro Akashi, Masayuki Yoshimura, Hiroko Kanoh, Toshiro Miura, Masunori Matsuzaki, Yamaguchi University, Ube, Japan

Background: Coronary plaque rupture is likely to occur at the shoulder of eccentric plaque as well as at the proximal side-portion of plaque hill. However, three-dimensional structural features in plaque rupture are still unclear.

Methods: Intravascular ultrasound (IVUS) images from 78 patients (64±9 y.o.) with a coronary plaque rupture were analyzed by a 3D image-processing program (Avizo, Mercury Computer Systems). Coronary lumen was traced in all frame images of IVUS. The traced lumen was transferred and rendered to form a three-dimensional surface structure of plaque rupture. The final image was examined from all angles as well as walk-through viewings.

Results: The cavity of plaque rupture has a mean longitudinal diameter of 4.0±2.4 mm, a mean short axis diameter of 1.4±0.7 mm, and its mean short/longitudinal ratio (SLR) of 0.4±0.24. A residual fibrous cap could be seen in 53 patients (68%). A slit-like fissure was observed in 36 cases (46%) at an edge of rupture cavity. Multiple ruptures in the same culprit coronary segment were seen in 19 cases (24%). A tunnel-like rupture with a fibrous cap bridge could be detected in 21 patients (27%). Patients with an oval rupture cavity (SLR > 0.3) had a greater maximum-CPK than those with a spindle cavity (SLR < 0.3)(p<0.02).

Conclusions: Coronary plaque rupture is not a simple phenomenon, but rather a complex one with a complicated variety of rupture process. This variability might determine the clinical outcome of patients with acute coronary syndrome.
Increased Levels of Circulating Bone Marrow-Derived Erythroid Immature Cells in Patients in the Acute Phase of ST Elevation Myocardial Infarction and Better Ventricular Function

Elena Corli, Erika Pagannone, Maria Beatrice Musumeci, Andrea Mannu, Marco De Giusti, Filippo Maria Cutuli, Eleonora Dito, Sebastiano Sciarretta, Camillo Autore, Massimo Voipe, II Faculty of Medicine, University of Rome, Italy, IRCCS Neuromed, Pozzilli (IS), Italy

Background: Large unstained cells (LUC), present also in normal subjects, were recently described as progenitors cells (PC) with hematopoietic commitment (CD34+). Erythroid PC are in turn committed towards endothelial and myeloid PC with repair and substitution function, in response to endothelial damage and myeloid ischemic necrosis. The role of circulating LUC in acute myocardial infarction (AMI) has not yet been clarified. We aimed to verify whether endogenous LUC output could exert a beneficial role with respect to infarct area and ventricular function (EF) in AMI (patients) pts, also in relation to treatment and revascularization efficacy and strategies.

Methods: We enrolled 135 consecutive pts admitted at our CCU with ST elevation AMI (98M, 37F, mean age 63±13), with time from symptom onset of 701±342 minutes, undergoing different treatment strategies: medical (n=20), primary (p) angioplasty (PCI) (n=105), rescue PCI (n=15), post successful fibrinolysis early PCI (n=0). For all pts, pre- and post-procedural TIMI flow, total number of diseased vessels, culprit vessel proximality, as well as haemoglobin (Hb), WBC, and LUC at time 1 (admission, LUMIC), 2 (3rd day of admission), and 3 (discharge), CKMB and troponin I peaks and AUCs, were recorded. As normally distributed, continuous variables were compared with Student t test, and the relation between LUC1,2, and 3 and measures of infarct area and EF corrected for age, gender, time from symptom onset, recanalization performed/not performed, TIMI flow and vessel proximality, was tested with multivariate analysis.

Results: Median LUC1 value separated two populations similar for Hb,Hct, WBC values at times 1, 2, 3. At the multivariate analysis detailed above, higher EF values were significantly and independently related with higher LUC 1 (β= -0.22, p<0.05), and post-procedural TIMI flow (β= 0.29, p<0.05).

Conclusions: Our data show that higher admission LUC are independently associated with a better ventricular function (EF), thus suggesting that bone marrow-mediated LUC output exert a favourable role on EF in AMI, regardless of type and efficacy of therapeutic strategy employed. Further investigation on topic is warranted.

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Type of MI</th>
<th>Type 2 MI</th>
<th>Non MI</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>143 (20.4%)</td>
<td>84 (9.1%)</td>
<td>411 (65.8%)</td>
</tr>
<tr>
<td>Peak TnI mg/l</td>
<td>23.95 ± 5.29</td>
<td>1.68 ± 0.40</td>
<td>1.26 ± 0.34</td>
</tr>
<tr>
<td>Without STEMI</td>
<td>12.26 ± 2.64</td>
<td>1.68 ± 0.40</td>
<td>1.26 ± 0.34</td>
</tr>
<tr>
<td>Age (y)</td>
<td>63.9 ± 1.6</td>
<td>64.2 ± 2.5</td>
<td>64.4 ± 0.8</td>
</tr>
<tr>
<td>Male</td>
<td>84 (56.7%)</td>
<td>35 (54.7%)</td>
<td>260 (56.4%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>61 (42.7%)</td>
<td>64 (92.7%)</td>
<td>170 (36.9%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>68 (98.1%)</td>
<td>63 (98.2%)</td>
<td>347 (90.5%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>66 (46.2%)</td>
<td>50 (64.6%)</td>
<td>208 (45.1%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>113 (79.0%)</td>
<td>65 (45.1%)</td>
<td>477 (62.9%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>23 (17.8%)</td>
<td>42 (26.5%)</td>
<td>122 (26.4%)</td>
</tr>
<tr>
<td>Illicit Drug Use</td>
<td>2 (1.4%)</td>
<td>1 (1.4%)</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>(Cocaine/Phenmetramine)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-hospital Angiogram</td>
<td>110 (77.6%)</td>
<td>71 (43.8%)</td>
<td>245 (62.6%)</td>
</tr>
<tr>
<td>Any Angiogram</td>
<td>124 (86.8%)</td>
<td>82 (50.0%)</td>
<td>215 (50.2%)</td>
</tr>
<tr>
<td>Significant obstruction</td>
<td>111</td>
<td>25</td>
<td>78</td>
</tr>
<tr>
<td>Non-obstructive/Normal</td>
<td>13</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>CK-MB peak</td>
<td>15 (10.5%)</td>
<td>8 (12.2%)</td>
<td>15 (10.5%)</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>102 (70.9%)</td>
<td>46 (35.1%)</td>
<td>195 (37.5%)</td>
</tr>
</tbody>
</table>

*pANOVA or Chi-Square
Conclusions: Patients with PP have higher inflammatory condition and positive remodeling with large plaque burden, and more post-stenting cardiac enzyme elevation compared with patients without PP. NC component is a major component of post-stented myonecrosis.

3:30 p.m.

1023-156

Primary Percutaneous Coronary Interventions for Stent Thrombosis

Guido Parodi, Gentian Memisha, Benedetta Bellandi, Renato Valenti, Angela Migliorini, Ruben Vergara, Nazario Carnabba, Gian Franco Gensini, David Antoniucci, Department of Cardiology, Careggi Hospital, Florence, Italy

BACKGROUND: There are very few (and conflicting) data about the effectiveness of primary percutaneous coronary interventions (PCI) for stent thrombosis (ST) treatment.

OBJECTIVE: We sought to evaluate the prevalence, efficacy and outcomes of primary PCI in patients with ST-elevation acute myocardial infarction (STEMI) due to ST.

METHODS AND RESULTS: Among 2,484 consecutive patients with STEMI treated by primary PCI, ST was the cause of the STEMI in 67 (3%) patients. Patients with ST showed a lower rate of significant collateral circulation (0% versus 6%, p=0.034) and a higher creatine kinase peak value (2,678±3,221 U/L versus 2,375±2,189 U/L, p=0.003) as compared to the other 2,387 STEMI patients. The PCI was successful (TIMI flow grade 3, and residual stenosis <20%) in 64 (96%) patients of the ST group and consisted in additional stenting (78%) or only balloon angioplasty (22%). Abximab and rheolytic thrombectomy were used in 75% and 31% of patients, respectively. Procedure time (39±26 versus 32±19 minutes, p<0.0001) and fluoroscopy time (13±10 versus 10±8 minutes, p<0.0001) were longer, and contrast medium amount (221±89 mL versus 194±103 mL, p=0.004) higher in patients with ST as compared to the de novo STEMI patients. Six-month death (12% versus 8%; p=0.216) and nonfatal reinfarction (10% versus 1%; p<0.0001) rates were higher in patients with ST as compared to those without. At 6-month angiographic follow-up (n=1,643±226), restenosis/reclosure rate was 54% versus 17% (p<0.0001) in patients with and without ST. CONCLUSION: The prevalence of primary PCI for ST is low. Additional stenting with or without thrombectomy is effective in restoring vessel patency in patients with ST, but restenosis and reclosure are frequent. ST treated with successful PCI is associated with large infarct size and poor outcome. New strategies to prevent ST are needed.

3:30 p.m.

1023-157

Prior Coronary Artery Bypass Graft Portends High Risk in STEMI Patients Treated With Primary Percutaneous Coronary Intervention

Robert C. Welsh, Christopher B. Granger, Cynthia M. Westerhout, James C. Blankenship, David R. Holmes, William W. O’Neill, Christian W. Hamm, Frans J. Van der Vel, Paul W. Armstrong, University of Alberta, Edmonton, AB, Canada

Background: Limited information exists regarding outcomes of STEMI pts with prior CABG undergoing primary PCI.

Methods: 128 pts (2.2%) with prior CABG were enrolled in APEX-AMI (n=5,745), a randomized, placebo-controlled trial of prasugrel in STEMI pts with primary PCI. Their preprocedural characteristics, whether the culprit coronary vessel (IRA) was a graft or native artery, and 90-day clinical outcomes were compared to those without prior CABG status.

Results: Pts with prior CABG were more frequently male, older, and had a higher incidence of comorbidities and multi-vessel CAD (Table). As compared to pts with prior CABG, primary PCI was not performed in 21% vs. 6.1% and TIMI-3 flow was restored in 80.2% vs. 91.5% pts with prior CABG (both p<0.001). Amongst those with prior CABG, the IRA was a graft (n=43) vs. native vessel (n=55) and their post-PCI TIMI 3 was 60.3% vs. 88.0% respectively (p<0.003). Prior CABG pts had a substantially increased hazard of 90-day death and the composite outcome of death/CHF/shock; however only death remained significant after baseline adjustment. When prior CABG pts were stratified by graft (n=43) vs. native vessel (n=55) there was further discrimination of increased mortality (10.9% vs. 3.7%, p<0.05).

Conclusions: In high-risk STEMI pts: those with prior CABG were less likely to undergo acute reperfusion and had worse clinical outcomes. This appears mediated in part by worse angiographic outcomes, especially when the IRA was a bypass graft.

Table. Selected patient characteristics and 90-day outcomes.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Prior CABG</th>
<th>Prior CABG</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>5617</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>Age, yrs (median, IQR)</td>
<td>61(52-71)</td>
<td>69(58-3-76)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female, %</td>
<td>23.3</td>
<td>14.1</td>
<td>0.014</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>49.0</td>
<td>70.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior MI, %</td>
<td>10.9</td>
<td>64.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior PCI, %</td>
<td>9.2</td>
<td>36.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior HF, %</td>
<td>3.3</td>
<td>16.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>15.7</td>
<td>25.0</td>
<td>0.004</td>
</tr>
<tr>
<td>Multivessel disease, %</td>
<td>40.2</td>
<td>81.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>90-day death, %</td>
<td>4.6</td>
<td>11.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Adj HR: 1.9, 95%CI(1.1-3.3)</td>
<td>p=0.025</td>
<td></td>
<td></td>
</tr>
<tr>
<td>90-day death, HF, shock, %</td>
<td>10.1</td>
<td>16.4</td>
<td>0.019</td>
</tr>
<tr>
<td>Adj HR: 1.1, 95%CI(0.7-1.7)</td>
<td>p=0.816</td>
<td></td>
<td></td>
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</tbody>
</table>
Recombinant Human Interleukin-11 Has a Novel Role in the Mobilization of Endothelial Progenitor Cells and Reduction of Infarct Size in Mice

Julius Atesbaaom, Siddharth Srivastava, Cam Patterson, University of North Carolina, Chapel Hill, NC

Background: Acute myocardial infarction (AMI) is the leading cause of death for both men and women in the western world, and studies in human subjects with coronary artery disease have shown that Endothelial Progenitor Cell (EPC) levels directly correlate with mortality after AMI. Currently, use of EPC for treatment of patients with ischemic heart disease involves delivery of ex vivo-processed EPC to patients during percutaneous coronary intervention or by direct injection of EPC to ischemic myocardium. A major limitation of EPC therapy in this patient population is lack of drugs to mobilize EPC in vivo.

Methods: In a preclinical study to evaluate the efficacy of mobilized EPC, saline or recombinant human interleukin-11 (HIL-11) was administered intravenously at a dose of 200 microgram/kg/day to 8-week old C57BL/6 mice (n=8 in each group) 24 hours prior to 30 minutes of coronary occlusion and reperfusion. Area at risk was assessed by Evans blue dye, infarct size by triphenyltetrazolium-chloride, and left ventricular volumes as well as ejection fraction by echocardiogram.

Results: There was a 5-fold increase in EPC mobilization within 24 hours of IL-11 infusion. The area at risk was significantly reduced by 24% at 72 hours post infarction. The post-infarct reduction of ejection fraction was improved, and the left ventricular end-systolic and end-diastolic volumes were reduced by 7 days when compared to control.

Conclusions: Taken together, these data show that HIL-11 has a novel role in reduction of infarct size and has a favorable effect on post-infarct remodeling suggesting a novel role of HIL-11 as an adjunctive therapy for patients with AMI.

3:30 p.m.

Left Bundle Branch Block Without Concordant ST-Elevation In Suspected ST-Elevation Myocardial Infarction Identifies Patients With High False Positive Rates: Insights From the APEX-AMI Trial

Renato D. Lopez, Hanly Shih, Yuling Fu, Paul W. Armstrong, Christopher B. Granger, Duke Clinical Research Institute, Durham, NC

Background: We sought to assess how left bundle branch block (LBBB) relates to the likelihood of ST-segment elevation myocardial infarction (STEMI) and need for primary percutaneous coronary intervention (PCI) in patients (pts) with suspected STEMI.

Methods: We evaluated cardiac biomarkers, coronary angiograms, outcomes according to LBBB in the 5473 pts included in the APEX-AMI trial. All electrocardiograms were interpreted in a core lab blinded to treatment and outcomes.

Results: LBBB occurred in 98 (1.7%) pts. Although pts with LBBB were intended to be eligible only if LBBB was "not known to be old" and with concordant ST elevation, 52 (53%) had concordant ST elevation and 46 (47%) did not. The associations of cardiac biomarkers, revascularization with primary PCI or coronary artery bypass graft (CABG) surgery, outcomes and LBBB are in the table. Patients with one definition of "false positive" STEMI (no biomarker elevation, or no initial TIMI 0 or 1 flow, or no primary PCI/ in-hospital CABG) were less common in LBBB with concordant ST elevation (30.8%) vs without (71.7%, P<0.001). Patients with LBBB and concordant ST elevation more often had primary PCI (84.6%) compared to no concordant ST elevation (71.7%).

Conclusion: In a clinical trial of pts requiring primary PCI, the incidence of "false positive" STEMI was high, especially if there was no concordant ST elevation. On the other hand, careful assessment of concordant ST elevation with LBBB is required to identify a population highly likely to require primary PCI.

Patient descriptors according to the presence of LBBB and concordance of ST-elevation

| LBBB | No LBBB | P-value
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>CK-MB &lt;=2x</td>
<td>13 (13.3%)</td>
<td>185 (3.3%)</td>
</tr>
<tr>
<td>Pre-PCI TIMI flow 0-1</td>
<td>60 (61.3%)</td>
<td>4164 (73.9%)</td>
</tr>
<tr>
<td>Pre-PCI TIMI flow 2-3</td>
<td>38 (38.8%)</td>
<td>1466 (26.1%)</td>
</tr>
<tr>
<td>Primary PCI or in-hospital CABG</td>
<td>79 (80.6%)</td>
<td>5401 (95.7%)</td>
</tr>
<tr>
<td>False Positive STEMI</td>
<td>49 (50.0%)</td>
<td>1639 (29.0%)</td>
</tr>
<tr>
<td>90-Day mortality</td>
<td>5 (5.1%)</td>
<td>2666 (4.7%)</td>
</tr>
<tr>
<td>1-Year death/shock</td>
<td>14 (14.3%)</td>
<td>572 (10.1%)</td>
</tr>
</tbody>
</table>

False Positive STEMI = no biomarker elevation, OR TIMI 0 or 1, OR no primary PCI/in-hospital CABG.

3:30 p.m.

Patient Characteristics Associated With the Choice of Triple Antithrombotic Therapy in the Setting of Acute Coronary Syndromes

Jeremiah P. Depta, Christopher P. Cannon, Gregg C. Fonarow, Xin Zhao, Deepak L. Bhatt, Cleveland Clinic, Cleveland, OH, VA Boston Healthcare System and Brigham and Women's Hospital, Boston, MA

Background: Evidence regarding the use of dual antiplatelet therapy and oral anticoagulation (i.e. triple therapy) in acute coronary syndromes (ACS) is lacking. We evaluated characteristics associated with the choice of triple therapy in ACS.

Methods: Using the Get With the Guidelines® national registry database, we studied patients presenting with ACS at 361 participating sites in the United States from 2000-2007. Multivariable logistic regression was used to assess the factors associated with the choice of triple therapy upon discharge. The Generalized Estimating Equation method was used to account for within-hospital clustering.

Results: A total of 86,304 patients presented with ACS during the study period. At discharge, 3,063 patients (4.6%) were prescribed triple therapy, whereas 60,716 patients (70.3%) received dual antiplatelet therapy, 2,348 patients (2.7%) received single antiplatelet plus oral anticoagulation, 19,065 patients received antiplatelet monotherapy (22.1%), and 242 patients (0.3%) received oral anticoagulation alone. Patients with a history of atrial fibrillation (odds ratio [OR] 6.56, 95% confidence interval [CI] 5.67 to 7.59, P<0.001), documented new onset atrial fibrillation (OR 3.57, 95% CI 2.70 to 4.70, p=0.001), or history of atrial flutter (OR 3.15, 95% CI 2.00 to 4.96, p=0.001) were more frequently discharged on triple therapy. Of patients with atrial fibrillation or flutter (n= 6,064), 1,139 patients (18.6%) were discharged on triple therapy, 2,508 patients (41.4%) received dual antiplatelet therapy, 1,444 patients (23.8%) received antiplatelet monotherapy, 973 (16.0%) patients received a different antiplatelet and/or oral anticoagulation regimen.

Conclusions: Atrial fibrillation or flutter were most strongly associated with the choice of triple therapy in patients with ACS, yet used less often compared to dual or single antiplatelet therapy in patients with those factors. Further study is needed to evaluate the safety/efficacy of triple therapy in ACS.

3:30 p.m.

Acute Myocardial Infarction--Therapy; Unstable Ischemic Syndrome/Long-Term Outcome

Monday, March 30, 2009, 9:30 a.m.-12:30 p.m.
Orange County Convention Center, West Hall D

Fibrinolytic Therapy and Bleeding Complications: Risk Predictors From SWEDHEART

Jonas Odgren, Lisa Werrooth, Ulf Srenestrand, Uppsala Clinical Research Center, Uppsala, Sweden, Dept of Cardiology, University Hospital, Linköping, Sweden

Background: Fibrinolytic treatment for ST-elevation myocardial infarction (STEMI) is associated with increased bleeding risk but is still widely used worldwide, mainly because of limited access to primary PCI. The aim of this study was to analyse contemporary fibrinolytic treatment patterns, in-hospital bleeding risk and prognosis during 2001 to 2005 in unscreened Swedish STEMI patients.

Methods: The SWEDHEART registry covers almost all Swedish patients treated for myocardial infarction. Major in-hospital bleeding was defined as lethal or intracranial bleedings or bleedings requiring surgery or blood transfusion. Survival status of the 14732 patients was obtained from the National Cause of Death Register.

Results: The proportion of patients receiving fibrinolysis decreased from 76 % in 2001 to 23 % of STEMI patients in 2005. Major in-hospital bleedings (including lethal or intracranial) increased from 1.4 % (0.8%) in 2001 to 4.0 % (1.6 %) in 2005, p<0.001. History of serious bleeding, higher age, female gender, clopidogrel treatment prior to admission, pre-hospital administration of fibrinolytics and fibrin-specific fibrinolytics were identified as predictors for bleeding. Major in-hospital bleeding was the strongest predictor of adverse prognosis with more than three-fold increase in one-year mortality.

Conclusions: During 2001 to 2005 the use of fibrinolytic treatment markedly decreased while the incidence of major bleedings was more than doubled, the latter might in part be explained by increasing use concomitant anti-platelet therapy, pre-hospital treatment and fibrin-specific fibrinolytics. Future close monitoring of bleeding complications is warranted, especially when considering the increased use of various combinations of antithrombotic drugs in conjunction with fibrinolysis and the great impact of bleedings on long-term mortality.
Trends in the Medical Management and Thirty-Day Mortality Among Patients With Renal Dysfunction Admitted With Acute Myocardial Infarction

Paul A. Santolucito, Dennis A. Tighie, Darlene Lessard, Robert J. Goldberg, University of Massachusetts Medical School, Worcester, MA

BACKGROUND: Patients with renal dysfunction are at increased risk for adverse outcomes after acute myocardial infarction (AMI). While comorbidities are often greater in these patients, lower usage of recommended therapies may also play a role. The purpose of this study was to examine recent trends in the hospital management and 30-day mortality among patients with renal dysfunction admitted with AMI.

METHODS: Data from 6,219 hospitalized AMI patients (mean age=70.7±43.7% women) during 6 bimannual periods from 1995-2005 in the Worcester Heart Attack Study were examined. Trends in AMI management and 30-day mortality were stratified according to degree of renal function [preserved renal function (eGFR ≥60), mild to moderate renal disease (eGFR 30-60), or severe renal disease (eGFR <30)].

RESULTS: Aspirin and beta-blocker use increased over time to a greater extent among patients with renal insufficiency, especially those with eGFR ≤30 (figure). Statin use increased similarly in all groups (figure) irrespective of eGFR. While 30 day mortality was higher among those with renal dysfunction during all study years (figure), significant declines in mortality over time were observed only among those with renal dysfunction.

CONCLUSIONS: Data from this large population based study demonstrate favorable trends in the medical management and short-term outcomes among patients with renal disease admitted with AMI. Despite these trends, patients with renal disease remain at increased risk for adverse outcome after AMI.
**Background:** First clinical studies on intracoronary stem cell infusion in patients with acute myocardial infarction (AMI) revealed promising results with regard to left ventricular ejection fraction (LVEF) improvement. Percutaneous intramyocardial cell injection (PICI) has shown to be superior to the intracoronary approach in preclinical studies, but PICI has only been reported in patients with chronic ischemic heart disease, so far.

**Methods:** On day 10.5±5 after AMI and PCI with stent implantation (culprit lesion: 18 LCA, 2 RCA) 20 patients (mean 60.4±11.4 years) received bone marrow derived mononuclear cells (BMC) in the vital low voltage region of the infarction area using left ventricular electromechanical mapping (EMM-guided) PICI. We injected 2.0±0.3x10^10 cells including 1.0±0.3x10^6 CD45-/CD34+ stem cells in each patient. EMM (NOGA), coronary angiogram was performed in 15 patients including 6-month follow-up. Echocardiography, laboratory data and clinical assessment (6-month and 12-month follow-up) were performed in all 20 patients.

**Results:** None of the patients showed peri-procedural complications or major adverse events during the 12-month follow-up. EMM showed an improvement from baseline LVEF 45.5±14.3% to 59.3±19.2% of normal voltage (p=0.016) and reduction of the low voltage area from 28.7±12% to 20.3±13.5% (p=0.016) in 15 patients with EMM follow-up after 6 months. Endocardial electrogram fragmentation showed no increase in the EMM. There was no ventricular tachycardia documented in the Holter-ECG's. During the 12-month follow-up in all 20 patients, LVEF improved from 40.8±6.8% to 47.0±10.5%.

**Conclusion:** Left ventricular EMM and percutaneous intramyocardial cell injection in patients with AMI was shown to be a safe procedure and is associated with improved electromechanical parameters and increased left ventricular function during a 12-month follow-up.

**DISCUSSION:**

- **References:**

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**1032-130**

**Percutaneous Intramyocardial Stem Cell Injection and Electromechanical Mapping in Patients With Acute Myocardial Infarction: First-in-Man Study**

Kerth T. Krause, Kai Jaquet, Carsten Schneider, Stefanie Haupt, Karl-Heinz Kuck, Asklepios Clinic St. georg, Hamburg, Germany

**Background:** First clinical studies on intracoronary stem cell infusion in patients with acute myocardial infarction (AMI) revealed promising results with regard to left ventricular ejection fraction (LVEF) improvement. Percutaneous intramyocardial cell injection (PICI) has shown to be superior to the intracoronary approach in preclinical studies, but PICI has only been reported in patients with chronic ischemic heart disease, so far.

**Methods:** On day 10.5±5 after AMI and PCI with stent implantation (culprit lesion: 18 LCA, 2 RCA) 20 patients (mean 60.4±11.4 years) received bone marrow derived mononuclear cells (BMC) in the vital low voltage region of the infarction area using left ventricular electromechanical mapping (EMM-guided) PICI. We injected 2.0±0.3x10^10 cells including 1.0±0.3x10^6 CD45-/CD34+ stem cells in each patient. EMM (NOGA), coronary angiogram was performed in 15 patients including 6-month follow-up. Echocardiography, laboratory data and clinical assessment (6-month and 12-month follow-up) were performed in all 20 patients.

**Results:** None of the patients showed peri-procedural complications or major adverse events during the 12-month follow-up. EMM showed an improvement from baseline LVEF 45.5±14.3% to 59.3±19.2% of normal voltage (p=0.016) and reduction of the low voltage area from 28.7±12% to 20.3±13.5% (p=0.016) in 15 patients with EMM follow-up after 6 months. Endocardial electrogram fragmentation showed no increase in the EMM. There was no ventricular tachycardia documented in the Holter-ECG's. During the 12-month follow-up in all 20 patients, LVEF improved from 40.8±6.8% to 47.0±10.5%.

**Conclusion:** Left ventricular EMM and percutaneous intramyocardial cell injection in patients with AMI was shown to be a safe procedure and is associated with improved electromechanical parameters and increased left ventricular function during a 12-month follow-up.

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**1032-131**

**Impact of Time to Therapy on the Efficacy of FX06 as an Adjunct to Primary Percutaneous Coronary Intervention in Acute ST Elevation Myocardial Infarction**

Jonas Hallen, Bernard Geudelin, Rainer Henning, Jurg Schwitter, Kurt Huber, Peter Petzelbauer, Peter Buser, Dan Atar, Fibrex Medical Research & Development GmbH, Vienna, Austria, Aker University Hospital, Div. of Cardiology, Oslo, Norway

**Background:** The “FX06 in IschemiaReperfusion Injury” (F.I.R.E)-trial found that FX06, a fibrin peptide, reduced infarct size (IS) by mitigating reperfusion injury after 5 days in patients with STEMI undergoing primary PCI. The aim of this analysis was to determine whether the efficacy of FX06 versus placebo was dependent on the timing of reperfusion therapy.

**Methods:** In this trial, 234 patients presenting with acute STEMI within 6 hours from onset of pain were randomized in 26 centres. IS was assessed at 5 days and 4 months after primary PCI in STEMI, reduces IS significantly at 5 days and at 4 months both in terms of LGE zone (not at 5 days) and NC zone in patients presenting early (pain-to-ballon < 3 hrs). In contrast, in late presenters, FX06 seems to exhibit an effect in the short term, but there is no significant effect compared to placebo in the long-term.

**Conclusion:** In this pre-specified subgroup analysis, FX06, when given as an adjunct to primary PCI in STEMI, reduces IS significantly at 5 days and at 4 months both in terms of LGE zone (not at 5 days) and NC zone in patients presenting early (pain-to-ballon < 3 hrs). In contrast, in late presenters, FX06 seems to exhibit an effect in the short term, but there is no significant effect compared to placebo in the long-term.

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**1032-135**

**ST-Elevation Myocardial Infarction Care and Outcomes for the Oldest-Old**

Daniel E. Forman, Anila Y. Chen, Stephen D. Wiviott, Tracy Y. Wang, David J. Magid, Karen P Alexander, Brigham and Women’s Hospital, Boston, MA, Duke University Medical Center, Durham, NC

**Background:** Data regarding use of reperfusion therapy and outcomes in the oldest-old (<85 yrs) STEMI patients (pts) are sparse.

**Methods:** We grouped STEMI pts from 286 sites enrolled in the NCDR ACTION Registry-GWTG between 1/1/2007 and 6/30/2008 by age: <75, 75-84, and >85 yrs and describe baseline characteristics, use of reperfusion, and in-hospital outcomes.

**Results:** Compared to pts <85 yrs, the oldest-old STEMI pts (median age 88 yrs, IQR 86-91) were more often female and had more comorbidity (Hypertension, Heart Failure, Peripheral Vascular Disease, and Prior MI, all p<0.001). They were also more likely to have reperfusion contraindications, less likely to be reperfused even if eligible, and had longer wait times to EKG and balloon inflation (Table). Primary PCI was the most common reperfusion strategy across all age strata. Unadjusted rates of in-hospital death increased with age groups (4%, 12%, and 19%). Compared to pts not reperfused, adjusted mortality was significantly lower for reperfused pts aged <75 yrs (OR 0.58, CI 0.40-0.84), but only trended to benefit for reperfused pts aged 75-84 (OR 0.93 CI 0.57-1.54) and >85 yrs (OR 0.86, CI 0.44-1.69).

**Conclusions:** The oldest-old STEMI patients were more likely to have reperfusion contraindications, less likely be reperfused when eligible, and had longer reperfusion wait times. While reperfusion conferred benefit among pts aged <75 yrs, pts 75-84 and >85 only trended to benefit, suggesting differences persist related to reperfusion across age.

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**1032-136**

**An Increased TIMI Risk Score is Associated With a Decrease in TIMI Patency in Patients Treated With Thrombolitics for ST-Elevation Myocardial Infarction**

Hans-Peter Hobbach, Uwe Zeymer, Peter Schuster, St. Marien-Krankenhaus Siegen, Siegen, Germany, Klinikum der Stadt Ludwigshafen, Ludwigshafen, Germany

**Background:** While primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy in ST-elevation myocardial infarction (STEMI) the majority of patients (pts) is admitted to hospitals without PCI facilities. For the most part these pts will be treated with thrombolysis. Therefore clinical models to predict the success of thrombolysis are still needed.

**Methods:** 314 pts (age 62±12 years) with STEMI (<6 hrs) were investigated; all pts received a thrombolytic therapy and underwent early (within 90 min of lytic) invasive management. A successful thrombolysis was identified by TIMI 3 flow in the infarct related artery, risk of pts was stratified by TIMI Risk Score (TRS).

**Results:** There was a significant linear relationship between STEMI pts and mortality (p for trend <0.001) as well as TIMI 3 flow (p for trend <0.001), we could identify TRS where we have to assume a lower efficacy of thrombolysis.

**Conclusions:** TRS for STEMI is a convenient clinical risk score for predicting mortality among pts with STEMI and may be also useful in assessing efficacy of thrombolytic therapy, increasing risk was associated with decreasing patency. STEMI pts with TRS > 4 treated with thrombolysis should be considered for an early invasive management and possible rescue PCI. Alternatively, they should be transferred urgently for primary PCI without administration of a thrombolytic agent.
Infarct Size in Off-Site Primary Angioplasty Versus Impact of Pretreatment With Clopidogrel on Initial Left Ventricular Function After ST-Elevation Myocardial Infarction

Randomized trials were included when the research subjects were unselected patients undergoing primary percutaneous coronary intervention (PCI) vs. optimal medical therapy (MED) alone.

Methods: Older, patients (age≥65 years, n=641) enrolled in OAT were compared with younger patients (<65 years, n=1560) with respect to baseline characteristics and outcomes by treatment with percutaneous coronary intervention (PCI) vs. optimal medical therapy (MED) alone.

Results: Older patients were more likely to be female, non-smokers, hypertensive and to have impaired renal function and multivessel disease. The 5-year primary outcome (death, MI or Class IV heart failure), and death and heart failure individually were more common in older pts (p=0.001) (Table). For the primary outcome, there was a trend toward a differential treatment effect based on age (p=0.03), and no difference between PCI and MED (OR 0.8 (0.7-1.1), p=0.37) in either age group. Among younger patients MI rates tended to be higher in PCI vs. MED (HR 1.80 (95% CI 0.93-3.53), p=0.02), with no difference in older pts. During 5 years follow-up, younger patients more often had angina vs. older pts (H.R. 1.28, p=0.003), but rates of death and heart failure were comparable between treatment centers (16±15 versus 14±12%, respectively p=0.35).

Conclusions: Older patients had higher rates of most adverse outcomes, irrespective of treatment. PCI reduced angina to a similar degree in the young and old. There was a trend toward a differential effect of PCI in the young vs. the old for the primary outcome, which is likely a chance finding.

5-Year Adjudicated Outcomes by Age Group and Treatment

9:30 a.m.

1032-136

Infarct Size in Off-Site Primary Angioplasty Versus Transferal to a Tertiary Center: A Single Photon Emission Computed Tomography Study

Victor A. Umanos, Paul Knaapen, Jan H. Cornel, Friso van der Zand, MCA, Alkmaar, The Netherlands

Background. Primary percutaneous coronary intervention (PCI) performed in large community hospitals without cardiac surgery back-up facilities (off-site) reduces door-to-balloon time compared with tertiary centers on-site. The present study was performed to explore whether off-site PCI for acute myocardial infarction results in reduced infarct size.

Methods. 128 patients with acute ST-segment elevation myocardial infarction were randomly assigned to undergo primary PCI at the off-site center (n=68) or to transferal to an on-site center (n=60). Three days after PCI, 510-Tc-sestamibi SPECT was performed to estimate infarct size.

Results. Off-site PCI significantly reduced door-to-balloon time compared with on-site PCI (94±54 versus 125±59 min, respectively, p<0.01), although time-to-treatment was not significantly reduced (257±211 versus 286±146 min, respectively, p=0.39). Infarct size was comparable between treatment centers (16±15 versus 14±12%, respectively p=0.35).

Conclusions. Off-site PCI reduces door-to-balloon time compared with transferal to a remote on-site interventional center but does not reduce infarct size. Instead, pre-PCI PCI 0.1% flow, anterior wall infarct localization, and development of Q-waves are more important predictors of infarct size.

9:30 a.m.

1032-137

Left Ventricular Function After ST-Elevation Myocardial Infarction in Patients Treated With Primary Coronary Angioplasty and Abciximab or Tirofibin: Insights From the Facilitated Angioplasty with Tirofibin or Abciximab (FATA) Randomized Trial

Nevio Testagori, Francesco Saia, Cinzia Marrozzini, Vincenzo Guiducci, Guido Rocchi, Elena Biagni, Giancarlo Piovaccari, Antonio Manari, Angelo Branzi, Antonio Marzocchi, Istituto di Cardiologia, Università di Bologna, Policlinico S. Orsola-Malpighi, Bologna, Italy, Unità Operativa di Cardiologia Interventistica, Ospedale S. Maria Nuova, Reggio Emilia, Italy

Background: Abciximab during primary percutaneous coronary intervention (PCI) has shown to ameliorate left ventricular function recovery (LVFR). High-Dose Bolus (HDB) tirofibin has similar effect on platelet inhibition. Whether or not this is associated with comparable efficacy on LVFR remains unclear. Then, we sought to compare the impact on left ventricular function of adjunctive therapy with HDB tirofibin or abciximab in ST elevated myocardial infarction (STEMI) patients treated with PCI. Further we sought to define the predictors of favorable (>50%) left ventricular ejection fraction (LVEF) and LVFR.

Methods: This study comprised 314 patients (abciximab, n=154; tirofibin, n=160) undergoing PCI in the randomized Facilitated Angioplasty with Tirofibin or Abciximab trial. LVEF and wall-motion-score-index (WMSI) were assessed within 48 h post-PCI and at 30-day. Among patients with left ventricular systolic dysfunction at baseline, LVFR was defined by one of the following: 1) increase of LVFR ≥10% as compared to baseline; 2) LVEF ≥50%.

Results: Similar LVEF was observed in the two groups either post-procedure (abciximab 49.7±10.1% vs. tirofibin 49.3±10.1%, p=0.09) and at 30-day (abciximab 53.1±15.8% vs. tirofibin 52.5±10.2%, p=0.6). Likewise, there was no difference in WMSI post-procedure
Influence of Time-to-Reperfusion on the Presence and Extent of Myocardial Salvage, Infarct Size and Microvascular Damage in Patients With ST-Segment Elevation Myocardial Infarction: Evidence From Cardiovascular Magnetic Resonance

Chiara Bucciarelli-Ducci, Chiara Bucciarelli-Ducci, Marco Francoce, Iacopo Carbone, Emanuele Canali, Raifaide Scardalda, Francesca Calabrese, Gennaro Sardella, Emanuela Ageri, Francesco Fedele, Roberto Passariello, Luciano Agati, University “La Sapienza”, Rome, Italy

Background: Previous studies evaluating the influence of time-to-reperfusion on infarct size (IS) and myocardial salvage over time in patients with ST-segment elevation myocardial infarction (STEMI) yielded conflicting results. Cardiovascular magnetic resonance (CMR) can visualize areas of irreversible myocardial and microvascular injury (infarct size, IS and microvascular obstruction, MVO, respectively) with late gadolinium enhancement (LGE) imaging and areas of salvaged myocardium at risk with T2-weighted imaging.

Methods: Seventy patients with first STEMI, successfully treated with primary PCI within 12 hours from symptom onset, underwent CMR 5±2 days after hospital admission. Patients were subcategorized into 4 quartiles on the basis of pain-to-ballon time distribution: <60 minutes (group A, n=19), 60 to 150 minutes (group B, n=17), 150 to 360 minutes (group C, n=17), >360 minutes (group D, n=17). Breath-hold T2-weighted and LGE CMR imaging was used to characterize reversible and irreversible myocardial injury.

Results: Shorter time-to-reperfusion (group A) was associated with smaller IS and MVO and larger salvaged myocardium at risk. A progressive increase in IS (8%, 11%, 12%, 18%, p<0.005, respectively), and MVD (0.5%, 1.5%, 3.7%, 6.0%, p<0.038, respectively) was observed, whereas salvaged myocardium at risk suddenly decreased after 60 minutes (8.5%, 3.2%, 2.4%, 2.1%, p<0.003, respectively). Lately reperfused patients (group D) had significantly larger areas of IS and MVO with higher prevalence of intramyocardial hemorrhage compared to group A, with an almost complete disappearance of salvaged myocardium at risk.

Conclusions: In patients with reperfused STEMI, time-to-reperfusion determines the extent of reversible and irreversible myocardial injury. CMR can identify and quantify areas of salvaged myocardium at risk representing an important tool to be used in large clinical trials assessing different reperfusion strategies.

9:30 a.m.

1032-141

Clopidogrel Therapy Following Acute Myocardial Infarction Hospitalization or Stent Insertion: What Are the Consequences of Stopping Therapy Before one Year?


Background: Clopidogrel has been shown to reduce the risk of recurrent acute coronary syndrome (ACS), as reflected by the ACC/AHA guidelines since 2002. Our goal was to evaluate the clinical impact of stopping clopidogrel therapy earlier than one year.

Methods: We conducted a retrospective observational cohort study of patients having an acute myocardial infarction (AMI; STEMI or non-STEMI) and/or coronary stent insertion from 2002-2007. Patients were enrolled in an integrated commercial health plan which provides care across the continuum of inpatient and outpatient settings. Patients having pharmacy claims indicating less than 30-day supply of clopidogrel were excluded. The occurrence of AMI and/or ACS-related procedures (CABG, PCI with/without stent insertion) was tracked up to one year after initial hospitalization. Multivariate Cox regression using a time-dependent covariate for clopidogrel therapy was used to assess the association between stopping clopidogrel and risk of AMI rehospitalization, ACS-related procedure, or all-cause mortality, while adjusting for demographics, comorbidities, cardiovascular procedures at initial hospitalization, and at follow-up.

Results: A total of 1,152 patients had an AMI hospitalization or coronary stent procedure followed by at least 30 days of clopidogrel therapy. Average duration of therapy was 131 days. Seventy-three percent (n=837) of the patients had not refilled their medication routinely for a full year. Stopping clopidogrel was associated with nearly a three-fold increase in the risk of subsequent AMI rehospitalization or ACS procedure (HR 2.71, 95% CI 1.63-4.50). When considering a composite endpoint of all-cause mortality, AMI rehospitalization or ACS procedure, stopping clopidogrel was associated with a two-fold increase in risk (HR 1.84, 95% CI 1.28-2.60).

Conclusion: Stopping clopidogrel prior to a full year of therapy following an AMI hospitalization or coronary stent insertion is associated with a significantly increased risk of death, AMI hospitalization, and/or ACS procedure. Healthcare decision makers should consider implementing evidence-based recommendations to minimize patients’ risk of recurrent events.

9:30 a.m.
Impact of Intracoronary Injection of Mononuclear Bone Marrow Cells in Acute Myocardial Infarction on Left Ventricular Perfusion and Function: Gated 99mTc-MIBI Single-Photon Emission Computed Tomography Study.

Piotr Lipieś, Maria Krzeminska - Pakula, Michal Plewka, Jakub Kusmierek, Anna Plachcinska, Remigiusz Szumiński, Tadeusz Robak, Anna Korycka, Jarosław D. Kasprzak, Medical University of Lodz, Lodz, Poland

Background: We sought to investigate the impact of intracoronary injection of autologous mononuclear bone marrow cells (BMC) in patients with acute ST-elevation myocardial infarction (STEMI) on left ventricular volumes, global and regional systolic function and myocardial perfusion.

Methods: 38 patients with first anterior STEMI, treated with successful primary percutaneous coronary intervention were randomly assigned to the treatment group or the control group in a 2:1 ratio. 3-10 days after STEMI patients underwent baseline ECG-gated 99mTc-methoxyisobutylisonitrile single-photon emission computed tomography (G-SPECT) with quantitative and qualitative analysis of left ventricular perfusion and systolic function. On the following day, patients from the BMC treatment group were subjected to bone marrow aspiration, mononuclear BMC isolation and intracoronary injection. No placebo procedure was performed in the control group. G-SPECT was repeated six months after STEMI.

Results: Baseline and follow-up G-SPECT studies were available for 36 patients. At 6-months in the BMC group we observed a significantly improved mean perfusion defect extent (p=0.02), left ventricular perfusion score index (p=0.03), infarct area wall motion score index (p=0.04) compared to the control group. However, the changes in left ventricular end-diastolic and end-systolic volumes, left ventricular ejection fraction and left ventricular wall motion score index did not differ significantly between both groups.

Conclusions: Intracoronary injection of autologous mononuclear BMC in patients with STEMI improves myocardial perfusion and infarct area systolic function at 6 months with no apparent benefit in global left ventricular systolic function.

Enoxaparin in Patients Not Undergoing Reperfusion for ST-Elevation Myocardial Infarction

Gabriel Tatu-Chioiu, Dragos Vinereanu, Maria Doborantu, Mirea Cintea, Maria Udaneu, Olivia Manțurî, Crina Sinescu, Elvira Craiu, Marius Vințila, Mariana Radoi, Răzvan Bujarioti, Spitalul Clinico de Urgenta ‘Floreasca’, Bucharest, Romania, University of Bologna, Bologna, Italy

Background: Enoxaparin therapy is beneficial in STEMI. Recent trials show fibrinolysis and/or percutaneous coronary intervention. Its efficacy in patients not undergoing reperfusion is still unproven.

Methods: We investigated the relative benefits of enoxaparin compared with unfractionated heparin in the Romanian registry of STElevation acute myocardial infarction (RO-STEMI), which enrolled 9288 consecutive patients from January 2000 to December 2007.

Results: There were 3812 (41.0%) patients who did not receive mechanical or pharmacological reperfusion, but administration therapy with enoxaparin (n=1462) or unfractionated heparin (n=2350). Logistic regression was used to adjust the outcome of inhospital death for baseline characteristics. Patients who were given enoxaparin were more likely to have history of hypertension (60.1% vs. 51.7%, p<0.001), lipid disorders (42.3% vs. 29.5%, p<0.001), and prior myocardial infarction (13.4% vs. 9.0%, p<0.001), and to present heart failure (48.6% vs. 34.3%, p<0.001). They were more likely to receive concomitant medication with aspirin and/or clopidogrel (93.7% vs. 83.5%, p<0.001). The rate of death was reduced by enoxaparin compared with unfractionated heparin (14.5% versus 16.9%; OR, reference unfractionated heparin: 0.83; 95% CI 0.69-0.99, p<0.05).

After adjustment for age, any chronic confounders and antiplatelet therapy with aspirin and/or clopidogrel, patients with enoxaparin had a 1.26-fold-lower risk of death (95% CI, 0.58 to 0.88, p<0.001).

Conclusions: In the RO-STEMI registry, patients who did not undergo reperfusion had greater absolute and relative risk reductions when treated with enoxaparin compared with unfractionated heparin as an admission therapy.
STEMI complicated by CS. The purpose of this study was to determine the prognostic significance of MR, in STEMI patients with CS on admission.

Methods: From January 1997 through March 2005, 292 consecutive STEMI patients presented with CS on admission and were treated by primary PCI. Early echocardiograms were performed in 147 patients, which constituted the final study cohort. Color doppler of MR was graded with a 0 to 3 scale (none, n=26; 1=mild, n=62; 2=moderate, n=40; 3=severe, n=19).

Results: Overall 1-year mortality was 27%. One-year mortality was 8%, 23%, 30% and 58% for patients with no, mild, moderate and severe MR respectively (p<0.001). For each grade of MR increase, the odds for mortality increased by 80% (OR 1.8; 95% CI 1.1-3.0; p=0.025) when adjusted for age >60 years, gender, previous myocardial infarction, left ventricular ejection fraction (LVEF) >40%, multivessel disease and no-reflow.

Conclusions: The early presence of MR is an independent predictor of 1-year mortality in STEMI patients with CS on admission treated by primary PCI. Early identification of MR allows risk stratification and triage of high-risk patients towards new therapeutic approaches.

Figure 1 Kaplan-Meier estimate of 1-year survival according to grade of MR (log-rank test p<0.01). Total n=147, no MR n=26, mild MR n=62, moderate MR n=40, severe MR n=19.

9:30 a.m.

1032-147 Improvement of Reperfusion Rates With Thrombectomy Catheter in Acute Myocardial Infarction

Rogério Moura, Fernando Barreto, Marcus Costa, Carlos Barreto, Luciano Brasileiro, Fernando Tavares, Hospital Babino, Rio de Janeiro, Brazil

Background: Despite the great effectiveness of primary percutaneous coronary intervention (PCI) in AMI with ST elevation (AMIEST), the distal embolization of atherothrombotic material is related to reduction of myocardial perfusion and worse outcome.

Objective: To demonstrate the importance of using thrombectomy catheters in patients with AMIEST and the effectiveness of these devices in improving myocardial reperfusion.

Methods: prospective randomized trial, which were consecutively included 152 patients with AMIEST (>8h). From them, 76 patients were submitted to conventional PCI with stent (CPCI) and 76 patients treated with thrombectomy aspiration catheter (TAC). Primary endpoints were evaluated as the >70% ST reduction and ≤2 myocardial blush grade. The secondary outcomes were occurrence of major adverse cardiac events (MACE), in-hospital, at 1 month and after 9 months (death, new AMI, stent thrombosis and target lesion revascularization).

Results: There was significant improvement in the incidence of myocardial reperfusion in patients in the TAC group: >70% ST reduction (88.2% vs. 43.4% p <0.001) and Blush grade ≥2 (89.5% vs. 61.8% p = 0.001). The need for liblllita inhibitors was lower in the TAC group (59% vs. 82% p <0.005). The macroscopic effective extraction of thrombotic material was achieved in 81.6% of cases. There was no significant difference in relation to in-hospital or late MACE occurrence up to 9 months. Conclusion: The use of thrombectomy aspiration catheter as an adjunct to primary PCI in AMIEST has proved to be safe and effective in improving the parameters of myocardial reperfusion in patients studied.

9:30 a.m.

1032-148 Noninvasive Tracking of the Survival, Proliferation, and Migration of Human Adipose Tissue-Derived Stem Cells Transplanted into the Infarcted Heart by Bioluminescence Imaging in Living Animals

Xiaowen Bai, Yasheng Yan, Yao-Hua Song, Brian Rabinovich, Roxana Metzele, Eckhard Alt, University of Texas, MD Anderson Cancer Center, Houston, TX

Background: Adipose tissue-derived stem cells (ASCs) show therapeutic value in the treatment of infarcted myocardium. However, there is little information about monitoring the fate of the injected ASCs in vivo. In this study, we used bioluminescence imaging for the first time to noninvasively evaluate the survival, proliferation and migration of human ASCs (hASCs) injected into the infarcted hearts of living mice.

Methods: hASCs were transduced with the lentiviral vector carrying luciferase gene. Half the first time to noninvasively evaluate the survival, proliferation and migration of human ASCs in vivo. In this study, we used bioluminescence imaging for the existence of hASCs in hearts, which confirms that the BLSs detected in the heart area in vivo was from the hearts.

Conclusions: This study demonstrates for the first time that bioluminescence imaging can feasibly be used to track transplanted hASCs in infarcted hearts of mice in vivo over the 28-day period. The injected cells were preferentially retained in injured myocardium rather than migrating to other organs or tissues. This finding provides further insight into the mechanisms underlying the effect of hASCs on cardiac function of infarcted myocardium.

9:30 a.m.

1032-149 The Effect of Failure Mode and Effect Analysis On Reducing Door-to-Balloon Time and Mortality in ST-Segment Elevation Myocardial Infarction

Feng-Yu Kuo, Wei-Chun Huang, Guang-Yuan Mar, Chin-Chang Cheng, Han-Lin Tsai, Kuan-Rau Chiu, Shue-REN Wann, Shoa-Lin Lin, Chun-Peng Liu, Cardiovascular Medical Center and Department of Emergency, Kaohsiung Veteran General Hospital, Kaohsiung, Taiwan,ROC, School of medicine, National Yang-Ming University, Taipei, Taiwan,ROC

Background: The aim of this study was to evaluate the efficacy of Failure Mode and Effect Analysis (FMEA) to reduce door-to-balloon (D2B) time, mortality and morbidity.

Methods: FEMA was used to evaluate our D2B process since 2007. We implemented changes into two systems: the emergency department (ED) system (reverse triage order) and the transfer system (a STEMI network with 14 cooperative transfer hospitals, 24-2-hour special phone lines to active catheterization laboratory from ED in transfer hospitals).

Results: The retrospective (2005-2006), interphase (2007) and prospective (2008 Q1-2) period had 83, 90 and 130 patients. The D2B median time decreased significantly (p<0.001) (Figure 1). In the subgroup analysis, the transfer patients via STEMI network had significantly shorter D2B median time (25.5 minutes) than on-site patients (47 minutes) (p<0.001) or transfer patients without previous contact (43.5 minutes) (p<0.001). The D2B less than 90 minutes ratio improved from 15% to 59%, and then to 95% (p<0.001). There was significant reduction in the ED stay median time (126 minutes vs. 13 minutes, p<0.001), unplanned readmission percentage within 30 days (8.1% vs. 1.6%, p<0.02) and in-hospital mortality rate (10.8% vs. 3.8%, p=0.04).

Conclusions: FMEA is a powerful tool to systematically identify the D2B system weakness and decrease D2B median time, ED stay, readmission rate and mortality. STEMl transfer network showed more efficiency than transfer without contact or on-site patients.

9:30 a.m.

1032-150 Comparison of Left Ventricular Wall Motion Recovery Between Primary Percutaneous Coronary Intervention With and Without Thrombosisuction in Patients With Acute Myocardial Infarction. Results of Long-Term Echocardiographic Follow-Up Study

Hyunmin Cho, Sung Yun Lee, Seung Hwan Lee, Min-Soo Ahn, Kyung Hoon Lee, Young Kim, Joon Hyung Doh, June Namgung, Won Ro Lee, Inje University, Ilsan Paik Hospital, Goyang-si, Gyeonggi-do, South Korea, Yonsei University, Won-ju College of Medicine, Won-ju-si, Kangwon-do, South Korea

Background: The thrombosisuction by use of export aspiration catheter (EAC) during primary PCI has been proved to be safe and effective method for coronary reperfusion. However, the changes of left ventricular (LV) wall motion after thrombosisuction have never been evaluated.

Methods: From April 2005 to January 2008, we analyzed 111 patients who were underwent primary PCI with and without thrombosisuction and completed Echocardiographic examination on 1st to 5th days (baseline) and 6 to 12 months (follow-up). We divided them into the suction group (n=58) and non-suction group (n=53) and then compared two groups by use of the LV regional wall motion score (WMS) and ejection fraction
Immediate ST-Segment Resolution Is Associated With Left Ventricular Function and Infarct Size Measured by Cardiovascular Magnetic Resonance in ST-Elevation Myocardial Infarction Patients Treated With Primary Percutaneous Coronary Intervention

Joost D. Haack, Niels J. Verouden, Wichert J. Kuijt, René J. Van der Schaaf, José P. Henriques, Marjolein M. Vis, Jan Baan, Jr., Jan J. Piiek, Jan G. Tijssen, Robbert J. De Winter, Mitchell W. Kruckoff, Karel T. Koch, Academic Medical Center - University of Amsterdam, Amsterdam, The Netherlands, Duke Clinical Research Institute, Duke University Medical Center, Durham, NC

Background: Infarct size and preserved left ventricular function are major determinants of the prognosis of ST-segment elevation myocardial infarction (STEMI) patients. We sought to investigate whether ST-segment resolution (STR) immediately after percutaneous coronary intervention (PCI), determined by continuous 12-lead ECG monitoring, relates to infarct size and left ventricular function, as assessed by cardiovascular magnetic resonance (CMR).

Methods: 186 STEMI patients received both continuous ST-segment monitoring (evaluated at Duke Clinical Research Institute eECG Core Lab) during primary PCI and CMR at 4 months. Immediate complete STR was defined as >70% STR at time of last contrast. CMR was used to determine infarct size and left ventricular function, as assessed by cardiovascular magnetic resonance (CMR).

Results: 110 patients had complete STR and 76 patients had incomplete STR immediately after primary PCI. Patients with complete STR had a higher ejection fraction (EF), lower left ventricular end-diastolic volume (LVEDV), lower left ventricular end-systolic volume (LVESV), and smaller infarct size. The association between complete STR immediately after PCI and CMR parameters was highly statistically significant (p<0.01).

Conclusions: Complete STR immediately after primary PCI for STEMI was associated with preserved left ventricular function, and smaller infarct size on CMR. These results suggest that STR immediately after primary PCI is more a clinical and simple tool for success of primary PCI.
ST-Segment Deviation Resolution After Primary Percutaneous Coronary Intervention Is Inversely Associated With Time to Reperfusion in Patients With Acute Myocardial Infarction

Niels J. Verheugt, Wichtert J. Kuul, Joost D. Haeck, Karel T. Koch, José P. Henriques, Jan Baan, René J. van der Schaar, Marjolein M. Vis, Jan G. Tijssen, Jan J. Piek, Robert J. de Winter, Academic Medical Center, Amsterdam, The Netherlands

Background: Incomplete ST-segment deviation resolution (STR) after epicardial flow restoration may represent microvascular obstruction and predicts an unfavorable outcome in patients with ST-segment elevation myocardial infarction (STEMI). We investigated whether time to reperfusion is associated with STR in a large cohort of STEMI patients undergoing primary percutaneous coronary intervention (PCI).

Methods: In this single-center study, 190 STEMI patients with a complete dataset underwent primary PCI between 2000 and 2006. Time to reperfusion was defined as time from symptom onset to first balloon inflation. STR was defined as the relative difference (in %) of the summed ST-segment deviation between the pre-PCI and the immediately post-PCI 12-lead electrocardiogram. STR of >70% was considered complete.

Results: Median STR immediately after PCI was 51% (IQR 23% - 71%). Stratified by time to reperfusion, patients with a shorter time to reperfusion showed significantly higher median STR compared to patients with a longer delay (P=0.017, Figure). Patients undergoing PCI within 3 hours of symptom onset showed complete STR significantly more often compared to patients with a longer time to reperfusion (OR 1.2, 95% CI 1.0 - 1.5, P = 0.04).

Conclusions: STEMI patients undergoing primary PCI earlier after symptom onset show more STR compared to patients with longer time to reperfusion. Therefore, treatment delays should be minimized to aim for microvascular rather than just epicardial reperfusion.

Comparison of the Pre-hospital or Cath-Lab Administration of High Dose Tirofiban in Patients Undergoing Primary Angioplasty: The AGIR2 Study

Carlos ElKhoury, Pierre Yves Dubien, Loïc Belle, Gulaume Debatty, Olivier Capel, Thibaud Perret, Dominique Savary, Patrice Serre, Eric Bonnefoy, for the AGIR2 study investigators, Hospices Civils de Lyon, Lyon, France; Université Lyon I, Lyon, France

Background: Prehospital treatment with a high dose of tirofiban brings benefits in patients with STEMI who undergo primary angioplasty. In these patients, prehospital high dose of tirofiban had not been directly compared to the administration of a high dose of tirofiban in the cath-lab.

Methods: The multicenter AGIR2 study, randomized 300 patients managed in a prehospital setting within 6 hours of a STEMI and who underwent primary angioplasty, to a pre-hospital high dose of tirofiban (25 μg/kg bolus + 0.15mcg/kg/min) or to a high dose of tirofiban in the catheterisation laboratory. All patients received a prehospital loading dose of clopidogrel (600 mg) and heparin. The primary end-point was TIMI flow grade 2-3 of the infarct-related vessel at initial angiography. The effect of a pre-hospital high dose of tirofiban on each TIMI flow grade, the ST segment resolution one hour after PCI, peak of the infarct-related vessel at initial angiography. The effect of a pre-hospital high dose of tirofiban in the cath-lab. Patients received PCI had higher prevalence of cardiogenic shock, and PCPS use as aspirin+clopidogrel). However, a proportion of these patients shows suboptimal levels of platelet inhibition. AMI patients may present nervous autonomic imbalance with sympathetic predominance, and it is well known that catecholamines increase platelet reactivity. Thus, in this study we tested whether cardiac autonomic function shows any relation with platelet reactivity in AMI patients treated with DAPT, aspirin+clopidogrel). However, a proportion of these patients shows suboptimal levels of platelet inhibition. AMI patients may present nervous autonomic imbalance with sympathetic predominance, and it is well known that catecholamines increase platelet reactivity. Thus, in this study we tested whether cardiac autonomic function shows any relation with platelet reactivity in AMI patients treated with DAPT.

Methods: We studied 14 AMI patients (55±12 years, 9 men) treated by primary PCI and discharged on DATP. At 1-month follow-up, we assessed platelet reactivity by measuring: 1) the aggregation time on the PFA-100 method, and 2) monocyte-platelet aggregates (MPA) by flow cytometry at baseline and after ADP-stimulated (10⁻⁴ M). Cardiac autonomic function was assessed by heart rate variability (HRV) on 24-hour ECG Holter recordings. An inverse correlation was found between HRV variables and platelet reactivity. Thus, in this study we tested whether cardiac autonomic function shows any relation with platelet reactivity in AMI patients treated with DAPT.

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Conclusions: The significant inverse relation between HRV variables and platelet reactivity 1 month after AMI suggests that autonomic sympatho-vagal imbalance may contribute to a lower response to DAPT in these patients. The clinical implications of this finding merit to be investigated in a large population of AMI patients.

Association Between Heart Rate Variability and Platelet Reactivity After Acute Myocardial Infarction

Giancarla Scalone, Ilaria Coviello, Pasquale Santangelo, Francesca Di Clemente, Lucy Barone, Roberto Mollo, Alfonso Sestito, Gaetano A. Lanza, Filippo Crea, Catholic University of Sacred Heart, Institute of Cardiology, Rome, Italy

Background. Patients with acute myocardial infarction (AMI) treated by primary percutaneous coronary intervention are treated with dual antiplatelet therapy (DAPT, aspirin+clopidogrel). However, a proportion of these patients shows suboptimal levels of platelet inhibition. AMI patients may present nervous autonomic imbalance with sympathetic predominance, and it is well known that catecholamines increase platelet reactivity. Thus, in this study we tested whether cardiac autonomic function shows any relation with platelet reactivity in AMI patients treated with DAPT.

Methods: We studied 14 AMI patients (55±12 years, 9 men) treated by primary PCI and discharged on DATP. At 1-month follow-up, we assessed platelet reactivity by measuring: 1) the aggregation time on the PFA-100 method, and 2) monocyte-platelet aggregates (MPA) by flow cytometry at baseline and after ADP-stimulated (10⁻⁴ M). Cardiac autonomic function was assessed by heart rate variability (HRV) on 24-hour ECG Holter recordings. An inverse correlation was found between HRV variables and platelet reactivity. Thus, in this study we tested whether cardiac autonomic function shows any relation with platelet reactivity in AMI patients treated with DAPT.

Conclusions: The significant inverse relation between HRV variables and platelet reactivity 1 month after AMI suggests that autonomic sympatho-vagal imbalance may contribute to a lower response to DAPT in these patients. The clinical implications of this finding merit to be investigated in a large population of AMI patients.
A332-159 Greater Adherence to the Mediterranean Diet Reduces the Risk for the Development of Left Ventricular Systolic Dysfunction in Patients Who Had Had an Acute Coronary Syndrome

Demetrios B. Panagiotakos, Christina Chryssohou, Panagiota Aggelopoulou, Ioanna Kehagia, George Metallinos, Christos Pitsavos, Christodoulos Stefanadis, Athens Medical School, Athens, Greece

Background: We evaluated whether adherence to this traditional diet is associated with the development of left ventricular systolic dysfunction (LVSD) in patients who had an acute coronary syndrome (ACS). Methods: During 2006-2007, 351 post ACS patients (65±13 years) who developed LVSD (ejection fraction<40%) immediately after the event and 386 patients (63±12 years) with preserved left ventricular systolic function (ejection fraction>50%), were included in the study. Detailed information regarding socio-demographic, clinical, lifestyle and anthro pometric characteristics, were retrieved from all patients. A semi-quantitative food frequency questionnaire was applied to assess the consumption of a variety of food groups, while the assessment of adoption of Mediterranean Diet conducted through the MedDietScore (range 0-55) that incorporates the inherent characteristics of this traditional dietary pattern. Results: Patients with LVSD reported less adherence to the Mediterranean diet, compared to those with preserved left ventricular systolic function (p<0.01). The MedDietScore showed good accuracy in predicting LVSD (AUC: 0.55±0.02; p=0.05). Moreover, one unit increase in the diet score (i.e., greater adherence) was associated with 3.5% lower risk of developing LVSD (95%CI 0.93-1.00), after adjusting for age, gender, BMI, clinical status and presence of the common cardiovascular disease risk factors. A value of 31/55 in the MedDietScore constitutes the optimal threshold for better diagnosing LVSD (sensitivity = 81%). Furthermore, the MedDietScore seems to be more accurate among people >65 years old (AUC:0.59±0.03; p=0.05), men (AUC:0.55±0.03, p=0.09) and diabetic patients (AUC:0.59±0.04, p=0.05). Conclusion: Greater adherence to the traditional Mediterranean diet seems to independently protect against development of LVSD after an ACS. The suggested MedDietScore is an accurate diet tool for screening ACS patients who are prone to develop LVSD. Our findings expand the beneficial effects of this traditional diet on human health, and should be further promoted.

9:30 a.m.

A332-160 How Serum Levels of Glucose and Inflammatory Biomarkers Upon Presentation Affect 1-Year Mortality in Non-diabetics With Acute Coronary Syndromes

Stefanos G. Fratzas, Michael N. Zairis, Stamatis Makrygiannis, Dimitris Mylas, Georgios Z. Tsioufis, Nikolaos Patocouros, Joseph Papadopoulos, Andreas Melidoni, Anastasis Koutosvaslis, Stylianos Handanis, Tzanio State Hospital, Piraeus, Greece

Background: Serum levels of glucose and inflammatory biomarkers upon presentation seem to confer incremental predictive value for no-diabetics (and diabetics) with acute coronary syndromes (ACS). We sought to investigate the possible interrelation of serum levels of glucose and inflammatory biomarkers as well as the interaction of these biomarkers in the prediction of 1-year death in this setting.

Methods: 848 STEMI and 666 NSTE-ACS consecutive pts, without history of DM, who presented in the first 12 and 24 h of index pain respectively, were studied. Serum glucose levels upon presentation and during hospitalization were ≤ 11 mmol/L in all pts. Each cohort was divided into 3 groups according to glucose levels: Group A (<6.1 mmol/L), Group B (6.1-7.7 mmol/L) and Group C (7.11 mmol/L). Serum levels of inflammatory biomarkers including hs-CRP, interleukin-6 (IL-6) and fibrinogen (FIB), were measured upon presentation.

Results: There was a significant gradual increase of levels of all inflammatory biomarkers from Group A to Group C in pts with STEMI and NSTEMI-ACS. The incidence of 1-year mortality in A, B, and C Groups was 11.2%, 16.2%, 20.4% and 8%, 12.6%, 19.1% for STEMI (p=0.02) and NSTEMI-ACS (p=0.002) respectively. Importantly, biomarkers were significantly related to the incidence of 1-year mortality in pts with STEMI and NSTEMI-ACS. Particularly, hs-CRP (p=0.001 and p<0.001), IL-6 (p=0.004 and p=0.008) and FIB (p=0.033 and p=0.002) were significantly related to 1-year death in STEMI and NSTEMI-ACS pts respectively. Multivariate Cox analysis (inflammatory biomarkers not included), glucose levels independently predicted 1-year death. However, by multivariate Cox analysis (inflammatory biomarkers included), glucose levels did not predict 1-year death.

Conclusions: According to the present results serum glucose levels upon presentation are strongly associated with the degree of inflammatory response in non-diabetics with ACS. This may at least partially explain the association of serum glucose levels upon presentation and adverse outcome in non-diabetics with acute coronary syndromes.

9:30 a.m.
The Effect of Angiotensin-Converting Enzyme Therapy TIMI Risk Index Predicts Long-Term Mortality in Prognosis in Diabetic Patients With Acute Myocardial Infarction in The TIMI-II Clinical Trial

Quang A. Truong, Christopher P. Cannon, Neil A. Zakai, Ian S. Rogers, Robert P. Glugliano, Stephen D. Wiviott, Carolyn H. McCabe, David A. Morrow, Eugene Braunwald, TIMI Study Group, Brigham and Women’s Hospital, Boston, MA, Massachusetts General Hospital, Boston, MA

Background: TIMI Risk Index (TRI) is a simple bedside score, calculated as heart rate x (age+10) x systolic blood pressure, that predicts 30-day mortality in ST-elevation myocardial infarction patients. We sought to evaluate whether TRI was predictive of long-term mortality and able to identify patients where an early invasive strategy would be beneficial post-thrombolysis.

Methods: In the TIMI II trial, 3154 patients (age 57 ± 10 years, 62% men) were randomized to invasive (n=1584) vs conservative (n=1570) strategy post-thrombolysis with median follow-up of 3 years. TRI was divided into 5 groups (Figure A).

Results: At 3 years, mortality was 25.4% (97/389) in Group 5 as compared to 5.1% (63/1368) in Group 1 and 2 (Figure B). When compared to Group 1, unadjusted hazard ratio (HR) was highest for Group 5 (HR 5.8, p < 0.0001), then Group 4 (HR 2.8, p < 0.0001), and Group 3 (HR 2.0, p < 0.0002) (c statistic 0.69). After controlling for multiple cardiovascular mortality risk factors, adjusted HR remained significant: Group 5 (HR 4.2, p < 0.0001), and Group 3 (HR 2.0, p = 0.002) (c statistic 0.69). At 3 years, mortality was 25.4% (97/397) in Group 5 as compared to 5.1% (23/457) in Group 1 and 2 (Figure A).

Conclusions: TRI is predictive of long-term mortality in TIMI II with a 4-fold increased risk in the highest TRI group as compared to the lowest, but could not identify a subgroup of patients who may benefit from an early invasive strategy after reperfusion therapy with thrombolysis.

Prognosis in Diabetic Patients With Acute Myocardial Infarction Is Related to Renal Function

Jacek Kowalczyk, Radoslaw Lenarczyk, Krzysztof Snojek, Janusz Gumprecht, Agnieszka Siedlecka, Tomasz Kukulski, Oskar Kowalski, Beata Sredniawa, Lech Polonski, Zbigniew Kalarus, 1st Department of Cardiology, Medical University of Silesia, Silesian Center for Heart Diseases, Zabrze, Poland, bDepartment of Internal Diseases, Diabetology and Nephrology, Medical University of Silesia, Zabrze, Poland

Background: The prevalence of diabetes mellitus (DM) and chronic kidney disease (CKD) is rapidly increasing. The aim of the study was to evaluate the impact of DM with or without CKD on prognosis in pts with acute myocardial infarction (AMI) treated invasively.

Methods: Single-centre prospective study encompassed 3334 AMI-pts, who were divided into two groups: 999 pts with DM diagnosed prior to or during index hospitalization and 2335 non-diabetics.

Conclusions: The prognosis in diabetics with AMI is significantly related to renal function. Diabetics without CKD had similar prognosis to non-diabetics. Multivariate models showed that unlike diabetes without renal dysfunction, DM-CKD was an independent risk factor for cardiovascular complications and total mortality.

Therapeutic Consideration In the Patient Undergoing CABG

Antonio Miceli, Faiza Zahir, Carlo Fino, Pradeep Narayan, Alan J. Bryan, Gianni D. Angelini, Massimo Caputo, Bristol Heart Institute, Bristol, United Kingdom

Background: Angiotensin-converting enzyme (ACE) inhibitors have been shown to reduce mortality and prevent cardiovascular events in patients with coronary artery disease. However, their preoperative use in patients undergoing coronary artery bypass grafting (CABG) surgery is still controversial. This study evaluates the effect of preoperative ACE inhibitors therapy on early clinical outcomes after CABG surgery.

Methods: This was a retrospective, observational, cohort study of prospectively collected data on 10,233 consecutive patients undergoing isolated CABG surgery between April 1996 to September 2007. Of these, 3,052 patients receiving preoperative ACE inhibitors were matched to a control group by propensity score analysis.

Results: Overall mortality was 1%. Preoperative ACE inhibitors therapy was associated with a doubling in the risk of death (1.3% vs 0.7%, odds ratio [OR] 2.01, 95% confidence interval [CI] 1.17 - 3.45, p = 0.014). There were a significant difference between the ACE inhibitors and control group in the risk of postoperative renal dysfunction (PRD, 7.1% vs 5.4%, OR 1.34, 95% CI 1.09 - 1.65, p = 0.005), atrial fibrillation (AF, 25% vs 20%, 1.33, 95% CI 1.18 - 1.5, p = 0.001) and use of inotropic support (45.9% vs 41.1%, 1.21, 95% CI 1.09 - 1.35, p = 0.01) respectively. Neither ACE inhibitors nor control group was associated with increased risk of postoperative myocardial infarction and cerebral events.

Conclusions: Preoperative therapy with ACE inhibitors is associated with an increased risk of mortality, post operative renal dysfunction and use of inotropic support. Omitting ACE inhibitors before surgery and restarting postoperatively might be a reasonable approach to improve early outcomes and retain the benefits of their cardioprotective effects after CABG surgery.
Aspirin-Insensitive Platelet Hyper-reactivity and Thromboxane Generation Are Independent Risk Factors for Early Vein Graft Occlusion After Coronary Artery Bypass Surgery

Jeffrey J. Rade, Tyler J. Gluckman, Rhodanly C. McLean, Jason B. Thompson, John G. Flower, Odda M. Hjelmesaeth, Katherine Laws, Jodi B. Segal, John V. Conte, Kathleen W. McNicholas, Todd C. Villines, Edward P. Shapiro, Steven P. Schulman, Thomas S. Kocker, Johns Hopkins School of Medicine, Baltimore, MD

Background: Aspirin (ASA) is routinely given to patients after coronary artery bypass (CABG) surgery to prevent early vein graft (VG) thrombosis. Little is known about the effect of ASA resistance or residual platelet reactivity on VG patency.

Methods: We prospectively studied 368 patients undergoing first-time CABG maintained on chronic ASA therapy. VG patency was assessed 6 months after surgery in 297 patients by multivariate analysis, a PFA-100 C/ADP CT >88 sec and UTXB2 level >321 pg/mg creatinine were associated with odds ratios for VG occlusion of 3.1 (p =0.002) and 1.9 (p =0.047), respectively. VGs in 74 (28.6%) patients at highest risk, defined by low PFA-100 C/ADP CT and high UTXB2 level, had 6.5 times the odds of occlusion (p =0.003) compared to VGs in 67 (28.1%) patients at lowest risk, defined by a high PFA-100 C/ADP CT and low UTXB2 level.

Conclusion: Despite suppression of platelet COX-1 activity by ASA, global platelet hyper-reactivity and persistent thromboxane generation are independent risk factors for early VG occlusion.

New Onset Postcoronary Artery Bypass Graft Atrial Fibrillation and Long-Term Survival

Giovanni Filardo, Cody Hamilton, Robert F. Hebejer, Jr., Baron Hamman, Paul Grayburn, Institute for Health Care Research and Improvement, Baylor Research Institute, Dallas, TX, Department of Statistical Science, Southern Methodist University, Dallas, TX

Background: The advancing age and generally increasing risk profile of patients receiving isolated coronary artery bypass graft surgery (CABG) is expected to raise incidence of new-onset post-operative atrial fibrillation (AFIB) resulting in potentially higher risk of adverse outcomes. In the early postoperative course, new-onset post-CABG AFIB is considered relatively easy to treat and is believed to have little impact on patients’ long-term outcome. However, little has been done to determine the effect of new-onset post-CABG AFIB on long-term survival, and this relationship is unclear.

Methods and Results: Survival was assessed in a cohort of 6,899 consecutive patients without preoperative AFIB who underwent isolated CABG at Baylor University Medical Center, Dallas, TX between 1/1/1997-12/31/2006—patients who died during CABG were excluded. Ten-year unadjusted survival was 52.3% [48.4%, 56.0%] for patients with new-onset post-operative AFIB and 69.4% [67.3%, 71.4%] for patients without it. A propensity-adjusted model controlling for risk factors identified by the Society of Thoracic Surgeons (STS) model coefficients were used to compare outcomes (death and composite of death, myocardial infarction, congestive heart failure and shock) associated with early (<48 h) vs. delayed (>48 h) CABG. Results: In-hospital CABG rates for NSTEMI and STEMI were 12.9% and 6.7% vs. delayed (>48 h) CABG.

Conclusions: Because prior studies identified increased risk with early CABG after acute coronary syndrome, guidelines recommend delaying CABG in stable patients. It is unknown whether delay remains appropriate in the modern era of accelerated treatment and discharge pathways.

Methods: Patients enrolled in the NCDR ACTION Registry — GWTG (1/2007 - 6/2008) who underwent in-hospital CABG after NSTEMI and STEMI without transfer were included. Logistic generalized estimating equations adjusting for differences in clinical characteristics were used to compare outcomes (death and composite of death, myocardial infarction, congestive heart failure and shock) associated with early (<48 h) vs. delayed (>48 h) CABG.

Results: In-hospital CABG rates for NSTEMI and STEMI were 12.9% and 6.7% respectively. Clinical characteristics by CABG timing are shown below. After multivariable adjustment, early CABG was associated with higher death (OR 2.53, 95% CI 1.33 - 4.82) and composite events (OR 3.11, 95% CI 1.61 - 6.00) compared with delayed CABG in STEMI patients. In contrast, outcomes did not significantly differ for early vs. delayed CABG in NSTEMI patients (death: OR 1.38, 95% CI 0.88 - 2.19; composite: OR 1.10, 95% CI 0.76 - 1.59).

Conclusions: While delayed CABG was associated with lower risk of adverse outcomes after STEMI, no difference was seen for NSTEMI. Further studies are needed to support this recommendation in NSTEMI patients as delaying surgery may increase resource utilization without improving outcomes.
Clinical Characteristics for NSTEMI and STEMI pts treated with early vs delayed CABG

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<td>p-value</td>
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<td>Age (yrs)*</td>
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<td>(55.0,72.0)</td>
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<tr>
<td>Diabetes (%)</td>
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<td>&lt;0.0001</td>
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<td>Prior MI (%)</td>
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<td>(21.8)</td>
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<td>0.01</td>
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<tr>
<td>Prior Revascularization (%)</td>
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<td>(21.2)</td>
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<td>0.01</td>
<td>0.30</td>
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<tr>
<td>Prior CHF (%)</td>
<td>3.9</td>
<td>1.0</td>
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<tr>
<td></td>
<td>(9.8)</td>
<td>(7.1)</td>
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<tr>
<td></td>
<td>&lt;0.0001</td>
<td>1.2</td>
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<td></td>
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<td>(0.8,3.0)</td>
</tr>
<tr>
<td>Prior Stroke (%)</td>
<td>5.6</td>
<td>4.1</td>
</tr>
<tr>
<td></td>
<td>(8.7)</td>
<td>(6.9)</td>
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<tr>
<td></td>
<td>0.04</td>
<td>0.26</td>
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<tr>
<td>Access to catheterization (hrs)*</td>
<td>8.4</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>(2.9,17.5)</td>
<td>(7.1,4.0)</td>
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<td></td>
<td>0.0001</td>
<td>1.2</td>
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<tr>
<td></td>
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<td>(0.8,3.0)</td>
</tr>
<tr>
<td>Clopidogrel within 24 hours of arrival (%)</td>
<td>27.9</td>
<td>39.5</td>
</tr>
<tr>
<td></td>
<td>(38.1)</td>
<td>(61.2)</td>
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<td>0.002</td>
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* Median (25th, 75th percentiles)

ACC.Poster Contributions

1041 Unstable Ischemic Syndrome/Long-Term Outcome; Stable Ischemic Syndrome

Monday, March 30, 2009, 1:30 p.m.-4:30 p.m.
Orange County Convention Center, West Hall D

1041-125 Oral Proton Pump Inhibitors and Their Impact on the Effectiveness of Dual Anti-platelet Therapy During the First Year After Elective Coronary Stenting

Georgios Z. Tsiapouris, Michael N. Zairis, Nikolaos Patsourakos, Stamatis Makrygiannis, Konstantinos Vogiatzis, Evirodiki Gougourela, Stelisios Karvounaris, Konstantinos Ritsatos, Konstantinos Fakolias, Stefanos G. Foussas, Tzanoi State Hospital, Piraeus, Greece

Background: Pts receiving dual anti-platelet therapy (clopidogrel and aspirin) after coronary stenting are commonly treated with oral proton pump inhibitors (PPIs) to protect against gastrointestinal bleeding. Due to the fact that clopidogrel is converted to its active metabolite by P450 isoenzymes, which are also involved in the metabolism of PPIs, there is a concern about whether the action of clopidogrel would be reduced in pts also taking PPIs. The 3C (Combined Clopidogrel and aspirin resistance in Coronary stenting) study afforded us the opportunity to examine the effect of the treatment with PPIs on the long-term prognosis in pts also treated with clopidogrel and aspirin following coronary stenting.

Methods: The 3C (Combined Clopidogrel and aspirin resistance in Coronary stenting) study was a prospective study which evaluated the impact of the resistance to the combined therapy with clopidogrel and aspirin on the 1 year incidence of death and myocardial infarction in a total of 612 consecutive pts who underwent elective coronary stenting for stable or unstable coronary artery disease. Information concerning to the drug therapy and the occurrence of the endpoints were collected during the follow-up.

Results: The present results have shown that PPIs drug therapy does not have any impact on the effectiveness of anti-platelet drug therapy during the first year following coronary stenting.

Conclusions: The combined therapy with clopidogrel (unrelated to the administered PPIs) is effective in reducing the mortality, non-fatal MI, CABG and stent thrombosis during the first year after PCI.

1041-126 Correlation of Inhibition of Platelet Aggregation After Clopidogrel With Post Discharge Bleeding Events: Assessment by Different Bleeding Classifications

Victor Serberbruny, Sunil Rao, Matthew Silva, Jennifer Donovan, Abir Kannan, Leonid Makarov, Dan Atar, Johns Hopkins University, Baltimore, MD

Background: Bleeding is a risk of dual antiplatelet therapy. There is an association between bleeding and cardiovascular mortality. However, the potential link of bleeding risk and inhibition of platelet aggregation (IPA) is not established.

Methods: We conducted secondary post-hoc analyses of 54m ADP-induced IPA and bleeding complications assessed by TIMI, GUSTO, and BleedScore™ scales in a dataset consisting of patients with documented CAD (n=246) and previous ischemic stroke (IS)

1041-127 Influence of Gender on Long-Term Mortality in Patients Presenting With Non-ST Elevation Acute Coronary Syndromes

Bahram J. Kumbhari, Mehdi H. Shishheborh, Anthony A. Bavy, Stephen G. Ellis, Venu Menon, Cleveland Clinic, Cleveland, OH, University of Florida, Gainesville, FL

Background: While an invasive strategy has been shown to benefit patients with non-ST elevation acute coronary syndromes (NSTE-ACS), its role in low-risk women is unclear. We examined gender differences in a real world registry of patients with NSTE-ACS, who underwent an invasive approach.

Methods: Consecutive patients with NSTE-ACS undergoing PCI from 2003-2007 at our center were included. Mortality was assessed from the Social Security Death Index. Multivariate Cox proportional hazards models were constructed to study the influence of gender on mortality (follow-up: 4.5 years). The interaction between age (>60, 60-75, >75 years) and gender was examined.

Results: The overall mortality rate in men (n=2,055) was similar to women (n=1,111): 11.5% vs. 13.6%, p=0.09. Women were older (67.1 vs. 64.5 years, p<0.0001), and had higher prevalence of obesity, diabetes, and anemia (all p<0.05). Gender was not significantly associated with mortality in the multivariate model, but the interaction term between age & gender was significant (p<0.009). On age-stratified analysis, mortality was higher in women >60 years than men (p=0.004) (Figure). On subgroup analysis, the differential impact of age was true for troponin (Tr) negative (p<0.005), but not Tr+ (p=0.26) women >60 years.

Conclusions: Low-risk women (Tr negative, age <60 years) with NSTE-ACS have a higher mortality with an invasive strategy than men. An adequately powered clinical trial exploring the role of an invasive strategy in women appears warranted.
pts) and low responsiveness group (240 pts) of clopidogrel. Cardiac death occurred in 7 pts (1.9%) of normal group and 14 pts (5.8%) in low group (p=0.009). Stent thrombosis occurred in 5 pts of normal group (0.7%, 4 definite and 1 probable) and 10 pts of low group (4.2%, 7 definite, 2 probable and 1 possible)(p=0.028). The associations between cardiac death and clopidogrel low-responsiveness were evaluated with multiplicative logistic regression models adjusted for age and sex. The adjusted Odds ratio for cardiac death was 3.242 (p=0.013, 95%CI: 1.281-8.205).

Conclusions: The low-responsiveness of clopidogrel measured with a point-of-care assay is an independent predictor of cardiac death and stent thrombosis in acute coronary syndrome patients undergoing PCI.

A336  ABSTRACTS - Myocardial Ischemia and Infarction

1041-129 Outcomes After Acute Coronary Syndromes in Patients With Rheumatoid Arthritis
Anbazhagan Prabhakaran, Anitha Rajamaniickam, Henri Roukouz, Anil Jain, Deepak L. Bhatt, Cleveland Clinic, Cleveland, OH
Background: Patients with Rheumatoid Arthritis (RA) have higher prevalence of cardiovascular disease compared to the general population. We assessed survival and cardiovascular outcomes in patients with RA after a Myocardial Infarction (MI).

Methods: Data was collected retrospectively in patients with RA who were admitted with MI between 11/99-5/06. Age and sex matched controls (CO) without RA, admitted with MI was randomly selected in a 2:1 ratio. Event free survival was analyzed using Kaplan-Meier method and proportional hazards model.

Results: 86 patients with RA (38.5% males, 70±12±2 yrs, 74% were on anti-rheumatic drugs), and 172 control subjects (38.4% male, age 72±12±5 yrs) were included. Patients with RA were less likely to be revascularized, compared with controls (38pts, 44.7% vs 103pts, 59.9%, p=0.02). All cause mortality was significantly higher in the RA group (figure, p<0.001). RA was an independent risk factor for all cause mortality (HR=1.66, CI: 1.13-2.45, p=0.01) and peripheral arterial disease related re-hospitalizations (HR=2.23, CI: 1.02-6.08, p=0.038). RA was not associated with significant cardiac related re-hospitalizations.

Conclusions: All-cause mortality is increased in patients with RA compared to patients without RA. Further studies are needed to evaluate the effect of anti-rheumatic drugs in patients with RA sustaining a MI and whether aggressive revascularization would improve survival.

1041-130 Combining Renal Function and Glucose Metabolism Data: A More Efficient Way to Assess Outcomes in Acute Coronary Syndromes Patients
Silvia Monteiro, Natalia Antonio, Carolina Lourenço, Rogerio Teixeira, Elaisbete Jorge, Rui Baptista, Fatima Saraiva, Francisco Goncalves, Pedro Monteiro, Mario Freitas, Luis A. Providência. Cardiology Department, Coimbra University Hospital and Medical School, Coimbra, Portugal

Background: Renal impairment and hyperglycaemia in acute coronary syndromes (ACS) are recognized predictors of in-hospital and post-discharge morbidity and mortality. However, the combined value of both parameters has not been assessed.

Aim: To evaluate, in an ACS population, the predictive combined value of creatinine clearance (CC) and admission glycaemia (GLY).

Population and methods: Retrospective analysis of 1023 consecutive patients admitted for ACS and followed for one year. Patients were divided in 4 groups according to their CC and GLY: A - CC<60 mL/min and GLY>=180 mg/dL (n=471); B - CC<60 mL/min and GLY<180 mg/dL (n=316); C - CC>=60 mL/min and GLY<180 mg/dL (n=112); D - CC>=60 mL/min and GLY>=180 mg/dL (n=124).

Results: After univariate analysis, in-hospital mortality (1.7% vs 6.4% vs 4.2% vs 17.5%; p<0.001) and mortality (1.3% vs 2.7% vs 4.1% vs 16.9%; p<0.001) were incremental and significantly different in the 4 groups, as was death at one year follow-up (3.4% vs 13.0% vs 14.0% vs 12.9%; p<0.001).

We then identified, by multivariate analysis, independent predictors of mortality and morbidity: regarding in-hospital events, the combination of low CC and high GLY was a strong independent predictor, as were age, elevated Troponin I and low body mass index, while events in the follow-up were best predicted by the combination of CC and GLY, high troponin I and kIpi class, previous hypertension and low ejection fraction.

Conclusion: In this ACS population, the combination of admission GLY and CC is a powerful tool to predict in-hospital and post-discharge outcomes, with incremental predictive power regarding each isolated component. This fact, never before described, underlies the importance of early assessment of renal function and metabolic abnormalities, in order to provide optimal management and risk stratification to ACS patients.

3:30 p.m.

1041-131 Impact of Microvascular Dysfunction on Long-Term Cardiovascular Outcomes After Primary Coronary Intervention for Acute Myocardial Infarction
Koichi Tamaki, Atsushi Yamamura, Shuichiro Kaji, Minako Katayama, Takeshi Kitai, Takakumi Yamanaka, Makoto Kinoshita, Natsuhiko Ebara, Yutaka Furukawa, Takashi Akasaka, Kobe General Hospital, Kobe, Japan, Wakayama Medical College, Wakayama, Japan

Background: It has been reported that even if TIMI 3 flow is achieved after primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI), microvascular dysfunction (MVD) results in insufficient reperfusion. Recent studies have shown that MVD can be assessed from coronary flow velocity (CFV) pattern. The aim of this prospective study was to examine whether the CFV pattern predicts the long-term cardiovascular outcomes after primary PCI in patients with AMI.

Methods: The study population consisted of 194 consecutive patients with a first anterior AMI successfully treated with primary PCI. We examined the CFV pattern immediately after PCI using a Doppler guidewire. According to our previous reports, we defined MVD as a diastolic deceleration time <600 ms and the presence of systolic flow reversal. Patients were divided into 3 groups: those who achieved TIMI 3 flow reperfusion without MVD (n=126; group 1), those who achieved TIMI 3 with MVD (n=35; group 2), and those with TIMI 2 flow (n=33; group 3). We then evaluated the association between the MVD and long-term major adverse cardiovascular event (MACE) rates.

Results: The age-adjusted data by multivariate analysis showed that the MVD was the strongest predictor for long-term MACE (hazard ratio: 4.02; 95% CI, 2.16-7.48; p=0.001).

Conclusion: The CFV pattern immediately after PCI is an accurate predictor of the long-term cardiovascular outcomes after primary PCI in patients with anterior AMI.

3:30 p.m.

1041-132 Impact of Two-Vessel Disease, Two-Vessel Disease and a Chronic Total Occlusion in a Non-infarct Related Artery on Long-Term Mortality After STEMI
Birger E. Claassen, Rene J. van der Schaar, Karel T. Koch, Marije M. Vis, Jan G. Tijssen, Robbert J. de Winter, Jan J. Piek, Jose P. Henriques, Academic Medical Center, Amsterdam, The Netherlands

Background: Patients with multivessel disease (MVD) constitute a patient group with a high risk of mortality after STEMI. Recently, it was reported that the higher mortality in patients with MVD is determined by the presence of a chronic total occlusion (CTO) in a non-infarct-related artery. However, previous studies did not distinguish between 2-vessel and 3-vessel disease. Therefore we study the effect of 2-vessel disease without CTO, 3-vessel disease without CTO and CTO based on the angiogram before PCI. Information on vital status was obtained from the Dutch national population registry per January 2007. Cox regression was used for multivariate analysis.

Results: STEMI was present in 2115 patients (66%), 2-vessel disease without CTO in 534 patients (16%), 3-vessel disease without CTO in 208 patients (6.3%) and a concurrent CTO in 420 patients (13%). Median duration of follow-up was 2.7 years (IQR 1.3-4.6 years). A total of 493 patients (15%) died; 227 (11%) in the MVD group, 70 (13%) in the 2-vessel disease group, 54 (26%) in the 3-vessel disease group and 142 (34%) in the CTO group (p=0.01). After correction for differences in baseline variables (age>60 years, residual LVEF<40%, diabetes, hypercholesterolemia, smoking, previous MI and shock) the presence of 2-vessel disease is not an independent predictor for mortality (HR 1.1, 95% CI 0.9-1.5, p=0.34), the presence of 3-vessel disease is an independent predictor for mortality with a HR of 2.2 (95% CI 1.6-3.0), and the presence of a CTO was an independent predictor with a HR of 3.2 (95%CI 2.5-4.0).

Conclusion: In STEMI patients without CTO, only patients with 3-vessel disease and not patients with 2-vessel disease have a significantly higher risk for mortality. Even after correction for the number of diseased vessels, a CTO in a non-infarct-related artery represents the patient category with the worst prognosis after STEMI.
A Novel Risk Score System for the Assessment of Clinical Outcomes in Patients With Acute Non-ST-Segment Elevation Acute Coronary Syndrome

Hyon Kuk Kim, Myung Ho Jeong, Young Keun Ahn, Shung Chull Chae, Jong Hyun Kim, Seung Ho Hur, Jeong Gwan Cho, Korea Acute Myocardial Infarction Registry (KAMIR) Study Group of Korean Circulation Society, Gwangju, South Korea

Background: Prognostic variables of Thrombolysis In Myocardial Infarction (TIMI) risk score have some limitations predicting short- and long-term clinical outcomes in patients with non-ST elevation acute coronary syndrome (NSTE-ACS). Utilizing a multivariable Cox regression analysis, multiple risk factors and angina symptom were associated with low predictability of death and myocardial infarction during one-year clinical follow-up in our database. The aim of this study was to develop a novel and simple assessment tool for the better risk stratification using objective parameters such as heart rate, systolic blood pressure and Killip class.

Methods: Between May 2005 and August 2007, 5,409 patients with NSTE-ACS (66.6% 12.4 years, 64.9% males) were enrolled in a nationwide prospective Korea Acute Myocardial Infarction Registry (KAMIR). New risk score was calculated by the removal of variables with low predictability such as multiple risk factors, angina and not-adjusted age and the substitution of TIMI risk index (heart rate x (age/10)²/systolic blood pressure, < 30 : 0 point, 30 - 60 : 1 point, < 60: 2 points) and Killip class= 1 point) for these variables. Our new risk score system was compared with the Global Registry of Acute Coronary Events (GRACE) and TIMI risk score for mortality during 6-month clinical follow-up.

Results: The accuracy for in-hospital mortality by TIMI, GRACE and new risk score system was 0.636 area under the curve (AUC) (CI : 0.599 - 0.674), 0.744 (CI : 0.717-0.770) and 0.767 (CI : 0.735 - 0.800) respectively. A significant difference is existed between TIMI and new risk score system (0.636 vs. 0.767, p < 0.0001).

Conclusion: The new risk score system for NSTE-ACS patients is a simple, objective, better risk scoring system than GRACE and TIMI risk score systems in the prediction of in-hospital and six-month mortality.
Conclusions: In patients presenting with ACS, a J-curve association exists between blood pressure (especially diastolic) and the risk of future cardiovascular events, suggesting that excessive lowering of blood pressure in this cohort may be dangerous and a target of 80-90 mmHg is optimal.

1041-137

Impact of Statin on the Regression of Coronary Atherosclerotic Plaque in Patients With Acute Coronary Syndrome (JAPAN-ACS) Study

Yukio Onishi, Shin C. Kan, Hiroaki Naruse, Masanori Okumura, Katsuki Hattori, Makoto Ikawa, Tomoko Kawai, Hiroto Hayagaya, Shigeno Matsui, Sadako Motoyama, Masayoshi Sano, Junichi Ishii, Hitoshi Hishida, Masanori Matsuzaki, JAPAN-ACS Study Group, Fujita Health University Hospital, Toyoake, Japan, Yamaguchi University Graduate School of Medicine, Ube, Japan

Background: Although cardiovascular disease is a major cause of death in women, it has not yet been well established whether the degree of atherosclerotic plaque regression derived from statin is similar between women and men.

Methods: We performed a prospective multicenter randomized study to assess plaque regression by serial IVUS examinations in 307 patients with ACS in 33 centers in Japan (JAPAN-ACS). All patients received either a new statin (atorvastatin; 40mg/day) or pitavastatin (20mg/day) for 8 to 12 months starting within 72 hours following IVUS-guided stenting for a culprit lesion in ACS. Non-culprit lesions located at +5mm distal or proximal to the stent were assessed by serial IVUS examinations in 252 patients from 8 to 12 months apart. While percent plaque volume (%PV) changes (i.e. PV follow-up minus PV post divided by PV post) were compared between atorvastatin and pitavastatin groups, no significant difference was observed between atorvastatin (-1.6±14.2%) and pitavastatin (16.9±13.9%, p=ns). Therefore, we compared the degree of %PV changes between 206 men and 46 women together with atorvastatin and pitavastatin groups.

Results: Coronary risk factors such as diabetes and hypertension were similar between men and women (p>0.05). Conclusions: Despite unfavorable baseline lipid profile in women as compared to men, statin conveyed greater plaque reduction in women than in men. Early intensive statin therapy would be more beneficial in women rather than in men with ACS.

1041-140

Impact of Newly Diagnosed Diabetes Mellitus as an Important Predictor of Long-Term Cardiac Events After Myocardial Infarction

Shuichi Kitada, Yoritaka Otsuka, Nobuaki Kokubu, Yoichiro Kasahara, Yu Katoaka, Mitsuru Abe, Yoichi Goto, Genjiro Kimura, Hiroshi Nonoguchi, National Cardiovascular Center, Osaka, Japan

Background: It has been reported that patients with acute myocardial infarction (AMI) but without previous known diabetes mellitus (DM) have a high prevalence of glucose abnormalities. The purpose of this study was to investigate whether newly diagnosed DM and impaired glucose tolerance (IGT) after AMI, is related to long-term cardiac events.

Methods: A total of 515 patients with first AMI were divided into 4 groups according to an oral glucose tolerance test (OGTT): 116 (23%) patients with normal glucose tolerance (NGT), 169 (33%) with IGT, 69 (13%) with newly diagnosed DM (NDM), and 161 (31%) with previous known DM (KDM). They were followed for major adverse cardiac events (MACE) defined as cardiac death, non-fatal acute coronary syndrome, heart failure, and revascularization (mean follow-up period: 2.21±3.32 years).

Conclusions: These data demonstrated that patients with newly diagnosed DM are at high risk of MACE as well as those with previous known DM. Early detection of newly diagnosed DM using OGTT may be important in the risk assessment of patients with AMI.
Persistent Elevated Levels of Plasma Myeloperoxidase as an Independent Predictor of Recurrent Cardiovascular Events in Patients With Unstable Angina Pectoris

Atsuko Furukawa, Takahiko Naruko, Yukio Abe, Ryoshi Komatsu, Akira Itoh, Kazuo Haze, Masashi Nakagawa, Chikako Kitabayashi, Nobufuku Shirai, Shoichi Ehara, Yoshihiro Ikura, Makiko Ueda, Osaka City General Hospital, Osaka, Japan, Osaka City University Graduate School of Medicine, Osaka, Japan

Background: There is increasing evidence that myeloperoxidase (MPO) contributes to cardiovascular disease. The present study was designed to investigate time-course changes in plasma MPO levels in patients with unstable angina pectoris (UAP). Furthermore, we investigated whether plasma MPO levels predict recurrent cardiovascular events.

Methods: Plasma MPO levels and serum high sensitivity C-reactive protein (hs-CRP) were measured in 144 UAP patients. Measurements were taken at the acute phase (on admission) and the chronic phase (14 days after discharge), and the findings were related to recurrent cardiovascular events. Cardiac events were defined as sudden cardiac death, fatal or non-fatal myocardial infarction, and other non-fatal events including UAP, or angioplasty, stenting, or coronary bypass grafting. Results: Serum hs-CRP levels at the chronic phase had increased significantly compared with the acute phase (acute phase, 0.49±1.52; chronic phase, 0.70±1.27 mg/dl, P<0.005). In contrast, plasma MPO levels at the chronic phase had decreased significantly compared with the acute phase (acute phase, 40.9±38.3; chronic phase, 16.3±10.5 ng/ml, P<0.0001). Over a mean follow-up period of 30.9 months, 33 patients (23%) had cardiac events. Patients were classified into 2 groups according to the median MPO value at the chronic phase (low-MPO group ≤ 16.0 and high-MPO group > 16.0 ng/ml). Kaplan-Meier survival curves showed that the high-MPO group had significantly (P=0.016 by log-rank test) worse outcomes than the low-MPO group. However, there were no significant differences in cardiovascular events among 2 groups according to the median hs-CRP value at the chronic phase (low-hs-CRP group ≤ 0.2 mg/dl and high-hs-CRP group > 0.20 mg/dl). Multivariate analysis showed that elevated plasma MPO levels at the chronic phase was the only independent factor associated with the cardiovascular events (OR, 2.58; 95% CI, 1.19 to 5.59, P=0.017). Conclusions: These findings suggest that persistence of an increased level of plasma MPO at the chronic phase is associated with the progression and destabilization of human coronary atherosclerotic lesions.

Different Contributuors to Thrombus Formation Between Sirolimus-Euting Stents and Paclitaxel-Euting Stents: Serial Angioscopic Observations

Tomoki Higo, Shinichi Hirota, Nobuyuki Ogasawara, Kazunori Kashiwase, Yasunori Ueda, Osaka Police Hospital, Osaka, Japan

Background: Late stent thrombosis after sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) implantation has emerged as a major concern. Previous angiographic and pathological studies have revealed prevalence of yellow plaques and incomplete neointimal coverage over drug-eluting stents greatly increase thrombotic risk. However, the mechanism of thrombus formation of SES and PES has not been clarified.

Methods: We examined 63 SES-implanted and 12 PES-implanted lesions. Angiographic and angiographic examinations of stent-implanted lesions were serially performed immediately (baseline) and 10.7 ± 3.8 months (follow-up) after implantation. Maximum yellow color grade (Max color grade: 0, white; 1, light yellow; 2, yellow or 3, intense yellow), neointimal coverage, use of stents and ACE inhibitors and SHIM score, only PWV (odds ratio (OR) 1.25 per 1 m/s increase, 95% confidence interval (CI) 1.03-1.52, p=0.01) and SHIM score (odds ratio (OR) 0.74 per 1 increase of SHIM score, 95% confidence interval (CI) 0.55-0.98, p = 0.03) remained independent predictors for presence of CAD. Conclusions: ED severity is associated with increased arterial stiffness and the latter is a predictor of CAD presence. Determination of arterial stiffness and severity of ED may help to identify underlying cardiovascular disease in men with ED.
different between SES and PES. In SES, newly formed atherosclerosis may contribute to thrombus formation, whereas in PES, high thrombogenic potential of stented lesions with incomplete neointimal coverage may contribute to it.

CONCLUSIONS:

(87%), make them live longer (87%), and prevent a future heart attack (87%). Also, most A majority also felt that their prescribed medications would improve their symptoms

RESULTS: Intramyocardial injection was performed without complications in all patients. Canadian Cardiovascular Society score improved from 3.0±0.6 at baseline to 2.3±0.7 at 3 months and to 2.0±0.6 at 6 months (P<0.01) in the BMC group, whereas no improvement was observed in the placebo group (2.9±0.7 vs. 2.6±0.8 vs 2.5±0.9, NS). Moreover, quality of life improved from 56±3% to 64±12% at 3 months and to 69±12% at 6 months (P<0.01) in the BMC group, compared to a smaller improvement in the placebo group (57±11% vs. 61±14% vs. 64±17%, P<0.01 compared to the BMC group).

The number of segments with stress-inducible ischemia per patient decreased from 3.1±1.5 to 2.4±1.8 (P<0.01) in the BMC group. The absolute decrease was significantly larger in the BMC group (-2.4±1.3 vs. -0.8±1.1, P<0.01 compared to the BMC group).

LV ejection fraction increased from 56±12% to 59±11% at 3 months in the BMC group

3.1±1.5 to 2.4±1.8 (P<0.01) in the placebo group. The absolute decrease was significantly

3.9±1.8 to 3.1±1.5 to 2.4±1.8 (P<0.01) in the BMC group, compared to a modest decrease from

3.9±1.8 to 1.5±1.5 (P<0.01) in the placebo group. The absolute decrease was significantly

larger in the BMC group (-2.4±1.3 vs. -0.8±1.1, P<0.01).

LV ejection fraction increased from 56±12% to 59±11% at 3 months in the BMC group (P<0.01), whereas no improvement was observed in the placebo group (from 54±10% to 53±10%, NS).

Conclusion: In no-option patients with angioplasty, intramyocardial BMC injection has a beneficial effect on anginal symptoms, myocardial perfusion and left ventricular function.

Multivariate Analysis of predictors for Extra-coronary Artery Disease

variable OR 95%CI P value

Hemodialysis

3.12 1.59 - 6.15 0.0010

Prior CABG

2.27 1.18 - 4.38 0.0142

Age > 70

2.10 1.50 - 2.93 <0.0001

HDL < 40 mg/dl

1.72 1.15 - 2.58 0.0086

Prior Stroke

2.00 1.25 - 3.20 0.0038

3:30 p.m.

1041-145

Patient Perceptions Regarding Benefits of Elective
Coronary Revascularization for Stable Coronary Artery Disease in the Current Era

Agurva Motiava, Jeanine Mckeever, Anna Kezerashvili, Paolo Gabriel, Jackie Harold, Mark Menegus, Mark Greenberg, Robert Ostfeld, Montefiore Medical Center, Bronx, NY

BACKGROUND: Recent evidence from the COURAGE trial has shown that elective PCI, while relieving angina, does not improve survival or reduce the incidence of a future myocardial infarction (MI) or optimal medical management in stable coronary artery disease. We sought to survey patients presenting to our catherization laboratory for elective PCI, to examine if they were adequately informed about its risks and benefits in addition to those of optimal medications, prior to their referral.

METHODS: Patients referred for a diagnostic catheterization to our laboratory since 03/10/08 were screened for eligibility. Patients with prior bypass surgery, PCI or acute coronary syndrome were excluded. Qualifying patients were asked to fill out a voluntary survey that included their demographics, medications and 12 questions, either in person or by telephone.

RESULTS: 60 eligible patients responded. The majority were males (55%) with a mean age of 67.8±9 years, 90% had an education level of high school or higher. Most felt under-informed about the possible risks of angioplasty (52%) or their medications (50%) by their referring physicians. A majority felt that an angioplasty would improve their symptoms (90%), would make them live longer (85%) and would prevent a future heart attack (88%). A majority also felt that their prescribed medications would improve their symptoms (87%), would make them live longer (87%), and prevent a future heart attack (87%). Also, most realized that consuming a healthy diet and regular exercise would help them live longer (97%) and prevent a future heart attack (90%).

CONCLUSIONS: Patients with stable coronary artery disease referred to our catherization laboratory for possible PCI remain erroneously over-optimistic about the additional benefits of this procedure in the current era. They feel under-informed about the risks of PCI and their medications by their referring physicians. These findings are similar to those published a decade ago, and highlight the importance of improved communication on risks, benefits, alternatives and findings of current literature to patients prior to referring them for an elective PCI.

1041-146

Heterogeneity of Neointimal Coverage Can Explain Larger Late Loss and Higher Risk of Late Stent Thrombosis of Paclitaxel-Eluting Stents Than Sirolimus-Eluting Stents: Angioscopic Observations

Tomoaki Higo, Shinichi Hirotani, Nobuyuki Ogasawara, Kazunori Kashiwase, Yasunori Ueda, Osaka Police Hospital, Osaka, Japan

Background: Several studies have shown that paclitaxel-eluting stents(PES) have larger late loss and higher risk of late stent thrombosis (LST) than sirolimus-eluting stents (SES). However, the reason for these clinical results has not been elucidated.

Previous pathologic studies have revealed that lack of neointimal strut coverage and

3:30 p.m.
The Prognostic Utility of Lipoprotein-Associated Phospholipase A Activity Versus Mass in Patients With Stable Coronary Artery Disease

Michelle O'Donnoghue, David A. Morrow, Sarah Sloan, Marc S. Sabatine, Brigham and Women's Hospital, Boston, MA

Background: Lipoprotein-associated phospholipase A (LP-PLA) is believed to contribute to atherogenesis. The relative prognostic utility of LP-PLA measured as enzyme activity versus mass remains undefined.

Methods: LP-PLA activity and mass (diaDexus) were measured at baseline in 3743 subjects in PEACE, a randomized trial oftrandolapril vs placebo in stable CAD. The primary endpoint (EP) was CV death, MI or coronary revascularization (median 4.8 year follow-up). Multivariable Cox regression was used to adjust for demographics, risk factors, and medications.

Results: Modeled separately, the adjusted risk for the primary endpoint per 1-SD increase was 1.23 (95% CI 1.16-1.31, P<0.001) for LP-PLA activity versus 1.12 (95% CI 1.04-1.19, P<0.002) for LP-PLA mass. Analyses by quartile are shown in Figure (left). In ROC analyses, LP-PLA activity (P=0.035), but not mass (P=0.16), significantly improved the C-statistic over traditional predictors. LP-PLA activity and mass were moderately strongly correlated (r=0.59, P<0.001). In a model that included both markers, activity (P<0.001) but not mass (P=0.70) remained significantly associated with outcomes. In quartile analyses, elevated LP-PLA activity was predictive of risk regardless of mass (Fig, right).

Conclusion: LP-PLA activity and mass each independently predict outcomes in patients with stable CAD. The two markers are moderately correlated, and LP-PLA activity appears to be the stronger independent predictor of outcomes.
Defective Recovery of QT Dispersion Predicts Late Cardiac Mortality After Percutaneous Coronary Interventions

Marco Zimario, Alessandro Corazza, Alfonso Tatsciione, Marcello Caputo, Nicola Maddestra, Cesare Di Iorio, Raaffaele De Caterina, Institute of Cardiology and Center of Excellence on Aging - University G. d’Annunzio, Chieti, Italy

**Background:** The inter-lead difference in QT interval, known as QT dispersion (QTD), has been suggested to provide a measure of repolarization inhomogeneity. The relationship between QTD and cardiac outcomes is controversial. We aimed at assessing the association between rapidly occurring changes in corrected QT (cQTD) following percutaneous coronary interventions (PCI) and long-term survival.

**Methods:** The 12-lead ECG was analyzed before, as well as 6 h and 18 h after PCI in 612 patients (median age 63 years, range 29-87). The variation in corrected QT dispersion (ΔcQTD) was calculated as the difference between baseline and 6 h after PCI measurements.

**Results:** PCI reduced cQTD in 343 patients (56%). QTd and cQTD were significantly reduced from baseline to 6 h after PCI (P<0.001 for all), while no significant change occurred between the 6- and 18-h assessments. Over 49±10 months, a total of 46 deaths (7.5%) occurred, 21 for non-cardiac and 25 for cardiac causes; all cardiac deaths were classified as arrhythmic. Patients in the lowest tertile of ΔcQTD (-i.e., those who increased cQTD after PCI - had a similar overall and event-free survival, but a higher cardiac mortality compared with other tertiles (log-rank P=0.01). In Cox regression analysis, a reduced ΔcQTD was an independent predictor of long-term cardiac mortality (HR=1.497; 95% Confidence Interval 1.081-2.075; P=0.015 for each 20 ms decrease), together with the number of treated lesions (P=0.008), diabetes (P=0.028), peak CK-MB (P=0.029), age (P=0.034) and the presence of 3-vessel disease (P=0.037). The area under the ROC curve for cardiac mortality was 0.712 for ΔcQTD and 0.645 for peak CK-MB. The 82 patients (13%) who were in the first tertile of ΔcQTD and experienced a post-procedural increase of CK-MB above normal limit had a 4-year cardiac mortality rate of 14.6%, significantly higher than the remaining population (2.9%, P<0.001).

**Conclusions:** QTD decreases after PCI. A defective recovery of cQTD suggests the persistence of myocardial areas with repolarization inhomogeneities and is related to long-term cardiac mortality, likely due to a relationship with sudden death.

**3:30 p.m.**

Neopterin Predicts Left Ventricular Function in Patients With Chronic Stable Angina Pectoris

Rodrigo Estevz-Loureiro, Alejandro Recio-Mayoral, Juan A. Siera-Rodriguez-Morel, Ernesto Trallero-Araguas, Juan Carlos Kaski, St. George’s Hospital, London, United Kingdom

**Background:** Left ventricular ejection fraction (LVEF) is the strongest predictor of survival in patients with CSA. Inflammation plays a pathogenic role in atherosclerosis, and an enhanced inflammatory status is known to impair patient outcome. A link exists between inflammation and LV dysfunction. Neopterin, a marker of inflammation and macrophage activation, is a predictor of risk in patients with CSA. We investigated whether increased neopterin levels correlate with the presence of left ventricular dysfunction in patients with chronic stable angina pectoris (CSA).

**Methods:** We prospectively assessed 181 CSA patients (symptoms stable for >3 months; age 69±9 years; 76% male) undergoing diagnostic coronary angiography. High sensitivity CRP and neopterin serum concentrations were measured immediately before angiography. LVEF was assessed angiographically and LV dysfunction defined as LVEF <45%.

**Results:** A significant negative correlation was found between neopterin levels but not CRP and LVEF (r=-0.222; p=0.003 and r=-0.097; p=0.194, respectively). After adjustment for relevant confounders, including extent and severity of coronary disease, neopterin was independently associated with LVEF (Beta=-2.36, CI 95% -4.56 to -0.17, p=0.034). Moreover, high neopterin levels were an independent predictor of LV dysfunction (OR 8.52, CI 95% 1.10-65.64; p=0.040). Receiver operating characteristic analysis for neopterin showed an area under the curve of 0.73 (CI 95% 0.59 - 0.87, p<0.009) for prediction of LV dysfunction.

**Conclusions:** Serum neopterin concentrations correlate with LVEF and high neopterin levels are a predictor of LV dysfunction in patients with CSA, irrespective of the extent and severity of coronary artery disease. Neopterin may thus be clinically useful for patient risk stratification.

**3:30 p.m.**

Intravenous Administration of Subtendorse Platelet Dose of Short-Acting Beta-Blocker Landiolol Before Percutaneous Coronary Intervention May Reduce the Incidence of Myocardial Infarction in Stable Angina

Hideaki Morita, Tatsuji Kono, Shuji Suzuki, Shogo Murakami, Tatsuya Umeda, Akiko Soyama, Yasushi Kitaura, Osaka Medical College, Takatsuki, Japan

**Background:** Myocardial infarction (MI) after percutaneous coronary intervention (PCI) defined as an increase in cardiac biomarkers is associated with higher incidence of late adverse clinical outcomes. We hypothesized that intravenous administration

of subtendorse dose of short-acting beta-blocker Landiolol before coronary artery occlusion may reduce the incidence of post-PCI MI.

**Methods:** Patients with stable angina undergoing PCI (n=26) were randomized in a prospective double-blind fashion to Landiolol at a dose of 3μg/kg/min (n=10) or placebo (n=13). Drug administration was started one hour before PCI and was continued for 24 hours. Evidence of post-PCI MI was defined as an increase in Troponin T >2 times the upper limit of normal within 24 hours of PCI.

**Results:** Intravenous administration of subtendorse dose of Landiolol decreased incidence of post-PCI MI compared with placebo (7.7% vs. 46.1%, p=0.037) without affecting the hemodynamic determinants of myocardial work including heart rate and systemic blood pressure.

**Conclusions:** Intravenous administration of subtendorse dose of short-acting beta-blocker Landiolol before coronary artery occlusion may reduce the incidence of post-PCI MI in stable angina.
Concomitant presence of effort angina, positive exercise stress test, and normal coronary arteries defines cardiac syndrome X. Its pathogenesis, although mostly attributed to dysfunction of coronary microcirculation, is still unclear. In addition, it is not known which clinical data might help identifying patients at higher risk of cardiovascular events. This condition is rare, and most information comes from single-center studies, recruiting a small number of patients. The Italian Registry of Syndrome X (RISIX) is a multicenter prospective registry collecting clinical and prognostic data of patients with syndrome X.

Methods: Inclusion criteria were (all): effort angina, positive exercise stress test, angiographically normal (>20% stenosis) coronary arteries. Follow-up was performed by ambulatory visits.

Results: 259 patients [51±11 years/old; 184 (71%) female], from 7 centers are currently in the registry. Incidence of risk factors for atherosclerosis was: hypertension 65.6%, hypercholesterolemia 58.7%, family history of coronary heart disease 25.9%, smoking 22.4%, diabetes 10%. At a median follow up of 40 months (Interquartile range 30.0-108.3), cardiovascular events were rare: 1 patient suffered acute coronary syndrome (0.4%) and 2 developed heart failure (0.8%). However, 83% of women and 46% of men (p<0.05) still complained of angina: among them, 60% have >1 annual episode/week, in 30% of cases severe enough to require at least one hospitalization. At multivariate logistic regression analysis, the only clinical findings predictive of persistence of angina were female gender (adjusted Odds Ratio 3.7; 95% C.I. 1.36-10.01; p<0.01).

Conclusion: Cardiac syndrome X is characterized by a good prognosis in terms of cardiovascular events. However, despite regular follow up visits at specialized centers, half of these patients still complain of frequent annualepisodes. Thus, while seemingly a benign condition, syndrome X is plagued by persistence of symptoms, which seriously limits quality of life of patients, and represents a major clinical and social issue.

**Bivalirudin Versus Heparin Alone in Low-Risk Percutaneous Coronary Intervention: Indirect Versus Direct Comparison**
Sanjay Kaul, Babak Azarbal, Prediman K. Shah, George A. Diamond, Cedars-Sinai Heart Institute, Los Angeles, CA, UCLA Medical Center, Los Angeles, CA

**BACKGROUND:** Indirect comparisons (IC) have been previously validated as effective tools for estimating relative effects of competing interventions when evidence from direct comparison (DC) is not available.

**METHODS:** Relevant studies chosen for IC included a common comparator (abciximab + Heparin) and different anticoagulants (Bivalirudin vs Heparin in PCI) and different antithrombotic treatments (abciximab + Heparin). The IC was performed according to the formula: RR_IC = (RR_DC1 x RR_DC2)/RR_DC3. The studies were comparable in terms of population, outcomes, and concomitant therapies (>85% thrombolysis or pretreatment). An interaction test was conducted to assess whether treatment outcomes differed between IC and DC.

**RESULTS (Table):** Compared with Heparin, IC yielded a nonsignificant 27% increase in TIMI major AMI compared with Heparin (0.46-0.94) (interaction P value >0.05).

**CONCLUSION:** The IC accurately predicted the observed in a direct head-to-head comparison that Bivalirudin does not provide superior efficacy or safety compared with Heparin alone during low-risk PCI.

**Bivalirudin vs Heparin Alone in Low-risk PCI**

<table>
<thead>
<tr>
<th>30-day Outcome</th>
<th>Bivalirudin vs Heparin</th>
<th>PFA</th>
<th>CRP</th>
<th>LDL-C</th>
<th>HDL-C</th>
<th>HDL-C/LDL-C</th>
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<tbody>
<tr>
<td>30-day Outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Death/ MI</td>
<td>1.21 (0.93-1.58)</td>
<td>1.05 (0.69-1.59)</td>
<td>1.32 (0.77-2.08)</td>
<td>1.16 (0.57-4.19)</td>
<td>0.75</td>
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<tr>
<td>Death/ MI</td>
<td>1.21 (0.93-1.58)</td>
<td>1.05 (0.69-1.59)</td>
<td>1.32 (0.77-2.08)</td>
<td>1.16 (0.57-4.19)</td>
<td>0.75</td>
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<tr>
<td>MI major bleeding</td>
<td>0.73 (0.41-1.32)</td>
<td>1.50 (0.62-3.68)</td>
<td>1.10 (0.38-3.17)</td>
<td>0.48 (0.32-0.98)</td>
<td>0.21</td>
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</tr>
<tr>
<td>MI major bleeding</td>
<td>0.73 (0.41-1.32)</td>
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<td>1.10 (0.38-3.17)</td>
<td>0.48 (0.32-0.98)</td>
<td>0.21</td>
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<tr>
<td>Transfusion rate</td>
<td>0.06 (0.04-0.94)</td>
<td>2.60 (1.25-5.37)</td>
<td>1.72 (0.96-4.01)</td>
<td>0.07</td>
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<tr>
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<td>1.72 (0.96-4.01)</td>
<td>0.07</td>
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**Data are shown as RR and 95% CI. Abcix: abciximab, TVR: target vessel revascularization, MI: myocardial infarction.**

**Changes of lipid parameters, CRP and PFA**

<table>
<thead>
<tr>
<th>S 80 (n=25)</th>
<th>E 10 / S 20 (n=22)</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>After 6 weeks p</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>83 (64-133)</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>47 (18-62)</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>6.0 (1.2-14.5)</td>
</tr>
<tr>
<td>PFA (s)</td>
<td>157 (147-157)</td>
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**Anticoagulation**

**Bivalirudin**

**Heparin**

**Effects of Ezetimibe Plus Moderate-Dose Simvastatin Versus Higher-Dose Simvastatin Alone on C-Reactive Protein and Platelet Function in Patients With Stable Coronary Artery Disease**
Antonio E.P. Pessaro, Carlos V. Serrano, Jr., Herlon Saravia Martins, James De Lemos, Paulo R. Parra, Juliano L. Fernandes, Renata T. Ladeira, Roberto Rocha C.V. Giraldes, José J.C. Nicolau, Heart Institute (InCor), University of Sao Paulo, Medical School, Brazil, Sao Paulo, Brazil

**Background:** It is not clear if intensive cholesterol reduction, obtained either by ezetimibe plus moderate-dose simvastatin (E/S) or by higher-dose simvastatin alone (S), have similar anti-inflammatory and anti-platelet effects. The aim of this study was to compare the effects of E 10 mg / S 20 mg vs S 80 mg on C-Reactive protein (CRP) and platelet aggregation (platelet function analyzer - PFA) of patients with stable CAD.

**Methods:** Patients (n=47, 63.5±9.03 years, 24 men), previously on S 20 mg, were randomly allocated to receive either E 10 mg / S 20 mg or S 80 mg for 6 weeks. Lipid profile, levels of CRP and PFA were measured before and after lipid-lowering.

**Results:** See table. Baseline characteristics (age, sex, diabetes, hypertension and smoking) were similar in both groups. Liver and muscle parameters were unaffected. CRP was reduced by S 80 (p=0.01), but not by E10/S20 (p=0.85), despite a similar reduction of LDL-C (28.2% vs 28.1%, respectively; p=0.68). In a comparison of CRP reduction between groups, we identified a trend towards S 80 efficiency (25.8% vs 3.5% ; p=0.09). PFA increased similarly for both strategies (6.7% vs 11.0%, respectively; p=0.20).

**Conclusions:** S 80 and E10/S20, are effective to reduce cholesterol and platelet aggregation in patients with stable CAD. However, only S 80 was able to reduce CRP effectively. Higher simvastatin doses may be necessary to provide a larger pleiotropic effect.
New Frontiers in Risk Assessment: From Genes to Proteins
Monday, March 30, 2009, 4:30 p.m.-6:00 p.m.
Orange County Convention Center, Room W307A
4:30 p.m.

**Differential Protein Biomarker Expression and Their Time-Course in Patients With a Spectrum of Stable and Unstable Coronary Syndromes in the Integrated Biomarker and Imaging Study-1 (IBIS-1)**

*Joanna J Wykrzykowska, Hector Garcia-Garcia, Andrew Zalesski, Patrick W Serruys, Thoraxcenter Erasmus MC, Rotterdam, The Netherlands, GiaxioSmithKline, Philadelphia, PA*

**Background:** Inflammation is an established component of coronary disease pathogenesis and inflammatory biomarkers have been correlated with increased risk of events. IBIS-1 was a single center pilot study to assess invasive and non-invasive methods of identifying plaques with high risk/vulnerable features and to correlate this with circulating biomarker expression. We assessed the expression of standard biomarkers at index catheterization, three and six months post-procedure. We screened for novel markers using MSI amplified protein microarray (170 analytes).

**Methods and Results:** CRP and IL6 as well as Lip/PLA2 levels were observed to decrease in patients with acute coronary syndromes over time. With the exception of CRP and IL6, the expression of classical biomarkers did not correlate with the presence of echogenic plaque on IVUS gray scale imaging or palmpography. Protein microarray testing was performed in duplicate in 66 of the 89 patients with stable angina or acute coronary syndromes (including non-ST elevation MI and ST elevation MI). 78 analytes showed expression above the lower limit of detection for at least one post-procedure time point in a subgroup of patients. This complex data set was further compressed using hierarchical clustering and principal component analysis and yielded two subsets of proteins demonstrating differences in abundance between two groups. The first subset displayed initial up-regulation and decreased over time in one patient subgroup (D-dimer, Hepatocyte Growth factor, CXC L9/ MIG, platelet factor 4/ CXC L4, CTACK, C-6 Kine, follistatin, GDF-7). The second subset increased over time (PAI-1 anti-apoptotic protein and I-309 - chemokine induced on the human endothelium by Lp(a)). Only two analytes (dHR 2.0, 1.1-3.9) showed change in expression at steady-state from 3 to 6 months.

**Conclusions:** Biomarkers identified by this exploratory analysis all appear to denote increased pro-coagulability, endothelial activation/injury or monocyte trafficking into the plaque. All these mechanisms are at the root of pathogenesis of vulnerable plaque. Further large vulnerable plaque natural history studies are needed to better define patients at risk.

4:45 p.m.

**Growth-Differentiation Factor-15 for Risk Assessment in Patients With an Ongoing Non-ST-Elevation Acute Coronary Syndrome and After Clinical Stabilization**

*Kai M. Enges, Kai C. Wollert, Bo Lagerqvist, Berit Lindahl, Lars Wallentin, Bertil Lindahl, Lars Wallentin, Tibor Kempf, University Hospital Uppsala, Uppsala, Sweden, Hannover Medical School, Hannover, Germany*

**Background:** Growth-differentiation factor-15 (GDF-15) is a stress-responsive TGF-β cytokine family member that has emerged as a prognostic biomarker in patients with a non-ST-elevation acute coronary syndrome (NSTE-ACS). The aim of the present study was to assess the time course and the prognostic relevance of GDF-15 levels in patients with an ongoing NSTE-ACS, and during a 6-month period after clinical stabilization.

**Methods:** GDF-15 was measured at randomization, after 6 weeks, 3 and 6 months in 950 NSTE-ACS patients included in the FRISC II (FRagmin and Fast Revascularization during InStability in Coronary artery disease)-study. Patients were followed for the composite endpoint of death or recurrent myocardial infarction for 5 years.

**Results:** Median GDF-15 levels decreased from 1357 ng/L at randomization to 1302 ng/L at 6 months. Patients randomized to an invasive strategy had a more pronounced decrease of GDF-15 (1316 to 1238 ng/L; p=0.001) as compared to patients randomized to a conservative strategy (1305 to 1269 ng/L; p=0.11). GDF-15 was correlated relatively during the 6-month observation period to cardiovascular high-risk features such as traditional risk factors, biomarkers of renal dysfunction (eGFR), inflammation (CRP) and hemodynamic stress (NT-proBNP). GDF-15 was an independent predictor for the composite endpoint both at randomization (adjusted HR 1.8 [1.1-2.8]; p=0.02) and 6 months (adjusted HR 2.1 [1.3-3.9]; p=0.02). Patients with persistently elevated GDF-15 levels > 1800 ng/L had a very high risk of the composite endpoint (n=47/141 [33.3%]) whereas patients with GDF-15 < 1200 ng/L at randomization had a low risk regardless of 6-month GDF-15 levels.

**Conclusions:** GDF-15 is a strong and independent risk predictor in both ongoing NSTE-ACS and at later follow-up. The changes of GDF-15 levels between both randomization arms might reflect the prognostic benefits related to an invasive strategy with early coronary revascularization. The relative stability of GDF-15 levels over time together with the results from the prognostic evaluation indicate a clinical utility of cut-offs of 1200 ng/L and 1800 ng/L both in ongoing NSTE-ACS and during later follow-up.
**Background:** Several single-nucleotide polymorphisms (SNPs) have been linked to progression of atherosclerosis, coronary plaque size and incidence of acute cardiac events. However, only few data from intravascular ultrasound (IVUS) studies on plaque size and correlation with SNPs are available.

**Methods:** In 173 out of 734 patients with established coronary artery disease from the ENCORE trials coronary plaque volume was assessed by IVUS and vessel size by quantitative coronary angiography. All 173 patients were genotyped for polymorphisms of CD14 C(-260)T, CRP C(+1444)T, and MMP3 promoter 5A/6A, using the single-nucleotide polymorphism-polymerase chain reaction (SNP-PCR) approach.

**Results:** Higher ratios of plaque volume/vessel size were observed in patients with the CRP 1444TT (n=84), MMP3 A5A5 (n=48) and CD14 260TT (n=62) genotypes (p = 0.002, p=0.016 and p=0.026, respectively). Baseline characteristics were comparable for all groups except for use of beta-blockers in the MMP group (p=0.033).

**Conclusion:** In patients with established and stable coronary artery disease the CRP 1444TT, MMP3 A5A5 and CD14 260TT variants are associated with larger coronary plaque volume independently of concomitant cardiovascular risk factors.

<table>
<thead>
<tr>
<th>CD14 (n=33)</th>
<th>CC</th>
<th>0.285 ± 0.103</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD14 (n=78)</td>
<td>CT</td>
<td>0.294 ± 0.113</td>
</tr>
<tr>
<td>CD14 (n=62)</td>
<td>TT</td>
<td>0.332 ± 0.132</td>
</tr>
<tr>
<td>CRP1444 (n=11)</td>
<td>CC</td>
<td>0.286 ± 0.123</td>
</tr>
<tr>
<td>CRP1444 (n=78)</td>
<td>CT</td>
<td>0.284 ± 0.110</td>
</tr>
<tr>
<td>CRP1444 (n=84)</td>
<td>TT</td>
<td>0.331 ± 0.122</td>
</tr>
<tr>
<td>MMP3 (n=50)</td>
<td>6A/6A</td>
<td>0.268 ± 0.126</td>
</tr>
<tr>
<td>MMP3 (n=75)</td>
<td>5A/6A</td>
<td>0.310 ± 0.108</td>
</tr>
<tr>
<td>MMP3 (n=48)</td>
<td>5A/5A</td>
<td>0.344 ± 0.114</td>
</tr>
</tbody>
</table>

**Abbreviations:** eGFR, estimated glomerular filtration rate; ACR, albumin-to-creatinine ratio; OR, odds ratio; CI, confidence interval; PWV, pulse wave velocity; CAD, coronary artery disease; ECP, extracorporeal percussion; WISE, Women's Ischemia Syndrome Evaluation; IVUS, intravascular ultrasound.
Incident Diabetes Mellitus in Patients With Stable Coronary Artery Disease
Apurva Badheka, Neha Garg, Mohammad A. Kizilbash, Samrat Bhat, Ankit Rathod, Sony Jacob, Luis Afonso, Wayne State University, Detroit, MI

Background: Predictors and significance of new onset diabetes (NOD) in patients with stable coronary artery disease (CAD) are poorly understood. Whether disparities in incidence of NOD exist among substrata of CAD patients is unclear.

Methods: The NHLBI Limited access dataset of the multicenter Prevention of Events with Angiotensin Converting Enzyme Inhibition Trial (n=8290) comparing trandolapril versus placebo in patients with CAD and preserved ejection fraction was used. Patients with documented myocardial infarction (MI) formed Group I (n=3685). Groups II and III (n=954) comprised patients post revascularization (CABS and PTCA respectively) without history of MI. Group IV (n=651) included patients with non obstructive (<50%) vessel stenosis (NOCAD) without prior MI or revascularization.

Results: Incident NOD occurred in 733 patients over mean follow-up of 4.6 yrs. Statistically significant covariates (HR, 95% CI) associated with NOD were use of beta blockers and trandolapril reduced risk while elevated BMI and angina pectoris. Incident diabetes mellitus (DM) was evaluated by local site reads and by a blinded quantitative coronary angiography (QCA) core lab.

Conclusion: Use of beta blockers and trandolapril reduced risk while elevated BMI and presence of NOCAD or PTCA conferred higher risk for developing NOD. Incident diabetes mellitus portends poor prognosis in stable CAD.
Significant Impact of Genetic Variants on Chromosomal Locus 1p13.3 on Serum LDL-Cholesterol and on Angiographically Characterized Coronary Artery Disease

Christoph H. Saety, Axel Muendlein, Simone Geller-Rhomburg, Gudrun Sonderegger, Philipp Reen, Stefan Beer, Alexander Vonbokan, Heinz Drexel, Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria, Private University in the Principality of Liechtenstein, Triesen, Liechtenstein

Background: Recently, genome-wide association studies identified a significant impact of a novel locus on chromosome 1p13.3 on serum LDL-cholesterol, which is causally linked to coronary artery disease (CAD). Potential associations between variants on this locus and angiographically characterized coronary atherosclerosis are unknown.

Methods: We performed genotyping of variants rs599839, rs646776, and rs4970834 on chromosome 1p13.3 in a large cohort of 1610 consecutive Caucasian patients undergoing coronary angiography for the evaluation of CAD.

Results: The rare alleles of variants rs599839, rs646776, and rs4970834 were significantly associated with decreased serum LDL-cholesterol (p=0.003, p<0.001, and p=0.005, respectively).

Further, carriers of the rare alleles of variants rs599839 and rs646776 were at a significantly lower risk of significant coronary stenoses <50% than subjects who were homozygous for the frequent allele, with OR of 0.78 [0.63-0.98], p=0.019 and 0.74 [0.60-0.91], p=0.004, respectively. After multivariate adjustment including LDL cholesterol, the protective effect of the rare allele of variant rs646776 on CAD risk remained significant (OR= 0.77 [0.61-0.97], p=0.026).

Conclusion: We conclude that chromosomal locus 1p13.3 is significantly associated with both serum LDL-cholesterol and angiographically characterized coronary atherosclerosis.

9:30 a.m.
Incidence of Infection in Patients With Sudden Cardiac Death Treated With Therapeutic Hypothermia Versus Conventional Care

Brian E. Gubins, Andrea C. Hall, James Constable, Punt S. Parasher, Christopher Y. Kim, Raghavendri Motun, Tayyab Mohyuddin, Saubir Sanon, Santiago Segovia, Ramal Weragoda, H. V. Anderson, Stefano Sridharoga, Richard W. Smalling, Ali E. Denktas, Memorial Hermann Heart and Vascular Institute - Texas Medical Center, Houston, TX, The University of Texas Health Science Center, Houston, TX

Background: Mortality for successfully resuscitated patients with sudden cardiac death (SCD) remains high. Our hospital utilizes therapeutic hypothermia in SCD patients in an attempt to improve survival and meaningful neurological recovery. A potential complication of therapeutic hypothermia is infection due to hyperglycemia and a decrease in white blood cell motility. We sought to establish whether the use of therapeutic hypothermia is associated with an increased incidence of infection. Methods: Patients with out-of-hospital cardiac arrest admitted to the CCU between 1/2004 and 12/2007 were reviewed, excluding transfers from outside facilities and patients with missing infection data. We evaluated the baseline characteristics, survival, and meaningful neurological recovery of patients with and without infection. The incidence of any infection, pneumonia, sepsis, and urinary tract infection (UTI) was compared in patients receiving therapeutic hypothermia versus conventional care.

Results: In 1,441 patients evaluated, the incidence of any infection was 70%, pneumonia was 49%, sepsis was 50%, and UTI was 8%. Among infected patients, 69% had pneumonia, 71% had sepsis, and 11% had UTI. Baseline characteristics were similar between patients with and without infection, except for witnessed cardiac arrest (95% versus 81%, p<0.02) and the mean minimum temperature (33°C versus 34.4°C, p<0.001), respectively. There was no difference in survival or meaningful neurological recovery between patients with and without any infection. There was a significant decrease in survival in patients with pneumonia (33% versus 57%, p=0.004). There was a significant increase in the incidence of any infection (70% versus 49%, p=0.02) and pneumonia (74% versus 54%, p=0.02) in patients treated with therapeutic hypothermia vs. conventional care.

Conclusions: In patients with SCD, use of therapeutic hypothermia was associated with an increase in the incidence of any infection and pneumonia. Pneumonia was associated with a decrease in survival. Further studies should be performed to determine whether patients treated with therapeutic hypothermia should receive empiric antibiotic therapy.

9:30 a.m.

Exertional and Nonexertional Sudden Deaths: Re-examining the Role of Hypertrophic Cardiomyopathy

Laudino M. Castillo-Rojas, David A. Appel, Jennifer A. McNear, Lena Avedissian, John E. Atwood, Lisa A. Pearse, Robert N. Potter, Allen P. Burke, Ladd Tremaine, Eric A. Shry, Philip J. Gentlesk, Stephen S. Reich, Robert E. Eckart, Department of Defense Cardiovascular Death Registry Group, Brooke Army Medical Center, San Antonio, TX, Armed Forces Institute of Pathology, Washington, DC

Background: Some types of genetic disease have a predilection towards a temporal association of sudden death with exertion. We sought to identify the activities associated with sudden death in a young cohort.

Methods: Records from the Office of the Armed Forces Medical Examiner from 1998 to 2008 were reviewed for sudden death in those less than 40 years with known activity at the time of death.

Results: There were 381 sudden deaths identified (age 30.2±6.9 years, 96.1% male). Exertional death was exertional death (124, 68.0%), non-exertional death (124, 68.0%), non-cardiac death (22, 11.6%), and cardiac death (124, 68.0%). Exertional death was the most common cause of death (41.7%, 13.5%), and non-exertional death was the second most common cause of death (35.5%, 11.6%). The most common cause of death was atherosclerosis (41.5%, 13.5%), hypotrophic LV hypertrophy without disarray (21.5%, 7.0%), and hypertrophic cardiomyopathy (21.5%, 7.0%). The activity associated with sudden death was most commonly physical fitness training (41.5%), recreational sports (41.5%), or military training (38.4%). Death during running and basketball were commonly cardiac (71.4%), while death during swimming was commonly idiopathic (50.0%). In a population age 18 to 40 years, idiopathic sudden death and atherosclerosis account for the majority of exertional sudden death (129, 35.6%) while hypertrophic CM (10, 2.7%) and non-exertional LV hypertrophy without disarray (19, 10.3%) are less common.

Conclusions: In a cohort of young adults with exertional death, idiopathic and atherosclerotic deaths are common causes, and examination of activity associated with death may be useful for therapy. Hypertrophic cardiomyopathy is much less common than previously reported in a population undergoing active surveillance and autopsy.

9:30 a.m.

Exertional Sudden Death Among Younger Adults in the Community: Results of Anatomical Metabolic and Genetic Evaluation

A. Seluk Adabag, Gary Peterson, Fred S. Apple, Jack Titus, Richard King, Russell V. Luepker, University of Minnesota, Minneapolis, MN

Background: Identifying the community-dwelling persons at risk for sudden cardiac death (SCD) is challenging. Few studies have investigated the victim with contemporary laboratory techniques and few have focused on a community-based population. We hypothesized that a comprehensive examination of out-of-hospital SCD victims in the community will reveal clues about the risk factors for SCD.

Methods: It is mandatory to report all out-of-hospital SCD to the Medical Examiner’s (ME) office in Hennepin County (population 1.2 million), Minnesota. We studied all SCD victims between the ages 25-60 years without an initially apparent cause of death and evaluated by the ME. We reviewed clinic records, conducted next-of-kin interviews and performed autopsies of laboratory studies and genetic analysis for mutations in genes associated with the long-QT syndrome. From August, 2001 to July, 2004, 114 cases were eligible. The next-of-kin consented to the study in 71.

Results: Mean age was 49.5±7 years, 86% were male and only 2 subjects had history of coronary heart disease (CHD). Coronary risk factors were highly prevalent for age (e.g. smoking 61%, hypertension 27%, hyperlipidemia 25%). On autopsy, 80% of the victims had high-grade coronary stenoses (>75% obstruction). Acute coronary lesions and previous silent myocardial infarction were found in 27% and 34% of the victims, respectively. Further, 60% had recently ingested analgesics. Possible deleterious mutations of the ion channel genes were detected in 5 (7%) of the victims. Of these, 4 were in the sodium channel gene SCN5.

Conclusions: Overwhelming majority of the younger SCD victims in the community have severe subclinical CHD, including undetected previous myocardial infarctions. Mutations in the long-QT syndrome genes were detected in a small minority. Analytic use shortly before death suggests that the victims were feeling ill. Traditional coronary risk factors were prevalent and under-treated. These findings imply that improvements in the detection and treatment of subclinical CHD in the community are needed to prevent SCD.

9:30 a.m.

The Significance of ST Elevation in Right Precordial Leads in Acute Anterior Myocardial Infarction

Alan Barshefshek, Hanech Hod, Dan Oero, Athanasios Michalidis, Ilan Goldenberg, Michael Glikson, Michael Eldar, Shlomi Mateczyk, Heart Institute, Sheba Medical Center, Tel Hashomer, Israel

Background: The clinical implications of ST-segment elevation in the right precordial leads in the circumstances of acute anterior myocardial infarction (AMI) are unknown.

Methods: We assessed the clinical utility of ST-segment elevation in leads V3R and V4R in anterior AMI.

Results: Group A included 39 patients (age mean±SD 59±11, male gender 82%) and group B included 81 patients (age 58±14, male gender 84%). Group A patients were more likely to experience early primary VF and comprised more patients who suffered from heart failure (HF) compared with group B (For VF 8/39 (20%) vs. 2/81 (2%), p=0.019, for HF 15/39 (38%) vs. 14/81 (17%), p=0.021). Patients in group A compared with group B had a trend towards less spontaneous repolarisation (14% vs. 32%, p=0.063) and had higher incidence of multivesSEL coronary artery disease [median (interquartile range) of 2 (1-3) vs. 1 (1-2), p=0.057]. There was no significant difference in the size of the infarct analyzed by peak CPK, sum of ST segment elevations or wall motion score index by echocardiography between the two groups.

Conclusions: In anterior myocardial infarction, ST-segment elevation in the right precordial leads is associated with increased risk for early primary VF and HF during hospitalization, independent of infarct size. Right precordial leads should be a routine part of the initial electrocardiogram in patients with acute myocardial infarction.

9:30 a.m.

Association of Body Mass Index on Survival After In-Hospital Cardiac Arrest

Renuka Jain, Brahmadee K. Nallamothu, Karl B. Kern, Paul S. Chan, University of Michigan, Ann Arbor, MI, Saint Luke’s Mid-America Heart Institute, Kansas City, MO

Background: Survival after in-hospital cardiac arrest may be influenced by patients’ Body Mass Index (BMI), which may affect the quality and effectiveness of resuscitation measures.

Methods: From 2006 to 2007, there were a total of 34,588 cases of cardiac arrest at 328 hospitals within the NRPCR. Of these, 22,266 patients (64.4%) had available data on height and weight and formed the study cohort. We examined the association between BMI categorized as underweight (<18.5 kg/m2), normal weight (20.5-24.9 kg/m2), overweight (25.0-29.9 kg/m2), obese (30.0-34.9), and very obese (>35.0 kg/m2), and survival to discharge using multivariable logistic regression, after stratifying by cardiac arrest rhythm type and adjusting for differences in patient and hospital characteristics.

Results: Of 4,499 patients with a pulseless arrest due to ventricular fibrillation or tachycardia, 1,825 (40.6%) patients survived to discharge. Compared with overweight patients, patients at other BMI levels had lower rates of survival (Table 1).

Conclusions: BMI is associated with differential rates of survival after in-hospital cardiac arrest. Future studies are needed to evaluate the interaction of BMI with CPR, defibrillation, and medication effectiveness.
**ABSTRACTS - Myocardial Ischemia and Infarction**

**A349**

Other hospital characteristics, including geographical location, academic status, cardiac arrest volume, and presence of automatic external defibrillator or medical emergency team programs were not associated with delayed defibrillation. Similarly, there was wide variation in hospital rates of survival to discharge (5.3% to 63.6%). Although most hospital factors were not associated with survival, hospitals in the top-performing quartile for defibrillation time had better overall rates of survival to discharge (OR of 1.41 [1.11, 1.77]; p < .001).

**Conclusions:** Rates of delayed defibrillation vary widely among hospitals but are largely unexplained by available hospital factors. Given its association with improved survival, future research is needed to better understand best practices in defibrillation speed among top-performing hospitals.

**1050-145**

**Outcomes of Therapeutic Hypothermia With Iced saline and Endovascular Cooling in Shockable and Nonshockable Rhythms**

Vinod S. Kurugollu, Niles Sood, Jeffery Kluger, Joseph Taliercio, Justin Lundby, Hartford Hospital, Hartford, CT

**Background:** Randomized studies of therapeutic hypothermia demonstrated improved outcomes in survivors of out-of-hospital cardiac arrest due to ventricular fibrillation (VF). The reported trials used surface cooling, which is slow, labor intensive and incomplete and were restricted to patients with VF only. We investigated the efficacy, safety, and outcomes of therapeutic hypothermia by infusing cold normal saline and endovascular cooling in patients (pts) with both VF and non-shockable rhythms.

**Methods:** We assessed consecutive 29 pts who were resuscitated from cardiac arrest and underwent endovascular therapeutic hypothermia at our institution. Of these, 22 pts received 2 liters of ice cold (4 °C) saline prior to endovascular cooling with Cool Gard 3000 and underwent endovascular therapeutic hypothermia at our institution. Of these, 22 pts were time to reach target temperature from initiation of hypothermia, feasibility of maintaining outcomes in survivors of out-of-hospital cardiac arrest due to ventricular fibrillation (VF).

**Results:** Out of 29 pts, 17 (58.6%) had VF and 12 (41.4%) had non-shockable rhythms.

**Conclusions:** In this study we found that the VF waveform of survivors had significantly higher frequency and amplitude characteristics, which might reflect the total duration of ventricular fibrillation. These measures can be used for future research to refine shock protocols in treatment of ventricular fibrillation.
Calcification at the Distal Anastomosis Is a Novel Predictor of Early Asymptomatic Vein Graft Failure in First-Time CABG Patients

Phrdnaghn C. McGlancy, Susanna M. Nzarazian, Tyler J. Gluckman, Edward P. Shapiro, Steven P. Schuman, John V. Conte, David R. Thiemann, Jeffrey J. Rade, Johns Hopkins School of Medicine, Baltimore, MD

Background: Saphenous vein grafts (SVGs) are the most frequently used conduits for coronary artery bypass graft (CABG) surgery. Despite advances in the surgical technique, up to 20% of SVGs continue to become occluded within the first year after CABG surgery.

Objective: The goal of the present analysis was to evaluate the demographic, clinical and anatomic findings associated with early asymptomatic SVG failure in the modern era, as measured by multidector computed tomography (MDCT) coronary angiography.

Methods: Patency was assessed in 611 SVGs in 291 patients from the prospective, multicenter Reduction in Graft Occlusion Rates (RIGOR) study. The odds of SVG patency 6 months post-operatively were analyzed using multilevel multivariate logistic regression with clustering on patient.

Results: At a mean of 6.5 months following CABG, MDCT revealed that 20.7% of SVGs were occluded. On univariate analysis, current tobacco use (OR 2.09, P = .03), female gender (OR 2.08, P = .04), and presence of calcification at the distal anastomosis (OR 2.24, P = .03) were predictive of greater odds of SVG occlusion. Target vessel size (OR 2.15, P = .001) and skip grafts (OR 2.49, P = .001) were also significantly associated with higher odds of SVG patency. In multivariate modeling, calcification at the distal anastomosis (OR 2.09, P = .05), smaller target vessel size (OR 2.37, P = .003), and female gender (OR 2.46, P = .01) remained statistically significant predictors of early SVG occlusion.

Conclusion: In this prospective clinical study, early SVG failure was associated with both demographic and anatomic factors. Optimal early SVG patency rates may be achieved through careful patient selection, as well as efforts to maximize target vessel size, utilize skip grafts, and choose anastomosis sites devoid of calcification. That the presence of calcification at the distal anastomosis is a predictor of early graft failure is an important new finding. Perhaps preoperative evaluation of the coronary vessels by MDCT may be useful to guide the approach of cardiothoracic surgeons in the future.

9:30 a.m.
Background: The choice of additional arterial conduit after the internal thoracic artery (ITA) in diabetic (DM) patients is controversial. Bilateral ITAs increase the risk of sternal infection while the radial artery (RA) may be prone to spasm causing decreased survival. We have thus compared our results of LITA and RA grafting in DM patients to non diabetic (non-DM) patients in order to clarify the role of the RA in DM patients.

Methods: From Jan, 1995 to Jan, 2008, 1483 consecutive patients (selected for age <65 yrs or no venous conduit) underwent isolated, primary CABG using the LITA and at least one RA. 34.5% of the patients were diabetic. These 511 DM patients had the same age (57 yrs, range 33-88 yrs) and EF (47%) as the 972 non-DM patients. The DM patients had significantly (p<0.01) more women (26.8 vs. 12.4%), previous strokes (7.8 vs. 2.7%), PVD (11.2 vs. 5.3%), and renal failure (2.3 vs. 0.9%) than the 972 non-DM patients.

Results: Operative and hospital mortality was 0% for the DM patients and 0.2% for the non-DM patients. DM patients had a trend towards higher rates of stroke (1.4 vs. 0.7%, p<0.30), sternal infections (1.6 vs. 0.9%, p=0.30) and respiratory failure (2.7 vs. 1.2%, p<0.06) than the non-DM patients. DM patients did have a significantly higher rate of hospital revascularization (57.0% vs. 45.8%, p<0.01). There was no difference in the rate of perioperative MI (1.0 vs. 0.9%) and renal failure (1.0 vs. 0.6%). The 1, 5 and 10 year Kaplan Meier survivals were 99%, 92% and 89% for the DM patients and 99%, 96% and 90% for the non-DM patients, respectively.

Conclusions: Myocardial revascularization using the LITA and RA results in excellent operative mortality and long term survival in DM patients despite a higher preoperative risk profile. DM patients had a trend towards a higher rate of postoperative morbidity. The RA appears to be an excellent choice as an additional arterial conduit in DM patients.

Background: Current antithrombotic regimens during percutaneous coronary interventions (PCI) include unfractionated heparin (UFH) or bivalirudin with or without GP IIb/IIIa inhibitors. Randomized studies have shown that bivalirudin plus provisional GP IIb/IIIa inhibitors is superior to UFH plus routine GP IIb/IIIa inhibitors in terms of net clinical outcome (composite of death, myocardial infarction, target vessel revascularization, and major bleeding). It is not known if prompt reversal of UFH by protamine after PCI results in decreased bleeding complications and no increase in ischemic complications.

Objective and Methods: To assess whether bivalirudin is superior to UFH plus protamine with respect to in-hospital REPLACE-2 major bleeding complications (primary end point) in elective PCI patients receiving a 600 mg clopidogrel loading dose 6-12 hours before PCI. GPIIb/IIIa inhibitor use was at the operator’s discretion. Secondary end points were ischemic events rate (composite of death, myocardial infarction, target vessel revascularization) and net clinical outcome at 6 months. We randomly assigned 850 patients to bivalirudin or to UFH (followed by 25 to 50 mg of protamine at the end of the procedure). Main exclusion criteria included: 1) PCI for chronic total occlusion and 2) severe renal insufficiency.

Results: The primary end point rate was 0.9% in patients randomized to bivalirudin and 2.8% in patients randomized to UFH (p=0.043). At 1 month (follow-up rate 100%), ischemic events were lower and net clinical outcome better in the bivalirudin arm as compared to UFH arm (2.8% vs 6.4% (p=0.014) and 3.3% vs 7.8% (p=0.004), respectively. At 6-month follow-up (93% follow-up rate at October 6, 2008), major bleeding rate was still lower in the bivalirudin group (1% vs 4.8%; p<0.001). Complete 6-month follow-up results will be presented.

Conclusion: In elective PCI patients bivalirudin as compared to UFH plus protamine is associated with less major bleeding complications. (Trial registration: clinicaltrials.gov Identifier: NCT00448461)

Results of Radial Artery Grafting in Diabetic Patients

Robert F. Trabanghi, Darryl M. Hoffman, Charles M. Geller, Loren J. Harris, Paul Steitzer, Bertsmann Cohm, Beth Israel Medical Center, New York, NY

9:30 a.m.

Comparison of Bivalirudin and Unfractionated Heparin Plus Protonate in Patients With Coronary Artery Disease Undergoing Elective Percutaneous Coronary Intervention: Final Six-Month Result of the Antithrombotic Regimen and Outcome (ARNO) Trial

Guido Paredi, Angela Migliorini, Renato Valenti, Benedetta Bellandi, Umberto Signorini, Piergiorgio Buonamici, Nazario Carabba, Giuia Moschi, David Antoniucci, Department of Cardiology, Careggi Hospital, Florence, Italy

9:45 a.m.

Long-Term Outcomes of Sirolimus-Eluting Stent Versus Off-Pump Coronary Artery Bypass Grafting in Diabetic Patients With Multivessel Coronary Disease Involving Proximal LAD

Hiroshi Tamura, Katsumi Miyauchi, Takahiko Kojima, Ken Yokoyama, Takeshi Kurata, Taira Yamamoto, Atsushi Amano, Hirohui Daide, Juntendo University, Tokyo, Japan

Numerous trials have compared coronary angioplasty with bypass surgery. However, there is no data regarding clinical comparison between off-pump coronary artery bypass grafting (CABG) surgery (using the internal mammary artery) and sirolimus-eluting stent (SES) in diabetic patients. This study was designed to compare the long-term clinical outcome of off-pump CABG with SES in diabetic patients with multivessel disease involving proximal left anterior descending or left main coronary artery in single center. Of all the patients who were screened for this observation, a team consisting of a surgeon and an interventionalist decided that the anatomy was suitable for both CABG and PCI.
**Comparison of Optimal Medical Therapy With or Without PCI on Cardiovascular Endpoints in Patients With Silent Myocardial Ischemia: Post Hoc Analysis From the COURAGE Trial**

William E. Boden, Koon K. Teo, Pamela M. Hartigan, David J. Maron,

Background: Both SWISSII-II (n=201 patients [pts] with recent MI) and ACIP (n=558 pts with stable CAD) showed that PCI significantly reduced long-term mortality in pts with silent myocardial ischemia (SMI). Accordingly, we assessed the impact of adding PCI to OMT on clinical events among stable CAD pts in COURAGE without angina at baseline (BL) who had SMI (i.e., ECG ischemia and/or reversible stress myocardial perfusion imaging [MPI] defects).

Methods: A post hoc comparison was performed for the primary endpoint of death or MI, as well as for death (D), MI, and hospitalization for acute coronary syndrome (ACS); the composites of D/MI/stroke and D/MI/ACS; and subsequent revascularization (revasc) during a median 4.6 year follow-up.

Results: Compared to the 1,997 pts with angina at BL, there were no significant differences in age, sex, cardiac risk factors, prior MI or revasc, extent of angiographic CAD, or ischemia by ECG or MPI in the 283 pts (12%) with SMI at BL. Other than diabetes (OMT+43%; PCI+24%), there were no BL differences in SMI pts by treatment assignment.

Of note, SMI pts required less revasc (16%) than those with BL angina (27%), regardless of treatment assignment. P<0.001. Adjusted event rates reveal:

**Conclusions:** In COURAGE, the addition of PCI to OMT did not reduce long-term cardiac events in SMI pts with stable CAD. While SMI pts in SWISSII-II differ from both ACIP and COURAGE, the - 2-fold trend toward lower mortality with PCI suggests the need for a more definitive trial of PCI vs. OMT in SMI pts.

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**ACCORAL CONTRIBUTIONS**

**Hot Topics in Percutaneous Coronary Intervention**

Tuesday, March 31, 2009, 10:30 a.m.-Noon
Orange County Convention Center, Room W307A

10:30 a.m.

**0915-3**

A Randomized Comparison of Transradial Versus Transfemoral Approach for Coronary Angiography and Angioplasty

Martin Brueck, Dirk Bandomsi, Wilfried Kramer, Harald Tillmanns, Clinic of Wetzlar, Wetzlar, Germany

Background: Coronary angiography and angioplasty are usually performed via the transfemoral approach. Transradial access may offer some advantages in comparison with transfemoral access especially under conditions of aggressive antiocoagulation and antiplatelet treatment. The aim of the study was to evaluate the safety, feasibility and efficacy by the transradial approach compared to the transfemoral access in a standard population of patients undergoing coronary angiography and angioplasty.

Methods: By the 2000 and January 2008, 1024 patients were randomly assigned to transradial or transfemoral approach. Patients with an abnormal Allen test or history of coronary artery bypass surgery were excluded. Both groups were comparable concerning baseline clinical characteristics (age, sex, body mass index, cardiovascular risk factors, acute and recent myocardial infarction, LV ejection fraction, previous PCI). Procedures were performed by four experienced physicians.

Results: Table

**Conclusions:** The finding of the present study shows that transradial coronary angiography and angioplasty are safe, feasible and effective with similar results to those of the transfemoral approach. However, procedural duration, fluoroscopy time and radiation exposure are higher using the transfemoral access. In contrast to the transfemoral approach, the rate of major vascular complications was negligible using the transradial access.
**Comparative Efficacy of Primary Percutaneous Coronary Intervention, Facilitated Percutaneous Coronary Intervention and Fibrinolysis in Chinese Patients With ST-Elevation Myocardial Infarction: A Multicenter Randomized Controlled Trial**

Yun Zhang, Shi Liang Jiang, Xiao Ping Ji, The Shandong Clinical Trial Group, The Key Laboratory of Cardiac Vascular Remodeling and Function Research, Jinan, People’s Republic of China

**Background:** Primary percutaneous coronary intervention (PPCI) is superior to facilitated percutaneous coronary intervention (FPCI) and fibrinolysis in patients with ST-elevation myocardial infarction (STEMI) if the door-to-balloon time is less than 90 minutes. The purpose of this study was to find out whether PPCI is superior to FPCI and fibrinolysis in the Chinese patients with STEMI in the current clinical practice.

**Methods:** A multicenter clinical trial was conducted in 18 medical centers with PCI facilities in Shandong Province, China. A total of 513 patients with STEMI were enrolled and randomized to one of the three reperfusion strategies: (A) PPCI, (B) FPCI and (C) fibrinolysis. Patients assigned to group A received immediate PCI at a mean door-to-balloon time of 119.5±81.5 minutes. Patients assigned to group B were first given an intravenous bolus of 80mg rt-PA followed by an infusion of 42mg rt-PA over a period of 60 mins and then PCI. Patients in group C received a dose of 100mg rt-PA using a standard protocol.

The primary endpoint was 30-day cardiovascular death. The secondary endpoint was a composite of recurrent unstable angina pectoris (UAP), reinfarction, target vessel revascularization (TVR), congestive heart failure (CHF) and intracranial hemorrhage (ICH) at 30 days.

**Results:** There was no significant difference in the incidence of cardiovascular death among the 3 groups at 30 days (3.4%, 3.0%, and 6.4% in group A, B, and C, respectively, p=0.339). A significant increase in the event rate of the secondary endpoint was found in group C (36.8%) compared with that in group A (10.3%) and group B (8.9%) (both p<0.01). Subgroup analyses indicated that the difference in the secondary endpoint was mainly due to the reduction in the relative risk of recurrent UAP (3.4%, 4.8%, and 17.0% in group A, B, and C, respectively, both p<0.01) and revascularization (2.3%, 3.0%, and 25.7% in group A, B, and C, respectively, both p<0.01). No significant difference was found in primary and secondary endpoints between group A and group B.

**Conclusions:** Both PPCI and FPCI is superior to fibrinolysis in the treatment of Chinese patients with STEMI. The efficacy of PPCI is equal to that of PPCI if the door-to-balloon time is more than 90 mins.
and rapid progression of non-culprit lesion (38% vs 20%, p=0.0035). Multivariate analysis revealed that renal dysfunction (OR 2.10, 95% CI 1.01 to 4.46, p=0.05) and hsCRP (OR 1.70, 95% CI 1.09 to 2.68, p=0.02) were independently associated with rapid progression.

Conclusions: In patients with NSTE-ACS, renal dysfunction is associated with not only the severity of CAD but also rapid CAD progression. These findings may partly explain adverse outcomes in patients with renal dysfunction.

Cockcroft-Gault Is Better Than the Modification of Diet in Renal Disease Study Formula to Predict Outcome Following a Myocardial Infarction - Data From Swedish Register of Information and Knowledge

Karinna Sveumner, Stefan H. Jacobson, Pia Lundman, Johan Lindback, Ulf Stenestrand, Lars Wallentin, Tomas Jernberg, Karolinska University Hospital Huddinge, Karolinska Institutet, Stockholm, Sweden

Background: It is unknown which estimation of renal function best predicts outcome in patients with acute coronary syndrome.

Methods: All consecutive myocardial infarction (MI) patients (n=36347) admitted to a coronary care unit and entered in a nationwide register between 2003 and 2006 had glomerular filtration rate (GFR) estimated by both the Cockcroft-Gault (CG) and the Modification of Diet in Renal Disease formula (MDRD).

Results: The median (IQR) CG-GFR and MDRD-GFR was 68.3 ml/min (47.8-93.5) and 71.5 ml/min (55.5-87.9), respectively. The estimations correlated well (r=0.83, p<0.001).

At least moderate renal dysfunction (GFR<60) was identified more often with CG than with MDRD equation (39.9% versus 31.1%). Lower renal function indicated higher annual mortality by either estimation. However, within each quartile of MDRD-GFR, mortality increased with decreasing CG-GFR (Figure). A similar pattern was seen when patients were divided according to the classification of the National Kidney Foundation. In a ROC-analysis CG had a significantly stronger association to outcome (AUC 0.78; 95% CI (0.77-0.79) versus 0.73 95% CI (0.72-0.74)). After multivariable adjustment, CG still predicted one year mortality better than MDRD equation (1st quartile compared with 4th quartile: HR 2.36 (2.01-2.78) with the CG; HR 1.58 (1.42-1.76) with the MDRD).

Conclusions: Cockcroft-Gault is better than the MDRD equation to predict mortality following a myocardial infarction.

Anemia for Risk Assessment of Patients With Acute Coronary Syndromes

Francois Schiele, Nicolas Mereveux, Marie-France Seronde, Vincent Descotes-Genon, Joanna Dutth, Romain Chapard, Fiona Ecomont, Jean-Pierre Bassand, University Hospital Jean Minjoz, Besancon, France

Background: In patients admitted with acute coronary syndromes (ACS), those with anemia are at higher risk, but current risk score systems do not take into account the presence of anemia. We studied the impact of anemia on mortality and determined its incremental predictive value.

Methods: Demographic, clinical and biological characteristics at admission, as well as treatments and mortality were recorded in 1410 consecutive patients with ACS. The incremental value of adding the anemia information was determined by the changes in appropriateness of Cox models when anemia was added.

Results: Anemia was detected in 381 (27%) patients. They were older, had more co-morbidities, higher GRACE risk score, received fewer guidelines-recommended treatments and, as a result, had a four times higher mortality. When added to a prediction model based on the GRACE risk score, anemia remained an independent predictor of mortality. The addition of anemia improved both the discriminatory capacity and the calibration of the models. According to the GRACE risk score, the population was divided into 4 different risk groups: <1%, 1 to <5%, 5 to <10% and >=10%. The addition of anemia to the model allowed a reclassification respectively 9%, 43%, 47% and 23% of patients into different risk categories.

Conclusions: Our data confirm that anemia is an independent and important predictive factor of mortality, even after adjustment for co-morbidities, hemodynamic conditions and treatments used. Combined with the GRACE risk score, anemia allows improved risk classification at admission for patients with ACS.

Warfarin is Independently Associated With Lower Risk of Six-Month Death or Myocardial Infarction in Patients With Atrial Fibrillation Following Acute Coronary Syndromes

Renato D. Lopez, Aijing Starr, Sana M. Al-Khatib, L. Kristin Newby, Rajendra H. Mehta, Frans Van der Vel, Kenneth W. Mahaffey, Robert A. Harrington, Harvey D. White, Lars Wallentin, Christopher B. Granger, Duke Clinical Research Institute, Durham, NC

Background: Little is known about the use of and need for oral anticoagulant therapy in patients with atrial fibrillation (AF) complicating an acute coronary syndrome (ACS). We examined warfarin use at discharge (according to CHADS2 score) and its association with 6-month death or myocardial infarction (MI) in ACS patients complicated by AF.

Methods: Of the 23,208 patients enrolled in the PURSUIT, PARAGON A, and SYNERGY trials, 4.0% (917 patients) had AF as an in-hospital complication and were discharged with warfarin. Of the 23,208 patients enrolled in the PURSUIT, PARAGON A, and SYNERGY trials, 4.0% (917 patients) had AF as an in-hospital complication and were discharged with warfarin.

Results: Overall, 13.5% of patients with ACS complicated by AF were discharged on warfarin. Patients receiving warfarin more often had diabetes, heart failure, or prior MI compared with those not receiving warfarin. Warfarin use among AF patients was similar across CHADS2 score groupings (CHADS2=0, 13%; CHADS2=1, 14%; CHADS2=2, 13%). Among patients with in-hospital AF, warfarin use at discharge was independently associated with a lower risk of death or MI within 6 months of discharge (HR 0.35; 95% CI 0.14-0.91). Adjusted curves of 6-month death or MI according to warfarin use at discharge are shown in the figure.

Conclusion: Warfarin use is associated with better 6-month outcomes among patients with AF complicating an ACS, but use is infrequent and is not related to CHADS2 score. This study highlights the need to better understand optimal antithrombotic therapy for AF occurring in the setting of an ACS.