Myocardial Ischemia/Infarction--Basic

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

9:30 a.m.

1014-125 Three-Dimensional RGD-Modified Alginate Scaffold Designed to Enhance Efficacy of Cell Transplantation to Infarcted Myocardium

Hugo P. Sondermeijer, 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 transplant 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 3x10e6 neonatal rat cardiomyocytes (nrCM), 3x10e6 neonatal rat cardiac fibroblasts (nrCF) or 3x10e5 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), 1x10e6 hMSCs (low dose, n=13) or 3x10e6 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, nrCM viability inside scaffolds increased from 3.3±1.2% (0 mg/g cRGDfK) to 12.3±0.1% (10 mg/g cRGDfk) to 28.9±7.3% (10 mg/g cRGDfk + gelatin) ($p<0.05$). Clusters of beating myocytes could be detected. nrCF viability increased from 48.8±21% (0 mg/g cRGDfK) to 77.2±3.2% (10 mg/g cRGDfK) ($p<0.05$). 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 2.4±15.4% (without hMSCs) and 17.1±6.8% (3x10e6 hMSCs), whereas FS increased by 6.9±10.3% (1x10e6 hMSCs) ($p<0.05$).
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.

1014-126 Human Fetal Mesenchymal Stem Cells Exert More Powerful Cytoprotective Paracrine Effects Than Bone Marrow-Derived Mesenchymal Stem Cell.

Elisabetta Cervio, Patrizia Danieli, Chiara Ciuffreda, Andrea Di Marco, Roberto Bassani, Marianna Roccio, Gianluca Viarengo, Peter J. Schwartz, Massimiliano Gnecchi, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, Università di Pavia, Pavia, Italy

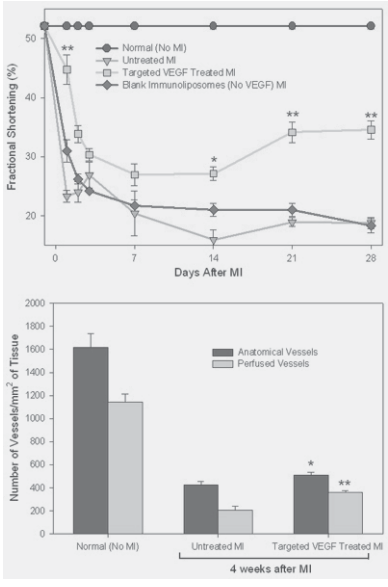
Background: We and others have shown that adult mesenchymal stem cells (MSC) repair experimental infarcted hearts mainly through paracrine mechanisms. In particular, MSC produce and release anti-apoptotic factors (AAF) that lead to cytoprotection. However, the production of AAF may be negatively influenced 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 rate of apoptosis was quantified by TUNEL staining. Cleaved Caspase 3 in H9c2 cells was evaluated by fluorimetric assay 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, cells from both the amnios and the BM displayed the antigen profile typical of MSC and efficiently differentiated into osteocytes, adipocytyes and chondrocytes. Compared with BM-MSC, A-MSC expressed significantly higher levels of PDGF-b (+ 6.6 folds), 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.

9:30 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. Rosano, Robert C. Scott, Zhanna Ivanov, Bin Wang, Parkson Lee-Gau Chong, Deborah L. Crabbe, 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 CD_{31} and $DiOC_7$ 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. After targeted VEGF, an increase in the number of anatomical and perfused vessels occurred at 4 weeks compared to untreated MI group. These improvements in vessel density were associated with increased fractional shortening by 4 weeks.
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 by complete occlusion of the left coronary artery followed by 2 hours of 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 mice. 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) compared to wild type mice (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 0.46±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 nmoles/mg protein, $p=0.0001$) as well as in wild type mouse hearts (from 3.82±0.4 to 2.3±0.01 nmoles/mg, $p=0.02$). However, wild type mice had significantly higher levels of ATP after IR injury

compared to UCP3-/- mice (p=0.008). Thus, lack of UCP3 in the mouse heart caused more severe necrosis and worse energetic status in the setting of IR injury.
Conclusion: Endogenous UCP3 prevents further myocardial necrosis during ischemia-reperfusion injury while maintaining nucleotide profile and cellular energetics, particularly ATP production. UCP3 plays a critical role in myopreservation under oxidative stress.

9:30 a.m.

1014-129 **Erythromycin Attenuates Myocardial Ischemia Reperfusion Injury in Rats via Inhibition of Microcirculatory Disturbance and Inflammatory Response**

Yusuke Jo, Toshihisa Anzai, Koji Ueno, Takashi Kohno, Kotaro Naito, Yuji Nagatomo, Yuichiro Maekawa, Toshiyuki 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. Macrolides 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/IR) or saline as control group (CON/IR), 30-minute prior to myocardial ischemia. Rats underwent 30-minute occlusion of left coronary artery, followed by reperfusion. Myocardial contrast echocardiography was performed an hour after reperfusion to assess microcirculatory impairment of the myocardium. Hemodynamic study, echocardiography and myeloperoxidase (MPO) staining were performed 24 hours after reperfusion. Real time RT-PCR was performed to assess myocardial mRNA expression in the area at risk 24 hours after I/R.
Results: Contrast echocardiography revealed that EM/IR had greater contrast intensity in the area at the risk compared with CON/IR (P=0.03). Hemodynamic study 24 hours after I/R revealed that LV end-diastolic pressure in EM/IR was lower and LV +dP/dt in EM/IR was higher than those in CON/IR (3±1 vs.5±2 mmHg, P=0.01, 8489±1036 vs. 5984±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). MPO staining revealed that neutrophil infiltration in EM/IR was significantly lower than that in CON/IR (P<0.05). Myocardial mRNA expression of IL-6 in the area at risk was significantly lower in EM/IR than that in CON/IR (P<0.05).
Conclusion: Intravenous administration of erythromycin attenuated ischemia-reperfusion injury through inhibition of microcirculatory disturbance, neutrophil infiltration and inflammatory response. Erythromycin may be effective as an adjunctive therapy to reperfusion for acute myocardial ischemia.

9:30 a.m.

1014-130 **Extracellular Matrix Processing Is Activated During Early Postischemic Reperfusion with Differential Effects of Temperature on Matrix Degradation and Endothelial Barrier Function**

Alexander Lauten, Ewa Majos, Thorsten Wahlers, Wilma Rademacher, Christian Jung, Juergen H. Fischer, Hans R. Figulla, Wilhelm Bloch, Friedrich-Schiller-University, Jena, Germany

Background: Acute ischemia is a well known inductor of extracellular matrix (ECM) remodelling, which leads to the development of congestive heart failure and is associated with left ventricular dilatation. Here we investigate the timecourse of ECM processing with release of endostatin (ES) and other low molecular weight fragments during early ischemia-reperfusion (I/R) of the heart.
Methods: In this blinded study, 30 pigs where randomized to 60min of global myocardial ischemia at either 4C or 37C or served as control. Five transmyocardial tissue samples and blood samples from the coronary sinus where collected at baseline and after ischemia within 150min of reperfusion. Collagen XVIII cleavage products of 10-75kDa including ES (25kDa) and Creatin Kinase (CK) as maker of myocardial injury where analyzed by the Western Blot and ELISA methods and by immunohistochemistry in tissue sections.
Results: We demonstrate that processing of the extracellular matrix protein collagen XVIII starts during early reperfusion, as a significantly increased expression of cleavage products at 10kDa and 75kDa as well as ES was observed at 150min of normothermic I/R. We further demonstrate a differential processing of collagen XVIII depending on temperature conditions during myocardial ischemia, as an increase in cleavage products was observed after normothermic ischemia only, however release of ES and other fragments remained unchanged after hypothermic ischemia and in controls. Increased postischemic processing of matrix proteins after normothermic ischemia correlated to increased CK-levels in this group. ES-levels in the coronary sinus where significantly lower at 30min and 150min after normothermic I/R as result of compromised endothelial barrier function.
Conclusion: This blinded study first demonstrates extracellular matrix processing during early ischemia-reperfusion with differential effects of temperature conditions and endothelial damage after normothermic I/R. These findings may contribute to a broader understanding of postischemic ECM remodelling and endothelial function.

9:30 a.m.

1014-131 **Islet-1 Promotes Cardiac Differentiation and Is Activated in Response to Myocardial Infarction in Adult Mouse Heart**

Satoshi Matsushita, Anthony J. White, James S. Forrester, Tarun Chakravarty, Eduardo Marbán, Raj Makkar, Cedars-Sinai Medical Center, Los Angeles, CA

Background: In the mammalian embryo, tissue injury heals without scarring, a response lost with the appearance of the inflammatory response. We hypothesized that a muted form of this healing response may persist in the adult, offering an opportunity for myocardial regeneration.
Methods: Myocardial infarction was created by ligation of the LAD coronary artery in C57BL/6 mice. Following a literature review of the transcription factors known to regulate cardiogenesis, expression of 8 transcription factors was determined in normal and infarcted myocardium by RT-PCR [baseline, 2, 7 and 14 d. following infarction (n=5 each)] and Western blotting. Immununohistochemistry was used to localize transcription factor(s) and c-kit to identify stem cells. Periostin and collagen expression were measured by RT-PCR and Masson's trichrome stain used to identify collagenous scar.
Results: Infarction was confirmed by upregulation of collagen (37.6±10.4-fold at 14 d), and by histology. Periostin expression increased 123.9±32.5 fold. Two transcription factors were consistently upregulated in infarct tissue compared to normal tissue: Isl1 (4.7±0.5-fold at 14d) and HAND1 (3.4±0.4-fold at 7d) [mean±SE, ANOVA<0.01]. Isl1, the most upregulated gene at 14 d, was also accompanied by an 18.3±4.6 fold increase in Isl1 protein. Immunohistochemistry revealed that Isl1 and the stem cell marker c-kit were expressed in the same small round cells.
Conclusion: Two embryonic transcription factors were upregulated in infarcted compared to normal myocardium, accompanied by markedly increased expression of Isl1 protein, which co-localized in the same cells with c-kit. Hand1 is known to co-operatively control development of the left ventricule in the embryonic heart. Isl1 is a marker of the embryonic second heart field, and its expression disappears as the cells begin to express cardiac markers. Periostin promotes reentry of adult cells into the cell cycle. These data suggest that a response paralleling cardiogenesis is activated following myocardial infarction, but that the balance of local factors favors scar formation. A change in the local environment toward the embryonic state could favor myocardial regeneration.

9:30 a.m.

1014-132 **Is the Cardioprotective Paracrine Action of Bone Marrow Cells Influenced by Clinical Conditions?**

Vien Khach Lai, José Linares-Palomino, Manuel Galiñanes, University of Leicester, Leicester, United Kingdom

Background: We have demonstrated that bone marrow cells (BMCs) have a potent cardioprotective effect. Here we have investigated whether clinical conditions such as diabetes and poor LV function influence the cardioprotection elicited by BMCs and whether the cause for any loss in protection resides in the BMCs or in the myocardium.
Methods: BMCs and right atrial appendage were obtained from patients undergoing elective cardiac surgery with and without diabetes, and from poor (EF<30%) and preserved LV function. Muscles were subjected to 90min ischemia/120min reoxygenation at 37°C. Tissue injury was assessed by creatine kinase (CK) released into the media during the reoxygenation period (IU/mg wet wt), and cell necrosis and apoptosis was determined by propidium iodide and TUNEL (% of aerobic control).
Results: CK release and cell necrosis and apoptosis induced by ischemia in the diabetic myocardium were not significantly affected by IP or the co-incubation with autologous or non-diabetic allogenic BMCs. However, when non-diabetic myocardium was co-incubated with autologous BMCs or with allogenic diabetic BMCs there was a significant reduction in CK release (from 1.41±0.18 to 0.48±0.11 and 0.44±0.14; p<0.05) and cell necrosis (from 9.54±0.98% to 3.29±1.32% and 0.60±0.50%; p<0.05) and apoptosis (from 11.59±3.13% to 0.92±0.46% and 1.01±0.63%; p<0.05, n=6/group). Muscles from patients with poor LV function were not protected by autologous BMCs but, importantly, CK release and cell necrosis were significantly reduced by allogenic BMCs obtained from patients with normal LV function (CK release from 1.16±0.10 to 0.61±0.14 and necrosis from 13.45±0.67% to 8.62±1.20%; p<0.05 in both instances, n=5/group) although apoptosis remained unaffected (from 8.09±1.53% to 6.08±1.02%; p=NS). By contrast, muscles from individuals with normal LV function could not be protected with BMCs obtained from patients with poor LV.
Conclusions: The cause for the loss of the cardioprotective paracrine action of BMCs in subjects with diabetes resides in the myocardium and not in the BMCs whereas in those with poor LV function the BMCs are responsible for the deficit in cardioprotection.

9:30 a.m.

1014-133 **Adjunctive Infusion of AZD6140, but Not Clopidogrel, With t-PA Enables Sustained Coronary Artery Recanalization With Recovery of Myocardium Perfusion in a Canine Model of Myocardial Infarction**

Kai Wang, Xiaorong Zhou, Yanming Huang, Mazan Khalil, Dominik Wiktor, Yu Peng, Marc S. Penn, The Cleveland Clinic, Cleveland, OH

Background: We assessed the effect of AZD6140, the first reversible oral $P2Y_{12}$ receptor antagonist, vs clopidogrel (CLOP) on platelet aggregation, thrombus formation, and myocardium perfusion in a dog coronary thrombosis model. **Methods.** Five min before administration of t-PA (1 mg/kg, 20 min), 10 animals received CLOP 10 mg/kg IV bolus for 5 min, 10 received AZD6140 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/h. **Results.** Reocclusion 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 ±2.67%) and CLOP (1.11 mm ±2.0%) vs control (26.3 mm ±23.5%, 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=0.221) compared to CLOP (50% recovery, P=0.051) and saline group (62% recovery, P=0.060). **Conclusion.** Administration of AZD6140 in combination with t-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.

	RR (%)	TR (min)	RD (min)	CFV (%)	Reocclusion (%)	Infarct size (cm2)
Control	90	24.4±7.7	87.4±44.9	30	50	13.63±4.19
CLOP	100	27.2±6.2	96.9±38.9	30	30	14.34±4.29
AZD6410	100	22.9±8.1	120±0.00*	0*	0*	6.31±2.86*

*P<0.05 vs CLOP and control groups. RR-reperfusion rate; TR-time to reperfusion; RD-reflow duration; CFV-cyclic flow variation. All data mean ± SD. Predetermined limit of observation after reperfusion was 120 min.

9:30 a.m.

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

Winston Shim, Genevieve Tan, Yacui Gu, Shiqi Li, Ling Qian, Yingying Chung, Sze Yun Lim, Ting Huay Ooi, Eugene Sim, Terrance Chua, Seng Chye Chuah, Tian Hai Koh, Philip Wong, National Heart Center, Singapore, Singapore, National University of Singapore, Singapore, Singapore

Background: Functional deterioration post myocardial infarction can be relieved by stem cell therapy. We investigate systolic and diastolic contribution of cell therapy on myocardial function.
Methods: Mesenchymal stem cells (MSCs) were derived from sternum of 46 patients. MSCs were differentiated into cardiomyocyte-like cells (CLCs) using cardiomyogenic induction medium. One week after ligating left anterior descending artery of Wistar rats, Vibrant DiI-labeled low dose MSCs (1x 10^6, n=9) and high dose MSCs (5 x 10^6, n=18) or CLCs (5 x 10^6, n=15) and serum-free medium (n=19) were injected into the peri-infarcted regions of myocardium. Left ventricular (LV) function was analyzed 6 weeks post transplantation by Millar's 2-F Mikro-tip pressure-volume (PV) catheter.
Results: High dose cell therapy significantly improved post-infarct remodeling by preventing expansion of end-diastolic and end-systolic volume. Furthermore, high dose CLCs (76.3 ± 8.1%, p<0.001) and MSCs (70.2 ± 11.1%, p<0.001), but not low dose MSCs (54.6 ± 18.8%), enhanced LV ejection fraction as compared to medium-injected control (48.1 ± 16.1%). However, both high and low dose MSC transplant impaired myocardial tissue compliance that elevated end-diastolic (13.9 ± 8.3 mmHg, p<0.05) and end-systolic pressure (163.8 ± 53.6 mmHg, p<0.01) respectively when compared to medium-injected animals (8.5 ± 3.1 mmHg [EDP] and 129.6 ± 27.7 mmHg [ESP]). In contrast, CLCs, but not MSCs, enhanced cardiac output (43674.2 ± 11854.6 uL/min, p<0.05) and stroke work (12303.3 ± 3174.1 mmHg*uL, p<0.05) by improving contractile dynamics of dP/dt_{max} (14734 ± 3306 mmHg/s, p<0.01) and dV/dt_{max} (5842 ± 2547 uL/s, p<0.05). The hemodynamic changes were correlated with engraftment of CLCs in collagen V-rich myofibers in peri-infarct region and preferential localization of MSCs within collagen I matrix and vascular structures in the infarct.
Conclusions: CLCs augment functional recovery by maintaining contractile efficiency and myocardial compliance at infarct borders. Cardiac differentiated stem cells may be more effective than undifferentiated stem cells in sustaining post-infarct recovery of myocardial function.

9:30 a.m.

1014-135 The N-Terminal Cleavage Product of PAR1 (Parstatin) Is a Potent Cardioprotective Agent Against Myocardial Ischemia and Reperfusion Injury by Recruiting NOS, ERK1/2, p38 MAPK, and K_{ATP} Channels

Jennifer L. Strande, Nikos E. Tsopanoglou, Anna Hsu, Jidong Su, John E. Baker, Medical College of Wisconsin, Milwaukee, WI, University of Patras, Patras, Greece

Background: The Protease-Activated Receptor 1 is fundamental to mediating thrombin's effects in cardiovascular injury. It has been implicated in atherosclerosis, acute coronary thrombosis, restenosis, and ischemia-reperfusion injury. Thrombin activates the receptor by proteolytic cleavage of the N-terminus to expose a tethered ligand, which then transactivates the receptor. Although much research has focused on the activated receptor, little is known about the 41 amino acid N-terminal cleavage product (Parstatin). We hypothesized that Parstatin would protect the heart against ischemia-reperfusion injury.
Methods/Results: Parstatin was synthesized at a peptide facility. We assessed the potential protective role Parstatin in an *in vivo* and *in vitro* rat model of myocardial ischemia-reperfusion injury. Parstatin (1-25 µg/kg) treatment before ischemia decreased infarct size by 26% in an *in vivo* model of I/R injury at an optimal dose of 10 µg/kg. Parstatin (0.1-10 µM) treatment immediately before ischemia decreased infarct size by 65% in the *in vitro* model and increased recovery in ventricular function by 23% following ischemia-reperfusion at a optimal concentration of 1 µM. The survival pathways known to be up-regulated by pharmacologic cardioprotectants were then explored. The cardioprotective effects of Parstatin were abolished by inhibition of NOS (L-NMA), ERK1/2 (PD98059), p38 MAPK (SB203508) and K_{ATP} channels (glibenclamide). L-NMA, PD98059, SB203508, and glibenclamide alone had no effect on cardioprotection *in vitro*.
Conclusion: A single treatment of Parstatin administered prior to ischemia confers immediate cardioprotection by recruiting NOS, ERK1/2, p38 MAPK, and K_{ATP} channels. This suggests a potential therapeutic role of Parstatin in the treatment of injury resulting from myocardial ischemia and reperfusion.

9:30 a.m.

1014-136 Ischemic Preconditioning Selectively Protects Subsarcolemmal Mitochondrial Respiration Against Ischemic Injury

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

Ischemic preconditioning (IPC) protects mitochondrial (mito) respiration from ischemia-reperfusion injury. It is unclear whether IPC induces mito protection from subsequent ischemic injury or from reperfusion injury and whether there is a selective protection of subsarcolemmal (SS) or interfibrillar (IF) mito. We studied pre and post ischemic SS and IF mito respiration to elucidate the timing of IPC protection and its effect on the different mito populations.
Isolated rat hearts were subjected to either A) CONTROL: 30 minutes (min) equilibration (EQ) and 30 min of ischemia or B) IPC: 10 min EQ, two 5 min episodes of IPC, and 30 min of ischemia. SS and IF mito were isolated at end equilibration and at the end of the 30 minute of ischemia. Mito respiration (state 2, 3, 4, respiratory control index (RCI: state 3/state 4), and ADP:O ratio) was measured by polarography using glutamate and malate as substrates in SS and IF mitochondria. Data is expressed as Mean±SEM.

End Equilibration										
n = 7	State 2		State 3		State 4		RCI (3/4)		ADP:O	
	SS	IF	SS	IF	SS	IF	SS	IF	SS	IF
CONTROL	29±4	20±2	103±10	80±9	35±4	22±3	2.9±0.2	3.6±0.2	2.9±0.2	3.3±0.1
IPC	27±3	21±2	97±7	83±8	34±2	24±3	2.9±0.1	3.6±0.2	2.8±0.2	3.5±0.2
End Ischemia										
n = 6	State 2		State 3		State 4		RCI (3/4)		ADP:O	
	SS	IF	SS	IF	SS	IF	SS	IF	SS	IF
CONTROL	34±2	19±1	70±7†	48±3†	42±2	29±2	1.7±0.1†	1.7±0.1†	2.2±0.1†	2.5±0.1†
IPC	33±2	22±4	94±3 *	53±5§	37±2	25±2	2.6±0.1*	2.2±0.1§	3.0±0.2*	3.0±0.2

(State 2, 3, and 4 are expressed as ng atoms O/min/mg protein) *p<0.05 vs End Ischemia CONTROL. † p<0.05 vs End EQ CONTROL. § p<0.05 vs End EQ IPC

Ischemia induces significant damage to both SS and IF mito as evidenced by impaired respiration (state 3, RCI, and ADP:O ratio). IPC prevents ischemic damage to SS mito as evidenced by preserved state 3, RCI, and ADP:O ratio at end ischemia compared to CONTROL. IPC did not prevent damage to IF mito. We conclude that 1) the protective effects of IPC on mito function is present at end ischemia, 2) that this protection against ischemic injury is selective to SS mito, and 3) this selective protection suggests that there are subcellular differences in IPC induced protection.

9:30 a.m.

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

Catriona J. Marshall, Tessa Mocatta, Judy McKenzie, Anthony Kettle, James Blake, John Elliott, David Smyth, Mark Richards, Dougal R. McClean, Department of Cardiology, Christchurch Hospital, Christchurch, New Zealand, Free Radicals Research Group, University of Otago, Christchurch, New Zealand

Background: The role of the neutrophil in inflammatory events leading to coronary plaque rupture and occlusive thrombus is controversial. Neutrophils and monocytes contain myeloperoxidase (MPO) and leukocyte elastase (LE) within azurophilic granules. We hypothesized that increased neutrophil and monocyte degranulation is found systemically and locally in the culprit coronary artery in patients with ST elevation myocardial infarction (STEMI).
Methods: Twenty eight STEMI patients having primary PCI were compared to eleven chronic stable angina controls having elective PCI. Blood was sampled from the femoral artery, and culprit coronary artery pre PCI at the site of occlusive thrombus with a fine sampling catheter. At 24 hours a peripheral venous sample was drawn. Flow cytometry measured neutrophil and monocyte MPO mean fluorescence intensity (MFI). Lower MPO MFI reflects increased degranulation. An ELISA measured plasma LE.
Results: Acute degranulation 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.
Conclusions: Acute neutrophil and monocyte degranulation in STEMI prior to restoration of epicardial flow suggests a possible role for neutrophil activation in the pathophysiology of occlusive plaque rupture.

Mean +/- SD	STEMI	Elective PCI	p value
Neutrophil MPO MFI			
Femoral Artery*	14.6+/- 7.8	33.9+/-21.8	<0.001
Coronary Artery pre PCI*	12.8+/- 6.5	29.8+/- 18	<0.001
24 hours	19.4+/- 9.4	21.1+/- 5.9	ns
Monocyte MPO MFI			
Femoral Artery*	4.9+/- 2.3	9.8+/-4.9	<0.001
Coronary Artery pre PCI*	5.1+/- 2.4	10+/- 4.8	<0.001
24 hours	7.9+/- 4.1	8.1+/- 2.3	ns
Plasma LE ng/ml			
Femoral Artery	21.8+/-10.6	11.6+/-6.3	<0.01
Coronary Artery pre PCI	28.8+/-28.3	17.5+/-9.0	0.01
24 hours	17.3+/-10.3	17.5+/-3.7	ns
*p<0.05 vs. 24 hrs in STEMI patients			

9:30 a.m.

1014-138 **An Insertion/Deletion Polyporphism in α_2-Adrenergic Receptor Gene Is a Genetic Risk Factor for Sudden Cardiac Death**

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

Background: A variant of the human α_{2B}-adrenoceptor 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 α_{2B}-adrenoceptor 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/D 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/D or I/D genotype had 1.95-fold (95% confidence interval, 1.07 to 3.55, P = 0.029) risk of sudden cardiac death and 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 α_{2B}-adrenoceptor 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, p=0.009) among those with previously diagnosed cardiovascular disease CVD but not among those without previous CVD.
Conclusions: The D/D and I/D genotypes of the α_{2B} -adrenoceptor are novel genetic risk predictors for unexpected sudden cardiac death and coronary heart disease mortality.

9:30 a.m.

1014-139 **Ischemic Preconditioning Robustly Reduces In Vivo Myocardial Infarction in Both Male and Female Mice With Short or Long Ischemic 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 Ohio State University, Columbus, OH

Ischemic preconditioning (IPC) is a powerful phenomenon that provides robust cardioprotection with reduced myocardial infarction. While it occurs in mammalian hearts with shorter periods of ischemia, little is known with prolonged periods of ischemia (I), and the relationship with aging and gender. Despite beneficial effects of nitric oxide (NO) in IPC, the role of endothelial NO synthase (eNOS)-NO is controversial. Therefore, we performed an extensive characterization of IPC in wild-type (WT) and eNOS-knockout (eNOS-KO) mice to evaluate whether the infarct limiting effect of IPC depends on ischemic periods, eNOS, ages, and gender. Classical IPC was induced by 3-cycles of 5-min regional coronary I (LAD occlusions) separated by 5-min reperfusion (R), and was followed by 30-min (30-IPC) or 60-min (60-IPC) index I and 24-hrs R. Control IR protocol had 30- or 60-min I followed by 24-hrs R, 30-IR or 60-IR, respectively. Protection was evaluated by measuring infarct size as a percentage of area at risk (Table). The major findings are that regardless of age and sex, WT mice exhibited robust IPC effects with significantly smaller infarct size, whereas, eNOS-KO mice failed to exert this effect. Both aging and prolonged ischemia caused significantly large infarction. Female WT mice had smaller acute IR injury compared to male WT. In conclusion, IPC protects WT mice against in vivo myocardial IR injury regardless of age, gender and/or ischemic duration, but, deletion of eNOS abolishes this potent cardioprotection.

Ischemic Preconditioning and Myocardial Infarction: Effects of Age, Sex, and Ischemic Periods

Gender / Age	Parameter	Protocols	WT (n)	eNOS-KO (n)
Male: 8-12 weeks	% Infarct size	30-I/R	42±1.1 (10)	49±2.2 (8)
Male: 8-12 weeks	% Infarct size	30-IPC	15.3±1.7*** (10)	47±2.5 (7)
Male: 8-12 weeks	% Infarct size	60-I/R	55±3.2 (8)	Lethal
Male: 8-12 weeks	% Infarct size	60-IPC	20±2.1††† (8)	Lethal
Male: 12-18 months	% Infarct size	30-I/R	54.1±3 (7)	ND
Male: 12-18 months	% Infarct size	30-IPC	27.1±3*** (7)	ND
Female: 8-12 weeks	% Infarct size	30-I/R	32.1±3.1 (7)	44.8±4.1 (6)
Female: 8-12 weeks	% Infarct size	30-IPC	20.4±2.8*** (7)	42.5±2.7 (5)
	I/R, ischemia-reperfusion;IPC, ischemic preconditioning	*** P<0.001 vs. respective 30-min I/R	††† P<0.001 vs. respective 60-min I/R	n = number of animals; ND = not determined

9:30 a.m.

1014-140 **Stabilization of Cardiac Electrophysiology in Ischemic Myocardium by Granulocyte Colony Stimulating Factor**

Natnicha Kanlop, Wasarut 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 cardioprotective effects during ischemic/reperfusion (I/R) period in *in vitro*. However, its effects on cardiac electrophysiology in *in vivo* is unclear. We tested the hypothesis that G-CSF can stabilize cardiac electrophysiology during I/R 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 (0.33*u*g/kg/min, n=6, Group1) and saline (n=4, Group2) were administered for 30 minutes prior to a 45-minute left anterior descending artery occlusion and at the time of reperfusion. The pacing threshold (DPT), ERP, VFT, DFT, QTc and QRS duration were determined in each pig before and during I/R period. In group3 (n=7), G-CSF was infused without artery occlusion.
Results: During ischemic period, G-CSF (group1) significantly increased the DPT, 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 DPT (0.7±0.2 vs. 0.3±0.1 mA, $p<0.05$) without altering other parameters.
Conclusions: G-CSF increases the ERP, DPT and VFT, thus stabilizing the cardiac electrophysiology and may prevent fatal arrhythmia in ischemic myocardium. However, G-CSF does not improve defibrillation efficacy during I/R injury.

G-CSF (Group 1)		Control	Ischemia	Reperfusion
VFT	volts	34±11	64±20*	49±16
	joules	0.10±0.05	0.30±0.20*	0.20±0.10
DFT	volts	480±115	539±13	490±145
	joules	18±9	24±12	20±13
ERP	ms	245±16	277±18*	243±36
DPT	mA	0.2±0.1	0.5±0.2*	0.7±0.2*

9:30 a.m.

1014-141 **Myocardial Regeneration With Autologous Mesenchymal Stem Cells in A Porcine Model Of Myocardial Infarction.**

Montserrat Rigol, Núria Solanes, Jordi Farré, Mercè Roqué, Laura Novensà, Antonio Berruezo, Neus Bellera, Santiago Roura, David Tamborero, Cristina Prat, Montserrat Batlle, Marta Sitges, José Ramírez, Josep Brugada, Antoni Bayés-Genís, Magda Heras, Hospital Clínic. 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: transendocardial culture media (n= 4); and Group 4: transendocardial 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 ventricle 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 ventricle MI between different groups (group 1: 19,3±5,2%; group 2: 24±0,6%; group 3: 22,2±6%; group 4: 21,7±7,2%).
Conclusions: This study demonstrates that neither cardiac function nor infarct size were significantly modified by the administration of ic or transendocardial MSCs in our porcine model of MI.

Ejection fraction measured by intracardiac echocardiography

	Intracoronary administration		Transendocardial administration	
	culture media	MSCs	culture media	MSCs
Before infarction	77±2%	79±1%	84±2%	80±1%
Ten days after infarction	55±10%	48±1%*	50±6%	54±4%*
3 weeks after treatment	58±8%	49±5%	50±5%	51±5%
* p< 0,05 vs before infarction				

9:30 a.m.

1014-142 **Increased Beta-Catenin Pathway Expression by a Remote Ischaemic Preconditioning Stimulus: First Evidence in Humans**

Hussain Contractor*, Houman Ashrafian*, Ishtiaq Rahman, Andrew N. Redington, Michael P. Frenneaux, C. Jorge Mascaro, Robert S. Bonser, Rajesh K. Kharbanda, University of Oxford, Oxford, United Kingdom, University of Birmingham, Birmingham, United Kingdom

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 PI3K/AKT/GSK-3β/β-catenin cell survival pathway has been proposed as 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-tubulin). 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=0.95). 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.

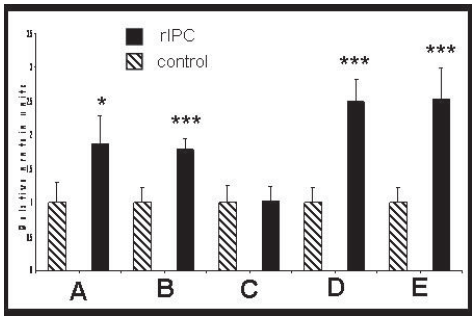


Figure 1: Relative expression of β-catenin pathway constituents in control and rIPC subjects. A=p-AKT, B=pan-AKT, C=p-GSK-3β, D=GSK-3β, E=β-catenin

9:30 a.m.

1014-143 **Ischemic Preconditioning Protects Mitochondrial Respiratory Function in Complex I and Complex II**

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 for each complex in the presence of ADP. Substrates for Complex I, II, and IV were glutamate and malate (4.7 mM) , succinate (7 mM) , tetramethyl-p-phenylenediamine (0.4 mM) respectively. Inhibitors for complex I, II, and III used were rotenone (188 nM), thenoyltrifluoroacetone (0.4 mM) , and antimycin A (18.8 nM) . Data is expressed as mean±SEM.

	Complex I		Complex II		Complex IV	
	SS	IF	SS	IF	SS	IF
CONTROL	83±4	55±4	53±2	24±2	59±2	46±4
IPC	130±7 *	112±5 *	70±3*	38±3 *	62±4	73±4
Data expressed in ng atoms O/mg protein. * p<0.05 vs CONTROL						

Ischemia reperfusion impairs mitochondrial complex I, II and IV activity. IPC preserves both complex I and II activity in subsarcolemmal and interfibrillar mitochondria at end reperfusion. Complex IV activity is not affected by IPC. Selective protection of mitochondrial complex I and II during reperfusion is the mechanism responsible for preservation of respiration by IPC.

9:30 a.m.

1014-144 **Deterioration of Left Ventricular Function in Patients With Non-ST-Elevation Myocardial Infarction Awaiting Coronary Angiography**

Bjornar Grenne, Christian Eek, Benthe Sjoli, Helge Skulstad, Svend Aakhus, Otto Smiseth, Thor Edvardsen, Harald Brunvand, 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 (NSTE-ACS) 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 NSTE-ACS 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.

	Strain (%) at admittance	Strain (%) before coronary angiography	Mean difference (95% CI)	p value
NSTEMI (n=32)	-15.8 ±3.0	-14.9 ±2.8	-0.9 (-1.4, -0.5)	<0.001
Unstable angina (n=14)	-17.6 ±2.4	-18.1 ±2.2	0.5 (-0,1 1.1)	0.083
Non-coronary chest pain (n=15)	-19.8 ±1.9	-19.8 ±2.1	0.05 (-0.9, 1)	0.92

Strain values are mean ± S.D.
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.

1014-145 **The Loss of MKK7 Is Critical for Cardiac Physiology**

Bernhard J. Haubner, Gregory Neely, Jakob Voelkl, Christian Kremser, Otmar 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 (MKK7), 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 MKK7, using a muscle specific knock-out strategy, in the cardiac pathology remained unclear.
Methods: We therefore generated muscle specific MKK7 knock-out (KO) mice and investigated their myocardial phenotype compared to MKK7 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 MKK7 KO mice during myocardial stress.
Results: We found significantly reduced fractional shortenings (WT: 56,2±2,1 vs. KO: 43,6±1,9%, n=7, p<0,05; CMR data) combined with marked dilatation (transversal diameter WT: 3,004±0,084 vs. KO: 3,511±0,105 mm, n=7, p<0,05; CMR data) in MKK7 KO rodents at the age of 12 weeks. In contrast, the extent of ischemia/reperfusion injury was significantly reduced in MKK7 KO compared to WT mice. Following 30 minutes of ischemia and 3 hours of reperfusion, MKK7 mutagenic rodents presented significantly reduced levels of troponin T (WT: 2,97± 0,39 vs. KO: 1,78± 0,26 ng/ml, n=13, p<0,05). This early decrement of troponin T in the transgenic cohort was followed by smaller areas of infarction after 1 week (WT: 3,58±0,50 vs. KO: 1,77±0,30mm², 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 MKK7 WT mice compared to the transgenic strain.
Conclusions: Our data provide the first *in vivo* knock-out evidence for the critical role of MKK7 in the heart: Whereas MKK7 KO hearts display reduced cardiac functions, they are partly protected from myocardial ischemia/reperfusion injury.

9:30 a.m.

1014-146 Remote Ischemic Preconditioning Modifies Cardiac Micro RNA Expression In Vivo: First Observations in a Mouse Model

Jing Li, Wanli Xuan, Pingzhao Hu, Rajesh K. Kharbanda, Andrew N. Redington, The Hospital for Sick Children, Toronto, ON, Canada

Background: Remote ischemic preconditioning (rIPC) 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. We have previously described important effects of the rIPC stimulus on gene expression profiles in mouse myocardium and human neutrophils, but our understanding of the mechanisms by which rIPC exerts its effects on cell signaling remains incomplete. MicroRNAs (miRNAs) are a recently discovered classes of endogenous, small, noncoding RNAs that downregulate posttranscriptional gene expression. There are no data regarding their role in ischemic preconditioning, but they are increasingly recognized as modifiers of myocyte growth and stress responses. We therefore hypothesized that the rIPC induces changes in myocardial miRNA expression.
Methods and Results: Sham procedure (n=3) or rIPC (four cycles of 5 min of hind-limb ischemia and 5 min of reperfusion, n=5) was performed immediately prior to heart harvest in mature wild type mice. Extracted RNA was subjected to analysis using a mouse miRNA microarray containing 382 miRNA probes. The resulting data was standardized by a quantile normalization method, and SAM (significance analysis of microarrays) analysis was used for statistical comparisons of control and rIPC profiles. Overall, 19 miRNA's were significantly 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 miRNA 346, fold change 10.31; p<0.005). Most of the miRNA's modified by rIPC have hitherto unknown roles in myocyte 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 miRNA's will enhance our understanding of the mechanism of protection afforded by rIPC, and may establish new therapeutic targets.

9:30 a.m.

1014-147 Impact of Antioxidative and Antiapoptotic Effects of Mesenchymal Stem Cells on Salvaging Ischemic Heart Injury: Role of Transient Overexpression of Heme Oxygenaze-1

Toshinari Tsubokawa, Chiaki Nakanishi, Kunimasa Yagi, Atsushi Nohara, Noboru Fujino, Hidekazu Ino, Shotoku Tagawa, Masakazu Yamagishi, Hatsue 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 $^{HO\text{-}1}$MSC were exposed to culture conditions with serum deprivation (SD) and hypoxia and characteristics of cell damage were analyzed by flow cytometry. Cell viability was determined by MTS assay after exposing MSC or $^{HO\text{-}1}$MSC to H_2O_2 as an oxidative stress. VEGF level in the supernatant of each cells culture after the load of H_2O_2 were measured by using ELISA. In rat infarction model, MSC ($5\times10^6 \pm 0.4 \times10^6$ cells/rat) or $^{HO\text{-}1}$MSC 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. $^{HO\text{-}1}$MSC 17 ± 2 %, p<0.05) and were markedly resistant to cell death at 400μM H_2O_2 (2 ± 2% vs. 32 ± 3%, P<0.05). $^{HO\text{-}1}$MSC secreted a large amount, 2.5-fold more VEGF compared with MSC. When $^{HO\text{-}1}$MSC were delivery by intramyocardial injection, increased capillary density associated with decreased infarction size was observed in $^{HO\text{-}1}$MSCs (1332 ± 75 /mm^2 with 21.1 ± 2.4%) compared with MSCs and control groups (1224 ± 138 /mm^2 with 27.8 ± 2.5% and 609 ± 48 /mm^2 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.

9:30 a.m.

1014-148 Pro-arrhythmic Risk of Embryonic Stem Cell-Derived Cardiomyocyte Transplantation in Infarcted Myocardium

Song-Yan Liao, Chung-Wah Siu, Wing-Hon Lai, Ka-Wing Au, Yuan Liu, Ed Wu, Yin Wu, Pandora M. Yip, Ronald Li, Chu-Pak Lau, Hung-Fat Tse, Cardiology Division, Department of Medicine, Queen Mary Hospital, the University of Hong Kong, Hong Kong, Hong Kong

Background: Embryonic stem cells (ESCs) and their cardiac derivatives have been explored as potential cell sources for treatment of post-myocardial infarction (MI) left ventricular (LV) dysfunction, however, their potential proarrhythmic risk remains unclear.
Methods: We compared the functional effects and proarrhythmic risk of direct intramyocardial transplantation of $3\text{x}10^5$ undifferentiated mouse ESC (ESC group, n=20) and mouse ESC derived-cardiomyocytes (ESC-CM group, n=28) versus culture medium (Control group, n=24) at the infarct and border zone in mouse model of acute MI. Cardiac magnetic resonance imaging (MRI) was performed at 1 and 3 wks post-MI. Electrocardiogram telemetry was performed to monitor for proarrhythmias.
Results: At 4 wks, ESC-CM group had significantly higher mortality rate compared with those in control group and ESC group (Figure 1, P<0.05). Telemetry monitoring confirmed the presence of spontaneous ventricular tachyarrhythmias (VT/VF) as cause of death in majority of mice transplanted with ESC-CM (67%). Cardiac MRI showed a similar improvement in LV ejection fraction in those mice of ESC group and ESC-CM group compared with control group at 1and 3 wks post-MI (Figure 2, P<0.05).
Conclusions: Our results demonstrate that transplantation of undifferentiated ESCs and ESC-CMs provide similar improvement in cardiac function post-MI, however, ESC-CMs is associated with a significant higher prevalence of spontaneous VT/VF and early mortality after transplantation.

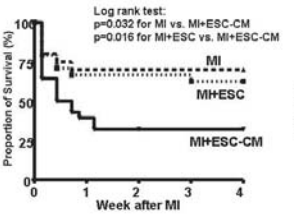


Figure 1

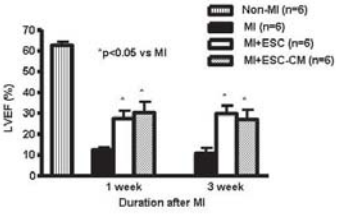


Figure 2

9:30 a.m.

1014-149 Increased Rho Kinase (ROCK) Activity in Hong Kong Subjects With Acute Coronary Syndrome (ACS)

Cheuk-man Yu, Ming Dong, Rui-jie Li, Mang Zhang, Qian-huan Zhang, James K Liao, The Chinese University of Hong Kong, Hong Kong SAR, Hong Kong

Background: Rho Kinase (ROCK) has been demonstrated to be involved in hypercontraction of vascular smooth muscle and implicated as playing a pathophysiological role in cardiovascular diseases such as coronary artery spasm. This study aimed to find out if ROCK activity is increased in Hong Kong population with acute coronary syndrome (ACS).
Methods: 112 Hong Kong subjects admitted for ACS and 20 matched controls were studied. ACS patients included 3 groups: ST elevation myocardial infarction (STEMI) (n=50), Non-ST elevation myocardial infarction (NSTEMI) (n=50) and unstable angina (UA) (n=12).
Results: ROCK activity, as determined by phosphorylation of myosin binding subunit (MBS) in leukocytes, was greater in STEMI (4.70±1.64), NSTEMI (4.68±1.55), and UA subjects (3.37±1.10) when compared with controls (1.38±0.35, all p<0.01). It was even higher in STEMI and NSTEMI subjects than in UA subjects (both p<0.05). Furthermore, ACS patients with elevated peak WBC level (>$10.1\text{x}10^9$/l) showed a higher ROCK activity than those with low level (≤$10.1\text{x}10^9$/l) (4.94±1.66 vs. 4.15±1.46, p<0.01). In addition, levels of troponin T (TnT), creatinine phosphokinase (CK), WBC, as well as total and LDL-cholesterol were associated with increased ROCK activity (Table).
Conclusion: This prospective study observed that ROCK activity was increased in patients with ACS, in particular those with myocardial infarction. The pathophysiological role of ROCK activity in ACS warrants further investigation.

Correlations between ROCK activity and clinical / biochemical parameters in ACS

	First TnT	Peak TnT	Peak CK	Peak WBC	TC	LDL
Correlation coefficient	0.304	0.374	0.275	0.226	0.221	0.226
P value	0.002	0.000	0.006	0.021	0.050	0.050

9:30 a.m.

1014-150 Neutralization of Interleukin (IL)-18 Ameliorates Ischemia/Reperfusion-Induced Myocardial Injury

William H. Boylston, Kaliyamurthi Venkatachalam, Sumanth D. Prabhu, Anthony J. Valente, Bysani Chandrasekar, Department of Veterans Affairs South Texas Veterans Health Care System, San Antonio, TX, University of Texas Health Science Center, San Antonio, TX

Background: Interleukin-18 is a proinflammatory, pro-apoptotic cytokine, whose expression increases during myocardial infarction and failure. We recently demonstrated that oxidative stress stimulates IL-18 expression in cardiomyocytes. Since ischemia/reperfusion (I/R) causes oxidative stress and potently induces proinflammatory cytokines, we hypothesized that IL-18 is induced following I/R and contributes to inflammation and tissue injury. Neutralization of IL-18 should thus lessen I/R-mediated tissue injury. We also asked whether simulated I/R *in vitro* induces IL-18 expression in cultured cardiomyocytes, and identified the underlying molecular mechanisms.
Methods: I/R studies were performed in a chronically instrumented, closed-chest mouse model. Male C57BL/6 mice underwent 30 min LAD coronary artery ligation followed by various periods of reperfusion. Sham-operated or ischemia alone (30 min) mice served as controls. A subset of animals was treated with IL-18 neutralizing antibodies (500 μg/mouse, *i.v.*) 1 h prior to LAD ligation. Ischemic LV tissue was used for analysis. Isolated

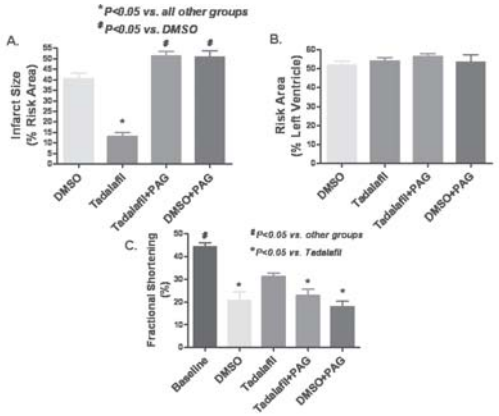
adult mouse cardiomyocytes underwent simulated I/R (30 min I/4 h R; sI/R) Downstream effectors were targeted by pharmacological inhibitors and adenoviral transduction of dominant negative expression vectors.
Results: Our results demonstrate low levels of NF-κB activity and IL-18 expression in naïve, 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 I/R-induced tissue injury (31% reduction in infarct size *vs.* sham). Confirming these *in vivo* results, sI/R 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 I/R 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

Fadi N. Salloum, Vinh Q. Chau, Jon-Erik Houser, Amit Varma, Nicholas N. Hoke, Antonio Abbate, Rakesh C. Kukreja, Virginia Commonwealth University Medical Center, Richmond, VA

Background: Emerging evidence suggests that the gaseous signaling molecule; hydrogen sulfide (H_2S) plays an important role in cardioprotection against ischemia/ reperfusion injury (I/R). Also, plasma levels of H_2S in patients with coronary artery disease (CAD) are significantly lower than in angiographically normal control subjects. Since H_2S-producing enzyme, cystathionine-γ-lyase (CSE) is expressed in the heart, we hypothesized that novel phosphodiesterase-5 (PDE-5) inhibitor, tadalafil (TAD) might utilize H_2S signaling in cardioprotection.
Methods: After obtaining baseline left ventricular (LV) function using transthoracic echocardiography (TTE), adult ICR mice were injected *i.p.* with TAD (1 mg/kg), vehicle (10% DMSO), TAD+dl-propargylglycine (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 I/R in patients with CAD. Moreover, these studies provide a novel mechanism involving H_2S 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 PPAR-γ Dependent Effect

Yumei 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 PPAR-γ agonist activity, protects against ischemia/reperfusion injury (I/R) 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 I/R 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 PPAR-γ inhibitor, on the effect of PIO on miR-29 levels in H2C9 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 (Caspase-3 activity) of H2C9 cardiomyocytes exposed to 16h hypoxia and 2h reoxygenation (SIR). Finally, we assessed the effects of miR-29 mimic and anti-sense inhibitor oligos on Mcl-1 (an anti-apoptotic Bcl-2 family member) cellular protein levels in H2C9 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 protected H9C2 cardiomyocytes 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-29s levels was blocked with GW9662. Overexpression of miR-29s reduced Mcl-1 cellular protein levels and transfection with inhibitor of miR-29 increased Mcl-1 levels. **Conclusions:** PIO downregulated miR-29a and miR-29c levels. This effect was dependent on PPAR-γ 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 I/R 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 non-IPC (0.82±0.1 vs 0.53±0.04 nmoles/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

Marlos R. Fernandes, Guilherme Silva, Cristiano Cardoso, Yi Zheng, Fred Baimbridge, 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 vs 1 episode at 5 and 10 days, respectively - p=0.08).There was no peri procedural death or tamponade. Overall, T sheep had LVEF 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/mm^2 - p=0.005) and a trend of higher cell proliferation (5.8±2.1 vs 3.9±1.7 positive nuclei/10^3 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.

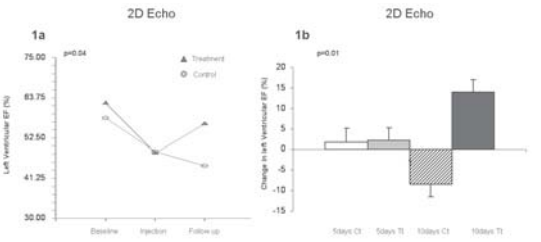


Figure 1: Left ventricular ejection fraction by 2D echocardiogram. a) results throughout the study; b) change of EF from baseline to follow up.

9:30 a.m.

1014-155 **Intravenous Infusion of Drag-Reducing Polymers: A New Approach to Improve Left Ventricular Function in a Rat Model of Myocardial Infarction**

Xianghui Chen, Kai Cui, Jiancheng Xiu, Yi Lao, Hui Xue, Daogang Zha, Jianping Bin, Yili Liu, Nanfang Hospital, Guangzhou, People's Republic of China

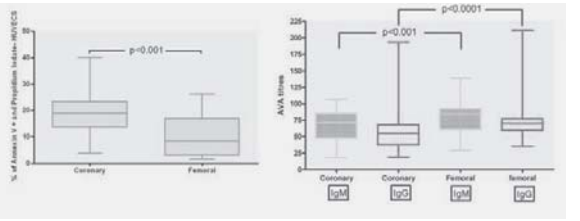
Background Blood soluble drag reducing polymers (DRPs) have been shown to reduce microvascular resistance and improve myocardial perfusion in a canine model of flow-limiting coronary artery stenosis. In animals with totally coronary artery occlusion, the effects of DRPs on cardiac function are unknown. In this study, we hypothesized the 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 50 μg/ml of DRPs (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. 24h after MI, noninvasive echocardiograpy 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 motion 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 24h post MI, DRP-treated animals had marked smaller LV end-systolic diameter (3.81±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, $p< 0.001$ and 1.91±0.35 *vs* 1.08±0.21mm, $p < 0.001$, respectively). Significant improvement in fractional shortening (34.84±10.35% *vs* 21.07±5.05%, p< 0.05) was also detected in rats infused with DRPs, paralleled with a lower wall motion score index (1.79±0.54 *vs* 2.52±0.15, p< 0.01) and smaller ratio of SM length to LV length (0.27±0.24 *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* 0.54±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 akinetic myocardium and extent of myocardial PD. This finding has important therapeutic implications to the treatment of acute coronary syndrome.

9:30 a.m.

1014-156 **Endothelial Cell Injury Induced by Intracoronary Sera in Patients With ST Elevation Myocardial Infarction**

Gopal Ghimire, Ann McCormack, Jonathan Spiro, Rajesh Kharbanda, Marlene Rose, Miles Dalby, 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 autoantigens, 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=26) were incubated for 4 hours with HUVECS in presence of complement. The cell injury was assessed with 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, 9.8) of the HUVECS incubated with the CA and 10.21 % (7.93) with FA underwent apoptosis (AV^+, PI^-), $p=6.7X1^{-5}$. 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), $p= 1.71X10^{-5}$ and 77.92 (23.7) , p= 0.00023.
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 compliment 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**

Jing Li, Wanli Xuan, Ran Yan, Emilie Jean-St-Michel, Michael Tropak, Andrew Redington, 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 PI-3 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 30min 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'-diindolylmethane (DIM) (which blocks transcriptional activity of β -catenin). rIPC significantly reduced infarct size (11.36±2.21% versus sham 39.31±7.02%, p<0.05) and this cardioprotection was reversed by pretreatment with Wortmannin or DIM (both p=ns compared with sham). Western blotting showed that rIPC significantly increased phospho-Akt (1.66±0.11 fold vs. sham), inhibited GSK-3b by increasing phosphorylated GSK-3b (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 PI-3K/Akt/GSK-3b signaling pathway, activation of which is associated with the novel finding of nuclear accumulation of β -catenin.

9:30 a.m.

1014-158 **In Vivo Myocardial Ischemia Reperfusion (I/R) Impairs Nitric Oxide Synthase (NOS) Activity: Potent Cardioprotection With BH4 Treatment**

Tiansheng Wang, Tse-Yao Wang, Jian Sun, Chun-An Chen, Fuchun Yang, M.A. Hassan Talukder, Jay L. Zweier, Davis Heart and Lung Institute, The Ohio State University, Columbus, OH

Tetrahydrobiopterin (BH4) is an essential cofactor of NOS that is highly redox-sensitive and causes NOS uncoupling during myocardial I/R. In an *in vitro* model of rat myocardial I/R, we have demonstrated that I time-dependently decreased cardiac BH4 content with concurrent decrease in eNOS activity and increase in NOS-derived superoxide. Supplementation of BH4 partially restored eNOS activity and suppressed eNOS-derived superoxide. It is well known that excessive superoxide formation and diminished nitric oxide generated by eNOS uncoupling have detrimental effects on myocardial I/R injury. Therefore, to address this issue in a clinically relevant model, in vivo regional myocardial I/R was performed in rats with measurement of myocardial NOS activity and infarction. Effect of BH4 treatment (100 μM *in vitro* or 10 mg/kg iv) was also investigated. Rats underwent 60-min regional myocardial I followed by R. Left ventricular samples from the area at risk (AAR) and non-ischemic area were harvested for NOS activity (L-arginine to L-citrulline assay). Myocardial NOS activity of AAR demonstrated a biphasic response where decreased NOS activity during I and early R (10-min) was followed by increased NOS activity. BH4 supplementation or treatment not only enhanced the NOS activity but also significantly reduced myocardial infarct size. These findings provide direct evidence that *in vivo* myocardial I/R results in NOS dysfunction, and that BH4 treatment restores NOS activity and enhances myocardial salvage.

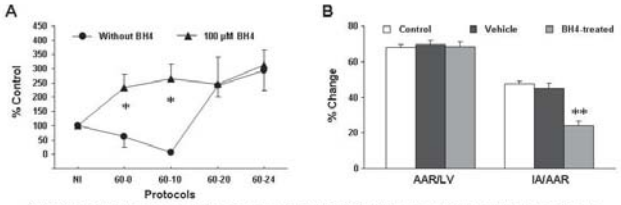


Figure legend: Values are presented as means ± SEM. **A (n = 3-4/group),** myocardial NOS activity of non-ischemic (NI) area and area at risk (AAR) at 60-min ischemia (60-0), 60-min ischemia and 10-min reperfusion (60-10), 60-min ischemia and 20-min reperfusion (60-20), 60-min ischemia and 24-hour reperfusion (60-24) without or with BH4 (100 µM) supplementation; NOS activity is expressed as percentage control (non-ischemic area). *P<0.05 vs. without BH4; **B (n = 5/group),** effects of preischemic BH4 (10 mg/kg/iv) treatment on left ventricular (LV) AAR and infarct area (IA) after 30-min LAD ligation and 24-hour reperfusion. Data is expressed as percentage change. **P<0.01 vs. vehicle.

9:30 a.m.

1014-159 **Candesartan and Omapatrilat Modulate Matricellular Proteins and Matrix Proteases and Limit Remodeling During Healing After Reperfused Myocardial Infarction**

Bodh I. Jugdutt, Arivazhagan Palaniyappan, Halliday Idikio, University of Alberta, Edmonton, AB, Canada

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 osteopontin (OPN) as well as other matrix metalloproteases (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, TIMP, 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-infarct 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 (IL)-6, tumor necrosis factor (TNF)-α, transforming growth factor (TGF)-β_1, Smad-2 and myelopeoxidase 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 Andenosine Monophosphate Kinase**

Kenneth R. McGaffin, Baobo 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 C57BL6 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 mean±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 1, a 37±6% decrease in FA binding protein, and a 46±3% decrease in FA translocase mRNAs by quantitative-PCR (all p<0.01). Leptin signaling, measured by phosphorylated/total (p/t) 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). Consistent with a switch to anaerobic metabolism, CAL caused a 32±3% decrease in p/t AMPK and 46±4% decrease in p/t ACC, with 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). In contrast, and consistent with the activation of oxidative metabolism, exogenous leptin increased p/t AMPK and ACC in sham hearts by 50±8% and 75±8%, respectively (both p<0.05 versus vehicle treated shams).
Conclusions: Combined, these data suggest that leptin mediates differential metabolic responses in normal and ischemic myocardium by regulating factors involved in both substrate transport and utilization, stimulating elements of aerobic metabolism when oxygen supply is abundant (sham mice) and glycolysis when oxygen is scarce (CAL mice).

9:30 a.m.

1014-161 **The Common Variant Rs9939609 in the FTO Gene Is Associated With Early-Onset Myocardial Infarction**

Diego Ardissino, Carlo Berzuini, Piera Angelica Merlini, Daniela Lina, Maria Francesca Notarangelo, Marco Tubaro, Pier Mannuccio Mannucci, Luisa Foco, Luisa Bernardinelli, David Altshuler, Sekar Kathiresan, Azienda Ospedaliero-Universitaria, Parma, Italy

Background: Type 2 diabetes and body mass index (BMI) are major risk factors for myocardial infarction. Recently, in several genome-wide association studies, a common variant, rs9939609, in the fat mass and obesity-associated (FTO) gene was discovered to associate with type 2 diabetes and body mass index (BMI). In the present study we investigated whether FTO rs9939609 relates to the risk of early-onset myocardial infarction.
Methods: The Italian genetic study of early-onset myocardial infarction is a nationwide prospective case-control study involving 1842 patients hospitalised for a first myocardial infarction before the age of 45 years, and 1842 healthy subjects matched for age, gender and geographical origin. The following baseline data were collected for each case and control: age, gender, family history, body mass index, smoking habits, hypertension, hypercholesterolemia, diabetes, cocaine use, physical activity and alcohol consumption. Genotyping was performed using the Sequenome MassARRAY platform.
Results: FTO rs9939609 was significantly associated with early-onset myocardial infarction (odds ratio 1,25, 95% confidence interval 1.08 to 1.45; p=0.000015) with a multiplicative model of the effect. The allele at FTO rs9939609 associated with higher BMI and risk for type 2 diabetes in earlier studies was associated with increased risk of myocardial infarction in the present study. After adjusting for type 2 diabetes, BMI, hypercholesterolemia and smoking FTO rs9939609 remained significantly associated with early-onset myocardial infarction (odds ratio 1.20, 95% confidence interval 1.05-1.38; p=0.006) suggesting that this variant may directly effect risk for myocardial infarction, independent of BMI. As previously reported FTO rs9939609 was also associated with BMI in this sample, more specifically the p-value of no association in the control group was equal to 0,01.
Conclusions: The allele at FTO rs9939609 corresponding to higher BMI and greater diabetes risk is associated with increased risk of early-onset myocardial infarction.

9:30 a.m.

1014-162 **Intramyocardial Injection of Human Adipose Tissue-Derived Stem Cells Improve Cardiac Function Following Acute Myocardial Infarction**

Xiaowen Bai, Yasheng Yan, Yao-Hua Song, Lilly H Droll, Daynene Vykoukal, Eckhard Alt, University of Texas, MD Anderson Cancer Center, Houston, TX

Background: Various stem cells have shown a the beneficial effect on cardiac regeneration after myocardial infarction (MI). Recently it has been shown that adipose tissue-derived stem cells (ASCs) from porcine improved cardiac function after MI. This study investigates for the first time the effect of human ASCs (hASCs) on the cardiac function after MI in mice.
Methods: MI was induced in mice by occlusion of the left anterior descending coronary artery (LAD). The mice were divided into two groups: 1) PBS group (n=8); 2) hASCs group (n=7). Half million hASCs from passage 4 in 30 µl PBS or PBS alone were injected into the infarcted hearts following the ligation of LAD. Cardiac function was assessed at 2-3 days before surgery (baseline), 1 week and 4 weeks after cell injection 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 end diastolic volume.
Results: MRI analysis showed that the left ventricular EF of PBS-injected hearts and hASCs-injected hearts was 63.74 ±3.32% (mean + SD) and 66.6 ±1.74% at baseline, respectively. EF in both groups declined by more than half (28.44± 9.92% for PBS 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 PBS-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 ± 9.42% with hASC treatment vs 18.7 ± 9.12% for PBS 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 TGFB1 and IGF1**

Brian Hynes, Arun HS Kumar, Sharon Weiss, Jeffery Schmeckpeper, Grainne 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 cardiotrophic 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 (25-28 Kg) 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, or CM + anti-TGFβ1, or CM + anti-IGF1, or X-vivo 15 (control) was administered in three 4 minute

cycles of balloon occlusion of the left circumflex artery. 24 hours post MI the animals were sacrificed and hearts sectioned from apex to base to quantify the infarcts. Cardiomyocyte apoptosis within the MI borderzone (50% MI and 50% normal myocardium/high power field) was evaluated by TUNEL assay, Caspase 9 activity and protein expression.
Results: Infarct sizes were not statistically different between the four groups. However CM significantly reduced the number of TUNEL positive cells/high power field vs. control (TUNEL 149.82±15.45 vs. 409.94±23.88). Caspase 9 protein expression (0.36±0.06 vs 1.00±0.10 Ab units) and activity (6.17±0.30 vs. 15.89±1.35/mg protein) was reduced in CM treated pigs. This response was significantly ($p<0.001$) attenuated by the addition of anti-TGFβ1 (308.98 ± 16.67 TUNEL positive cells/hpf; 0.71±0.08 Ab units; 11.16±0.63/mg protein) and anti-IGF1 (307.02 ±19.67 TUNEL positive cells/hpf; 1.01±0.13 Ab units; 15.83±1.13/mg protein) antibody to the CM.
Conclusion: EPC derived conditioned media reduces the apoptosis in the MI borderzone 24 hours post MI generation. This effect is mediated substantially through TGFβ1 and IGF1.

9:30 a.m.

1014-164 Collagen Matrix as a Delivery Vehicle Prevents Injected Stem Cells From Migrating out of Infarcted Myocardium to Remote Organs in a Rat Myocardial Infarction Model

Wangde Dai, Sharon L. Hale, Gregory L. Kay, Aarne J. Jyrala, Robert A. Kloner, Heart institute, Good Samaritan Hospital, Los Angeles, CA

Background: A limitation of cell therapy for heart disease is that stem cells injected directly into the myocardium are capable of entering the vasculature and migrating to remote organs. We determined whether collagen (COL) matrix as a delivery vehicle could prevent this migrating process.
Methods: A myocardial infarction (MI) was induced by ligation of the left coronary artery in Fischer rats. Seven days after MI, saline (SAL group, n=12), saline plus 2 million bone marrow derived rat mesenchymal stem cells (MSC) labeled with isotopic colloidal nanoparticles containing europium (NP) (SAL+MSC group, n=13), COL (COL group, n=13), or COL plus 2 million labeled MSC (COL + MSC group, n=13) were directly injected into the scar. Four weeks later, tissues from infarcted myocardium, non-infarcted myocardium, and remote organs (including lung, liver, spleen and kidney) were sampled. Distribution of grafted MSCs was quantitatively analyzed by measuring the NP radioactivity in these tissues.
Results: There was zero NP detected in the tissues that received saline or collagen alone. NP were detected in the heart and remote organs in SAL+MSC group. Labeled cells (expressed as cell number/g tissue weight) were present in 3/13 lungs (mean value equivalent to 12,724±7,060 cells/ g), 4/13 livers (12,301±5,924 cells/g), 11/13 spleens (57,228±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 2/13 lungs (4,631±3,176 cells/g, p=NS), 0/13 livers (0 cells/g, $p<0.05$), 4/13 spleens (24,060±17,373 cells/g, $p<0.05$), 0/13 kidneys (p=NS), 5/13 non-infarcted myocardium (51,522±21,548 cells/g, $p<0.05$). In COL + MSC group, NP were detected in 12/13 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.

ACC.POSTER CONTRIBUTIONS

1023

Myocardial Ischemia/Infarction--Basic; Unstable Ischemic Syndrome--Clinical; Acute Myocardial Infarction--Therapy

Sunday, March 29, 2009, 1:30 p.m.-4:30 p.m.
Orange County Convention Center, West Hall D

3:30 p.m.

1023-125 Extracellular Matrix Scaffold Restores Ventricular Function by Attenuating Adverse Ventricular Remodeling After Myocardial Infarction

John R. Frederick, J. Raymond Fitzpatrick, III, Ryan C. McCormick, David A. Harris, Ah Young Kim, Max J. Smith, Carine M. Laporte, Jeffrey R. Muenzer, Alex J. Gambogi, Y. Joseph Woo, University of Pennsylvania School of Medicine, Philadelphia, PA

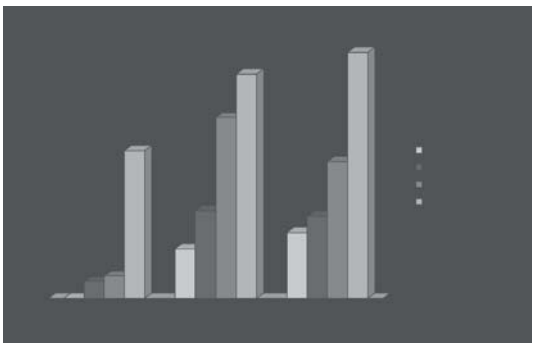
Background: Myocardial infarction (MI) causes cardiomyocyte death and subsequent scar formation, resulting in left ventricular (LV) dilation and progressive loss of cardiac function. Innate repair mechanisms are incapable of reversing this process. We hypothesized that the application of a scaffold of extracellular matrix (EMS) derived from decellularized porcine jejunal submucosa at the time of MI could mechanically reinforce the infarcted area of the LV. By adhering to surrounding normal myocardium, EMS could provide increased resistance to wall stress and reduce borderzone stretch, LV dilation, and subsequent adverse ventricular remodeling resulting in improved function.
Methods: Adult male Lewis rats (n=22) underwent LAD ligation to induce MI. At the time of ligation, EMS was affixed to the entire LV free wall which included the region of ischemia in the experimental group. Control animals received a similar array of sutures with no scaffold. Eight weeks following infarction, ventricular function was assessed by echocardiography, pressure-volume conductance, and cardiac output monitoring. Ventricular geometry was assessed by digital planimetric analysis of sectioned hearts.
Results: Compared to controls, echocardiographic analysis of experimental animals showed increased fractional shortening (21 vs 37%, p=.017) and increased ejection fraction (50 vs 71%, p=.013). The slope of contractility as measured by pressure-volume conductance was also greater in the experimental group (.3 vs .46, $p<.05$), as was cardiac output (27 vs 33mL/min, $p<.05$) Digital planimetric analysis of sectioned hearts showed increased borderzone thickness (1.5 vs 1.9mm, $p<.05$) as well as decreased scar fraction expressed as a percentage of the total section area (20 vs 15%, p=.001) and circumferential scar length (7.9 vs 5.4mm, $p<.05$).
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.

3:30 p.m.

1023-126 Very High Prognostic Value of Admission IL-6 Levels in Acute Myocardial Infarction. A Multiethnic Study

Nicole Cristell, Domenico Cianflone, Enrico Ammirati, Michela Banfi, Damiela Piraino, Alberto Monello, Alessandro Durante, Neal Uren, Hui Li, Dayi Hu, Attilio Maseri, Università Vita Salute San Raffaele, Milan, Italy

Background: Inflammation is implicated in many stages of Acute Myocardial Infarction (AMI) but its prognostic importance in a very early phase is not clear.
Methods: We enrolled 1099 patients with their first AMI as their first manifestation of coronary artery disease within 6 hours of symptom onset, in order to compare the prognostic value of C-Reactive Protein (CRP) and Interleukin-6 (IL-6) on in-hospital and 6-month adverse event rate in 3 ethnic groups: Italians, Scottish and Chinese from metropolitan areas. They had similar age, gender, risk factor and inflammatory marker elevation compared to controls.
Results: Patients presented with median levels of CRP and IL-6 more than double those of controls [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.



3:30 p.m.

1023-127 The Role of Heart-Type Fatty Acid Binding Protein in the Diagnosis of Acute Coronary Syndromes

Jonathan Rosman, Gita Kavala, Kotoro Obunai, Steven R. Bergmann, Beth Israel Medical Center, New York, NY

Background: Heart-type fatty acid binding protein (H-FABP) is a membrane bound protein which facilitates transport of fatty acid in the heart. It is being used outside the US for early diagnosis of myocardial infarction (MI). However, studies have shown inconsistent correlation with standard cardiac biomarkers.
Methods: Fifty patients admitted with ST-segment elevation MI (STEMI, n=25), non-STEMI (NSTEMI, n=15) or unstable angina (n=10) were evaluated. The CaridoDetect® med 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 58% (23); and the quantitative H-FABP was positive in 38% (15). No patient had a positive H-FABP with a negative initial troponin. The sensitivity and specificity of qualitative H-FABP assay for detecting MI were 0.57 (95%; CI= 0.41-0.73) and 0.8 (95%; CI= 0.44-0.97). The sensitivity and specificity of quantitative H-FABP assay for detecting MI were 0.38 (95%; CI= 0.23-0.55) and 1.0 (95%; CI= 0.69-1.00). The diagnostic accuracy of patients presenting within 6 hours is shown in Table 1.
Conclusion: Neither qualitative nor quantitative H-FABP appeared temporally earlier or provided increased sensitivity or specificity compared with troponin in diagnosing acute MI or unstable angina. Accordingly, the use of this biomarker as a diagnostic tool for MI is limited.

Table 1: Accuracy of initial troponin and H-FABP obtained on presentation in ACS patients presenting

	Sensitivity	95% CI	Specificity	95% CI
Initial Trop	0.78	0.56-0.93	0.83	0.36-1.00
H-FABP qualitative	0.57	0.34-0.77	0.67	0.22-0.96
H-FABP quantitative	0.50	0.28-0.72	1.00	0.54-1.00

3:30 p.m.

1023-128 **Ischemic Postconditioning Is a Powerful Antiarrhythmic Therapy With a Mechanism That Is Independent of Previous Standard Mechanisms Associated With the Cardioprotective Effects of Pre and Postconditioning**

Joan Dow, Anil Bhandari, Robert A. Kloner, Heart Institute, Good Samaritan Hospital, Los Angeles, CA, Keck School of Medicine at University of Southern California, Los Angeles, CA

Background: There have been few truly successful antiarrhythmic therapies in the setting of ischemic heart disease. Ischemic postconditioning has shown promise but its mechanism of action is unknown. **Methods:** Anesthetized female rats were subjected to five minutes of proximal coronary artery occlusion and five minutes of reperfusion. They were either not postconditioned (NP) or subjected to four cycles of 20 seconds reperfusion, 20 seconds reocclusion (postconditioning [Po]) before final reperfusion. ECG and blood pressure were monitored throughout. Proposed agonists and antagonists to Po, representing a number of mechanisms, were evaluated. **Results:** Po reduced the number of rats that exhibited any ventricular tachycardia (VT) from 9/10 in NP to 5/10 in Po and number with sustained VT (≥ 10 sec) from 7/10 in NP to 4/10 in Po. The median number of episodes of VT was 12 in NP and 0.5 in Po (p = 0.03), and the median duration of VT was 40 seconds in NP and 3.1 seconds in Po (p = 0.08). Cyclosporine A, a suppressor of the mitochondrial permeability transition pore (and a proposed agonist of Po) did not show a reduction in reperfusion induced ventricular arrhythmias compared to control NP rats (VT occurred in 11/14 NP rats and 10/15 Cyclosporine A treated NP rats); nor did Cyclosporine A reduce the episodes of sustained VT (5/14 in NP and 4/15 in Cyclosporine A NP rats). Thus Cyclosporine A did not mimic Po's beneficial effect on VT. The proposed antagonists of Po including Wortmannin (p13 kinase inhibitor; n = 7), 5 hydroxydecanoate (selective inhibitor of mitochondrial K^-_{ATP} channel; n =6), and 8 sulfophenyl theophylline (a blocker of adenosine receptor; n =10) failed to block the reduction in VT induced by Po (n = 26). **Conclusion:** Ischemic postconditioning is a powerful maneuver to reduce ischemia/reperfusion induced arrhythmias. However, the mechanism by which Po reduces reperfusion induced VT is independent of known pathways that have been implicated in the infarct sparing effects of Po including mitochondrial permeability transition pore, p13 kinase pathways, mitochondrial K_{ATP} channel and adenosine. Alternative protective pathways must exist to explain the antiarrhythmic effect of postconditioning.

3:30 p.m.

1023-129 **Intranasal Administration of Atrial Natriutetic Peptide Attenuates Left Ventricular Remodeling and Dysfunction Associated With Acute Myocardial Infarction in Rats**

Akiko Soyama, Tatsuji Kono, Yasushi Kitaura, Osaka Medical College, Takatsuki, Osaka, Japan

Background: Neuronally produced atrial natriutetic peptide (ANP) is a neuromodulator that inhibits the release of noradrenaline and angiotensin II from neurons. In rats with myocardial infarction (MI), a substantial decrease of ANP was found in the paraventricular nucleus (PVN) and supraoptic nucleus (SON), which are involved in cardiovascular and fluid regulation. We have demonstrated that alpha-hANP administered intranasally may access the brain directly. We hypothesized that alpha-hANP administered intranasally may attenuate progression of LV remodeling after MI. **Methods:**Forty rats were assigned to either alpha-hANP administered intranasally at a dosage 200μg in 10μL saline (ANP, n=20) or same amount of vehicle alone (MI, n=20), when the areas of ischemia (as a percentage of the free wall and septum) were determined by echocardiography at 30 minutes after left coronary artery ligation. Sham-operated rats (n=10) were used as controls. Hemodynamics and echocardiography were recorded at 3weeks later. **Results:**The areas of ischemia were similar, being 32±19 % and 29±9 % for the MI and ANP groups, respectively. Compared with the vehicle infusion, alpha-hANP significantly improved survival (53 % versus 17 %; *P*=0.04), attenuated left ventricular (LV) chamber dilation, and improved LV function. (*=*p*<0.05 vs. Sham, †=*p*<0.05 vs. MI) **Conclusions:**Alpha-hANP administered intranasally may access the brain compartment directly and may attenuate progression of LV dysfunction.

Table 1

	Sham (n=10)	MI (n=20)	ANP (n=20)
Heart rate (beats/min)	212±26	247±35*	222±35
LV systolic pressure (mmHg)	105±8	87±18*	91±6*
LV end-diastolic pressure (mmHg)	8±3	19±6*	12±4†
Peak dp/dt (mmHg/sec)	4070±610	2800±370*	3370±270*†
Negative dp/dt (mmHg/sec)	3750±380	1950±570*	2660±690*†
LV end-diastolic dimension (mm)	7.4±0.6	9.4±0.4*	8.6±0.7*†
LV ejection fraction (%)	52±2	19±3*	33±8*†

3:30 p.m.

1023-130 **Coronary Flow Velocity Reserve Gradually Decreases According to Glucometabolic State in Patients With Acute Myocardial Infarction**

Brian B. Løgstrup, Dan E. Høfsten, Thomas B. Christophersen, Jacob E. Møller, Hans Erik Bøtker, Kenneth Egstrup, Department of Medical Research, OUH Svendborg 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 ± 11.33 years) with first time AMI without any 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/kg/min). Coronary flow velocity reserve (CFVR) was calculated as the hyperaemic 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 the183 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_{TREND} = 0.005) 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.

3:30 p.m.

1023-131 **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 Kazmierski, Marcin Syzdol, Grzegorz Smolka, Wieslaw Cybulski, Edyta Paczkowska, Marek Krol, Andrzej Ochala, Boguslaw Machalinski, Mariusz Z. Ratajczak, Pawel 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 um), negative for lineage and CD45 markers, enriched for markers of embryonic pluripotent stem cells (Oct4, Nanog) and express CD133 and 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. MRI 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 pluripotent (Oct-4, 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) cells/μL; p<0.53]. VSELs 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 (0.1-4.9) 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 (0,04-0,5), 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.
Conclusion: Acute MI induced mobilization of VSEL SCs expressing pluripotent markers, early cardiac and endothelial markers, and chemokine receptor CXCR4.

3:30 p.m.

1023-132 **Relation of Coronary Thrombus Age With Plaque 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 Burzotta, Giampaolo Niccoli, Giovanni Paolo Talarico, Carlo Trani, Antonio Maria Leone, Rocco Mongiardo, Antonio G. Rebuzzi, Guido Fadda, 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 plaque rupture may long precede 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: 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 atherosclerotic elements were reported. Myocardial perfusion after PCI was assessed by the angiographic Myocardial Blush Grade (MBG) score and ST resolution (STR) > 70% on ECG.
Results: Forty five patients, 58±14 yrs old, 33 males entered the study. Detectable material, suitable for light microscopy analysis, was retrieved from 35 (78%) patients and 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 absence 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 ≥2, 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.

3:30 p.m.

1023-133 Ventricular Arrhythmias in Patients With Non-ST Elevation Myocardial Infarction: Incidence, Predictors and Mortality

Shuchita Gupta, Vincent Figueredo, Shweta Gupta, Albert Einstein Medical Center, Philadelphia, PA

Background: While serious ventricular arrhythmias are well-documented in patients with ST elevation myocardial infarction (STEMI), their incidence and behavior in patients with non-STEMI (NSTEMI) have not been examined in detail. We aimed to study the incidence, predictors and mortality rates for ventricular arrhythmias in patients with NSTEMI undergoing early invasive treatment.
Methods: Patients admitted between January and December 2004 with NSTEMI who underwent cardiac catheterization within 48 hours of admission were identified retrospectively. The presence and type of ventricular arrhythmias and mortality rate were noted. Data on cardiac risk factors, laboratory tests, findings on electrocardiogram (EKG), echocardiogram, cardiac catheterization and revascularization procedures done were collected. The need for defibrillation and/or anti-arrhythmic therapy was recorded.
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. VT/VF occurred within the first 12 hours in 40% of these patients. On univariate analysis, the presence of left bundle branch block (p=0.03), T wave inversions (p=0.005) on EKG, early coronary artery bypass grafting (p=0.012) and left ventricular ejection fraction (LVEF) (p=0.007) were significantly associated with VT/VF. Potassium and magnesium levels were not significantly associated (p=0.44 and 0.40 respectively). On multivariate analysis LVEF remained the only predictor of VT/VF. The risk of VT/VF increased by 33% for every 10% decrease in LVEF (odds ratio 0.97, 95% confidence interval 0.94-0.99).
Conclusion: The incidence of malignant ventricular arrhythmias in patients with NSTEMI was higher than reported previously (2.1 to 2.6%). The only significant predictor was LVEF. Among patients with NSTEMI who died, 50% had VT/VF. Further prospective studies are needed to better characterize ventricular arrhythmias in these patients.

3:30 p.m.

1023-134 Impact of Preventive Medications on Type of Clinical Presentation of Acute Coronary Syndromes

Robert W. Yeh, Malini Chandra, Alan S. Go, Kaiser Permanente of Northern California, Oakland, CA, University of California, San Francisco, San Francisco, CA

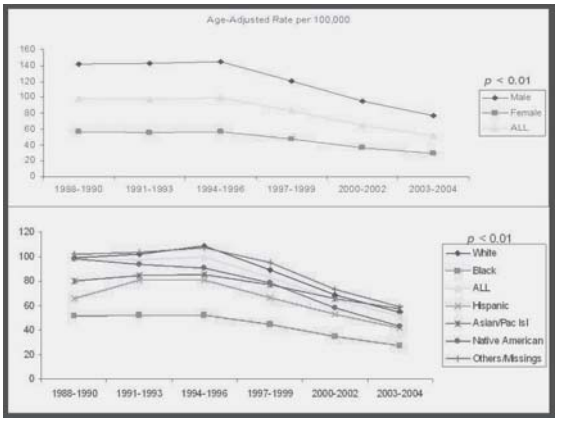
Background: Few studies have examined how preventive therapies may influence the nature of clinical presentation of acute coronary syndromes (ACS). We examined the association between receipt of preventive medications and the likelihood of presenting with unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI) or ST-elevation myocardial infarction (STEMI) among ACS patients.
Methods: We identified all adults hospitalized for diagnosed UA, NSTEMI or STEMI [using ICD-9 codes] between 1998-2007 within Kaiser Permanente of Northern California, an integrated healthcare delivery system caring for >3 million patients. Medication use was obtained from health plan pharmacy databases. The proportions of ACS patients presenting with UA, STEMI and NSTEMI were compared across study year. Multivariable regression was performed to examine whether prior cardioprotective drug usage affected the likelihood of presenting with UA, NSTEMI or STEMI, after adjustment for sociodemographics, vascular risk factors, and comorbidities.
Results: Between 1998-2007, 42,890 Kaiser patients were hospitalized for UA, 40,076 for NSTEMI and 20,895 for STEMI. The proportions of ACS patients presenting with UA and STEMI declined significantly over time (51.4% and 23.5% in 1998 vs. 31.7% and 16.4% in 2007, respectively, P<0.0001 for trend by year) while use of preventive therapies has increased. In multivariable regression, prior use of statins (OR 0.65), beta blockers (OR 0.64), ACE-inhibitors (OR 0.94) and thienopyridines (OR 0.84) were each independently associated with lower odds of presenting with MI compared with UA. In patients presenting with MI, prior use of statins (OR 0.91), beta blockers (OR 0.92), ACE-inhibitors (OR 0.88) and thienopyridines (OR 0.78) were all associated with lower odds of presenting with STEMI compared with NSTEMI, even after adjustment for potential confounders.
Conclusions: Patients with ACS were less likely to present with UA and STEMI over the past decade. This difference can be attributed, in part, to an increase in the use of cardiopreventive medications. Expanded use of preventive therapies appears to have favorably altered the pattern of presentation of ACS.

3:30 p.m.

1023-135 The Prevalence 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, Mehrtash Hashemzadeh, 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 State.
Method: 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 races 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.



3:30 p.m.

1023-136 Did Hurricane Katrina Affect the Incidence of Acute Coronary Syndromes in New Orleans?

Sandeep Gautam, Jonathan Menachem, Sudesh Srivastav, Patrice Delafontaine, Anand Irimpen, Tulane University School of Medicine, New Orleans, LA

Background: In August 2005, New Orleans was hit by Hurricane Katrina, the biggest natural disaster in the United States. Previous studies have shown an increase in acute myocardial infarction (AMI) in the immediate hours to weeks after natural disasters. The goals of our study were to detect any long-term increase in the incidence of AMI after Katrina and to investigate any pertinent contributing factors.
Methods: This was a single center retrospective cohort observational study. Patients admitted with AMI to Tulane University Hospital, in the two years before Katrina and in the two years after the hospital reopened (5 months after Katrina) were identified from hospital records. The two groups (pre- and post- Katrina) were compared for pre-specified demographic and clinical data.
Results: In the post-Katrina group, there were 246 admissions for AMI, out of a total census of 11,282 patients (2.18%), as compared to 150 AMI admissions out of a total 21,229 patients (0.71%) in the pre-Katrina group (p<0.0001). The post-Katrina group had significantly higher prevalence of unemployment (p=0.0003), lack of medical insurance (p<0.0001), medication noncompliance (p=0.0001), smoking (p=0.001), substance abuse (p=0.03), first-time hospitalization (p<0.001), local residents rather than visitors (p<0.0001), and people living in temporary housing (p=0.003). There was no significant difference in the racial distribution in the two groups.
Discussion: The role of chronic stress in pathogenesis of AMI is poorly understood, especially in the aftermath of natural disasters. Our data suggests that Katrina led to prolonged loss of employment and insurance, decreased access to preventive health services and an increased incidence of AMI. In addition, it appears that chronic stress

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-Menyar, Mohammed Zubaid, Wael Almahmeed, Kadhim Souliman, Ahmed Al-Motarreb, 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 8187 (1986 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). Atypical presentations (dyspnea and atypical chest pain) were more common in women than men (15.1% versus 8.1%; p=.001 and 8.0% versus 6.1% p=0.02). Women were less likely to be appropriately treated with thrombolytic therapy (79.9 %versus 83.6%), primary PCI (4.9 %versus 8.4%)β-blockers (57% versus 64%), clopidogrel (54% versus 60%), and glycoprotein IIb/III inhibitor (2.2% versus 9.5% p=.001) than men. Door to needle time was more prolonged in women (median, IQR: 40, 50 versus 35, 41 min). Women 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 4.0% 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.

1023-138 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. Mogabgab, Robert P. Giugliano, Marc S. Sabatine, Christopher P. Cannon, Stephen D. Wiviott, David A. Morrow, Satishkumar Mohanavelu, Elliott 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 8-hr intervals by symptom onset: morning (6AM-2PM), evening (2PM-10PM), overnight (10PM-6AM). We correlated pt characteristics with timing of symptom onset and calculated adjusted outcomes (using the baseline TIMI risk score) in InTIME-II-TIMI 17 (derivation set, N=15,031), with confirmation in ExTRACT-TIMI 25 (validation set, N=20,461).
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 MIs 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 2PM-10PM, but 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 lesser in-hospital delays with overnight lysis. Adjusted outcomes appear worst in pts with symptom onset from 2PM-10PM, in whom smoking is a major modifiable risk factor.

Characteristics/Outcomes of Patients with MI Pain Onset Time in 8 hour Intervals								
	InTIME-II-TIMI 17				ExTRACT-TIMI 25			
	Morning	Evening	Overnight	3-way P	Morning	Evening	Overnight	P value
Pain Onset	48.5%	30.2%	21.3%	<0.001	47.6%	31.3%	21.1%	<0.001
Mean Age(yr)	62.0	60.3	60.2	<0.001	60.5	59.4	58.9	<0.001
Obese (BMI≥30)	18.5%	20.4%	21.4%	0.002	20.3%	20.8%	23.4%	<0.001
Smoking	40.8%	50.0%	47.4%	<0.001	44.8%	49.8%	49.6%	<0.001
Prior MI	15.1%	16.3%	18.5%	<0.001	12.3%	13.1%	14.6%	0.001
Prior Revasc	5.8%	6.4%	7.1%	0.031	4.1%	4.0%	4.7%	0.165
Prior ASA	19.6%	18.8%	22.6%	<0.001	18.0%	15.9%	18.8%	<0.001
Prior BB	14.9%	14.9%	18.1%	<0.001	14.3%	13.1%	15.9%	<0.001
Anterior MI	42.3%	39.8%	44.7%	<0.001	43.7%	43.1%	45.6%	0.038
PTT >70	59.1%	45.0%	55.6%	<0.001	35.8%	34.6%	31.1%	0.001
CrCl >90	33.6%	34.6%	38.3%	<0.001	38.8%	38.9%	45.4%	<0.001
Mean SBP (mmHg)	138	140	138	0.007	133	134	133	0.064
Mean HR (bpm)	75	77	76	<0.001	75	77	76	<0.001
Pain-Lysis (hr)	3.1	2.9	3.3	<0.001	3.3	3.1	3.5	<0.001

30d Outcomes: Odds Ratios vs. Morning Pain onset Adjusted for TIMI Risk Score (P Values)						
	InTIME-II-TIMI 17			ExTRACT-TIMI 25		
	Morning	Evening	Overnight	Morning	Evening	Overnight
All Mortality	1.0	1.19(0.041)	0.97(0.72)	1.0	1.18(0.009)	1.01(0.90)
D/MI/Str/ Revsac	1.0	1.12(0.007)	1.12(0.011)	1.0	1.07(0.050)	1.17(<0.001)
D/C-Shock/ CHF	1.0	1.16(0.007)	1.08(0.19)	1.0	1.15(0.015)	1.06(0.41)

3:30 p.m.

1023-139 A Comparison of Cardiovascular Death Rates in the Same City During a Losing Versus Winning Super Bowl Championship

Robert A. Kloner, Scott McDonald, Justin Leeka, W. Kenneth Poole, Heart Institute, Good Samaritan Hospital, Los Angeles, CA, Keck School of Medicine at University of Southern California, Los Angeles, CA

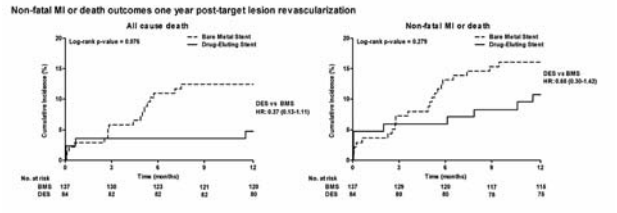
Background: A recent German Study suggested that viewing a stressful World Cup soccer match could increase cardiovascular events, but whether the Super Bowl could result in a similar phenomenon in the United States is unknown. The purpose of this study was to determine whether there were changes in local death rates and cardiovascular death rates, when a football team represented by that local population participated in the Super Bowl. To the best of our knowledge, this is the first study to investigate total and cardiovascular deaths surrounding a winning and losing Super Bowl within the same city. Los Angeles (LA) played in the Super Bowl twice, and within a four year time frame once on January 20, 1980 (LA Rams versus Pittsburgh Steelers in which LA lost), and on January 22, 1984 (LA Raiders versus Washington Redskins in which LA won). **Methods:** Data from Los Angeles County were analyzed for death rates from all causes; and deaths from circulatory, ischemic heart disease and acute myocardial infarction for three weeks surrounding the Super Bowl versus all other days (controls) from January 15 till end of February for 1980 to 1983 and 1983 to 1988. **Results:** The three weeks surrounding LA's losing 1980 game was associated with higher daily death rates in LA County (per 100,000 population) for circulatory deaths (1.2473 versus control 1.0660; p < 0.0001); death due to ischemic heart disease (0.8185 versus control 0.7144; p < 0.005); death from acute myocardial infarction (0.2664 vs. control 0.2316; p < 0.0193); and all deaths (2.3885 vs. control 2.0934; p < 0.0001). In contrast the three weeks surrounding the winning 1984 game were associated with a trend toward lower circulatory deaths (1.0556 versus control 1.1199; p = 0.0528), and a decrease in all deaths (2.1369 versus 2.3300; p = 0.0002). An analysis between 2000 to 2004, when LA did not have a professional team, did not show an increase in cardiovascular deaths surrounding the Super Bowl. **Conclusions:** These results suggest that the emotional stress of loss by a local sports team in a highly publicized rivalry such as the Super Bowl can trigger total as well cardiovascular deaths; in contrast, the positive emotions surrounding a win may actually lower deaths.

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. Kutcher, 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 1,451 (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 4% DES, p<0.001 and DES placement in 25% BMS versus 65% DES, p<0.001. At one year post-revascularization for TLR, the DES versus BMS hazard ration (HR) for all cause death 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.



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.

1023-141 Rationale of Decreasing LDL-Cholesterol Level <70mg/dL in Patients With Coronary Artery Disease: Intravascular Ultrasound-Virtual Histology Study

Jang-Ho Bae, Taek-Geun Kwon, Ki-Young Kim, Charanjit S. Rihal, Amir Lerman, Konyang University Hospital, Daejeon, South Korea, Mayo Clinic, Rochester, MN

Background: It is recommended that low dense lipoprotein-cholesterol (LDL-C) levels are reduced to less than 70mg/dL in patient with coronary heart disease. We sought to evaluate the effect of reduction of LDL-C level at coronary plaque composition by intravascular ultrasound-virtual histology (IVUS-VH).
Methods: We analyzed the distal and proximal segment (96 segments in 62 patients (mean 59.9years old) to the stent using IVUS-VH, which had residual plaque, during percutaneous coronary intervention and at routine follow-up coronary angiography after 7.7±1.5 months. Study subjects were taken lipid lowering agents (atorvastatin 10mg in 32 patients, rosuvastatin 10mg in 13 patients, pitavastatin 2mg in 17 patients) and divided into two groups according to LDL-C level measured at follow-up examination. Group1=LDL-C≤70mg/dL (19 segment), Group 2=LDL-C > 70mg/dL (74 segments).
Results: Total cholesterol, triglyceride and LDL-C were significantly decreased, whereas HDL-cholesterol was insignificantly increased during follow-up period. However, percent change of total cholesterol and LDL-C showed no significant difference among lipid lowering agents. In patient with LDL-C level less than 70mg/dL at follow-up examination, percent fibrous volume (1.11% vs. -1.07%, p=NS) and percent dense calcium volume (-1.84% vs. 2.62%, p=NS) showed no significant change. But percent fibrofatty volume (7.00% vs. -0.55%, p=0.015) was increased and percent necrotic core volume (-6.26% vs. 0.19%, p=0.007) was decreased in patients with LDL-C level less than 70mg/dL than those with LDL-C level over 70mg/dL. When we divided the study population into to groups based on the LDL-C level <100mg/dL, there was no significant differences of plaque compositions between 2 groups. Percent change of segment plaque burden showed no significant difference between two groups during follow-up period (-4.02% vs. 0.12%, p=NS).
Conclusions: This study showed that reduction of LDL-C level less than 70mg/dL, not 100mg/dL, is important in terms of the necrotic core of coronary plaque, which is a main component of vulnerable plaque.

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 Yin Chen, 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, 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 (68.95 ± 10.11 vs 62.83 ± 12.74, *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 thrombolysis compared with the pts without CVD. Intensive medical therapy was equally maintained in both groups.
Pts with CVD showed higher incidences of cardiac death [13.6% vs 5.1%, adjusted odd ratio (OR) 2.11, 95% confidence interval (CI) 1.60-2.79, *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*=0.003) 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 thrombolysis. 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.

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. 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: 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 represented the leading identifiable etiology (n=426, 56.1%). Of the cohort with disease of the coronary arteries, atherosclerosis was the leading abnormality; but less common in those <40 years (88.7%) compared to those ≥40 years (98.4%, p<0.001). Anomalous coronary artery (7.1% vs. 0.4%, p<0.001) and a significant coronary bridge (3.6% 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 vs. 25.3 kg/m^2, p=0.022).
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 Yin Chen, Seung Woon Rha, Yong Jian 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 4698 STEMI patients presented during working hours (weekdays 7 AM to 6 PM) versus off hours (weekends, holidays, and 6 PM to 7 AM weeknights).
Results: Overall, 2628 STEMI patients (55.9%) presented during off hours. Compared with patients presenting during working hours, off-hour 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 thrombolysis 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

Kjell C. Nikus, Markku 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 (29%), pathological Q waves without ST-elevation (23%), typical LBBB (6%), LVH without ST-elevation, except in leads aVR and /or V1 (7%), left main ECG (8%, n=97), other ST-depression and/or T-inversion (14%) and other findings, including normal ECG (13%).

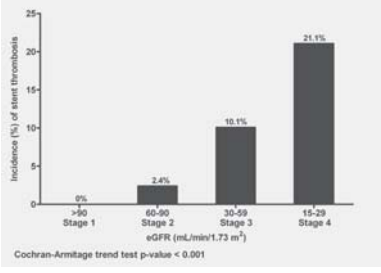
Results: All patients with the left main ECG pattern, who had a coronary angiography, had significant coronary artery disease, 8% had 1-vessel, 21% 2-vessel and 71% 3-vessel disease. In addition, 25% had significant, 50% or more, left main disease. In patients with other ECG patterns, the proportion 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

Nathan D. Lambert, Matthew T. Sacrinty, Terry R. Ketch, Samuel J. Turner, Renato M. Santos, Kurt R. Daniel, Robert J. Applegate, Michael A. Kutcher, David C. Sane, Wake Forest University Baptist Medical Center, Winston-Salem, NC

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 multivariate 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 towards increased risk for all outcomes.
Conclusions: In an acute MI population, stage CKD 3-4 (eGFR 15-59 ml/min/1.73m²) and proteinuria were identified as novel prognostic markers for ST. In addition, patients with both decreased GFR and proteinuria had higher incidences of all-cause mortality and non-fatal MI or death than patients with either condition alone.

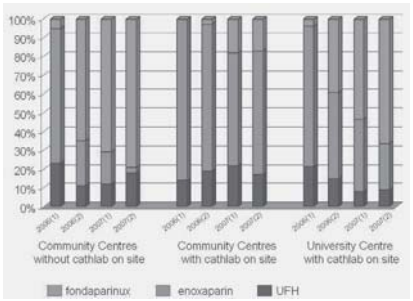


3:30 p.m.

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

Francois Schiele, Nicolas Meneveau, Marie-France Seronde, Vincent Descotes-Genon, Joanna Dutheil, 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 by 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-Ttreated 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-ACS 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.

	Tn+MB+	Tn+MB-	P value	Adjusted OR (95% CI)	P value
Acute ASA	97%	96%	0.056	1.19 (0.98-1.4)	0.08
Acute beta blocker	93%	92%	0.56	1.17 (1.01-1.35)	0.04
Acute clopidogrel	55%	50%	<0.01	1.22 (1.13-1.31)	<0.001
Acute GP 2b/3a	48%	32%	<0.01	1.87 (1.71-2.06)	<0.001
Acute Anti-thrombin	92%	89%	0.03	1.36 (1.20-1.54)	<0.001
Cath within 48 hours	71%	62%	<0.01	1.30 (1.19-1.42)	<0.001

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 variables, known CAD pts were less likely to receive early GP 2b/3a antagonists (OR 0.81 [0.78-0.85]), anti-thrombins (OR 0.87 [0.82-0.94]) and early angiography (OR 0.85 [0.82-0.89])(all p<0.01). In-hospital mortality was higher in known CAD pts, but after risk adjustment was no longer different (OR 0.91 95% CI 0.83-1.01). The most important independent predictors of in-hospital mortality (age, blood pressure, heart failure, dialysis, and peripheral vascular disease) were similar in the 2 groups. **Conclusions:** Pts with known CAD have a higher unadjusted in-hospital mortality compared to pts without known CAD that disappeared after risk adjustment. Known CAD appears to be a surrogate for other clinical variables for predicting in-hospital mortality in pts with NSTEMI.

	No Known CAD	Known CAD	P value
Age, yrs	65±15 (65)	69±13 (70)	<0.001
Systolic BP, mmHg	146±32 (145)	143±33 (142)	<0.001
Heart failure at presentation	18%	27%	<0.001
Dialysis	1.9%	3.8%	<0.001
Peripheral vascular disease	6.9%	19%	<0.001
Mortality	4.1%	4.9%	<0.001

3:30 p.m.

1023-150 Renal Dysfunction Adds Incremental Value to the TIMI Score

Jason Go, Ann Narmi, Aimin Chen, Dan Hilleman, Stephanie Maciejewski, John Sype, Aryan Mooss, Creighton University Medical Center, Omaha, NE

Background: The Thrombolysis in Myocardial Infarction (TIMI) risk score is a validated risk assessment tool to predict outcomes in patients with UA/NSTEMI. However, there are some concerns as to the broad applicability of the TIMI risk score in the real world setting because the score was derived from clinical trial cohorts and may not be as predictive in the general setting. Renal dysfunction is a well known independent predictor for adverse cardiovascular events in both clinical trials and community-based studies. It was not included in the original TIMI score criteria largely because the clinical trial cohorts excluded patients with renal dysfunction.
Objective: To evaluate if renal status adds incremental value to the prognostic utility of the TIMI risk score for UA/NSTEMI without sacrificing its ease of use and bedside applicability.
Methods: We did a retrospective study of 798 consecutive patients diagnosed with UA/NSTEMI from 2000-2003. The 7 TIMI risk variables were obtained along with renal status determined from the admission Creatinine. The Creatinine Clearance (CrCl) was computed using the Cockroft-Gault Equation. Patients were categorized as having renal dysfunction if their creatinine clearance was less than 45ml/min. Adverse outcomes were defined as an in-hospital composite of death, myocardial infarction, or severe ischemia requiring urgent revascularization. Logistic regression models were used to calculate Receiver Operator Characteristic (ROC) curves.
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: In a real world setting, addition of the renal status to the TIMI risk score added incremental value in prognostic accuracy without detracting from the ease of use and bedside applicability of the TIMI risk score.

3:30 p.m.

1023-151 Chronic Kidney Disease May Raise the Risk for Cardiovascular Disease by Increasing Number of Yellow Plaques in a Coronary Artery: Angioscopic Study

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

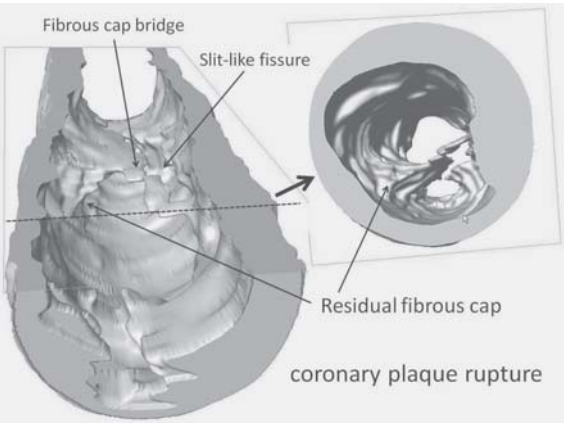
Background: Chronic Kidney Disease (CKD) has emerged as an independent risk factor of cardiovascular disease. On the other hand, we have revealed in the previous angioscopic study that number of yellow plaques (NYP) in a coronary artery is an independent indicator of cardiovascular events, and that patients 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 angioscopic examination were enrolled in this study. The infarct-related artery was angioscoically examined. NYP, maximum yellow color intensity (max YP; grade1, 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$\leq$ 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=0.041).
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.

3:30 p.m.

1023-152 Three-Dimensional Morphologic Analysis of Coronary Plaque Rupture Using Intravascular Ultrasound and Novel Stereoscopic Image-Processing System

Tatsuhiro 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 (S/L) of 0.43±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 (S/L > 0.3) had a greater maximum-CPK than those with a spindly cavity (S/L < 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.

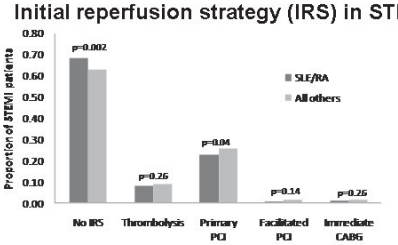


3:30 p.m.

1023-153 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
Results: 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 969 and SLE in 157 patients was reported. 17 patients had both RA and SLE. Baseline characteristics and medications were matched for gender, presence of ST-segment elevation on ECG; hospital transfer status, history of hypertension, diabetes mellitus, dyslipidemia, peripheral vascular disease, prior MI; and family history of CAD. Figure 1 illustrates an interesting trend towards *lower use of initial reperfusion strategy (p<0.05), primary PCI (p<0.05), facilitated PCI, and immediate CABG in patients with SLE or RA when compared to the other cohorts*. Though statistically insignificant, there is a trend towards longer length of in-hospital stay in patients with SLE or RA
Conclusions: During hospitalization for MI, patients with RA and SLE face a therapeutic disadvantage with lower use of all the modalities of reperfusion strategy



3:30 p.m.

1023-154 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 Conti, Erika Pagannone, Maria Beatrice Musumeci, Andrea Marra, Marco De Giusti, Filippo Maria Cauti, Eleonora Dito, Sebastiano Sciarretta, Camillo Autore, Massimo Volpe, II Faculty of Medicine, University of Rome, 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 myocardial PC with repair and substitution function, in response to endothelial damage and myocardial ischemia/ 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 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=5), post successful fibrinolysis early PCI (n=5). 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, LUC1), 2 (3rd day of admission), and 3 (discharge), CKMB and troponin I peaks and AUCs, were recorded. As normally distributed, continous 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 o 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.

3:30 p.m.

1023-155 Patient Characteristics in Myocardial Infarction (MI) and Non-MI Subsets Based Upon the New Universal MI Definition

Usman Javed, Waqas Aftab, John A. Ambrose, Deepak Thatai, Ralph Wessel, Mouatou Mouanoutoua, Fridolin Sy, Michael Weilert, Sundararajan Srikanth, Cyrus Buhari, UCSF Fresno, Fresno, CA

Introduction: Myocardial Infarction (MI) has recently been redefined and classified according to elevated Troponin I (TnI) and associated clinical criteria of myocardial ischemia. (*Circ* 2007;116;2634-2653). The incidence, demographic data, angiographic findings and hospital mortality of Type 1 (spontaneous plaque rupture/erosion), type 2 (altered supply demand) MI and non MI with increased TnI have not been previously reported.
Methodology: Over a 3 month period, all patients admitted to the hospital with TnI >0.04 ng/ml (MI cut off for TnI-Ultra, Siemens) were prospectively evaluated by the same physician. MI was defined as TnI >0.04 ng/ml, with either associated clinical, EKG and/or imaging findings. In-hospital or recent coronary angiograms were reviewed by the same two physicians.
Results (Table 1: Mean ± SEM): Of 701 patients with elevated TnI, 216(30.8%) had MI-143 (20.4%) had Type 1, 64 (9.1%) had Type 2 while 461 (65.8%) had no MI. 33(4.7%) could not be classified. Major risk factors were common in all groups.
Conclusions: Type 1 is the most common MI and is associated with higher TnI values (even without ST elevation MI) than the other groups and is more likely to undergo angiography. Type 2 MI is often associated with fixed disease and illicit drug use. Non MI patients with increased TnI commonly have non significant coronary disease in spite of a high in-hospital mortality.

Table 1. Patient Characteristics

	Type 1 MI	Type 2 MI	Non MI	p*
n	143 (20.4%)	64 (9.1%)	461 (65.8%)	
Peak TnI ng/ml	29.95 ± 5.29	1.68 ± 0.40	1.26 ± 0.34	<0.0001
Without STEMI	12.26±2.46	1.68 ± 0.40	1.26 ± 0.34	<0.0001
Age (years)	65.9 ± 1.6	64.2 ± 2.5	64.3 ± 0.8	0.68
Male	84 (58.7%)	35 (54.7%)	260 (56.4%)	0.83
Diabetes	61 (42.7%)	24 (37.5%)	170 (36.9%)	0.46
Hypertension	126 (88.1%)	53 (82.8%)	371 (80.5%)	0.11
Smoking	66 (46.2%)	30 (46.9%)	208 (45.1%)	0.95
Hyperlipidemia	113 (79.0%)	34 (53.1%)	243 (52.7%)	<0.0001
Obesity	54 (37.8%)	14 (21.9%)	122 (26.5%)	0.015
Illicit Drug Use (Cocaine/Methamphetamine)	2 (1.4%)	17 (26.6%)	21 (4.6%)	<0.0001
In hospital Angiogram	111 (77.6%)	14 (21.8%)	47 (10.2%)	0.0002
Any Angiogram	124 (86.8%)	32 (50.0%)	150 (32.5%)	<0.0001
Significant obstruction	111	25	78	<0.0001
Non-obstructive/Normal	13	7	72	<0.0001
ICU admission	15 (10.5%)	8 (12.5%)	74 (16.1%)	0.21
In-hospital mortality	15 (10.5%)	9 (14.1%)	67 (14.5%)	0.47

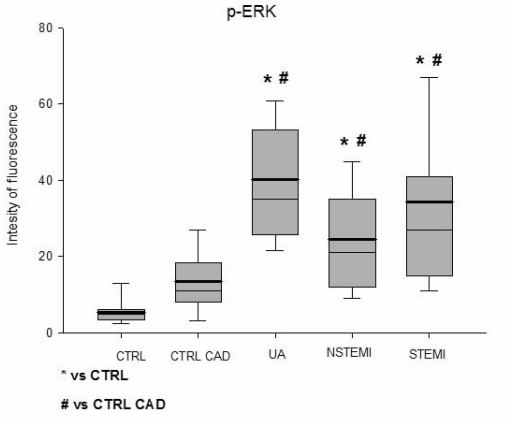
*ANOVA or Chi-Square

3:30 p.m.

1023-156 Mitogen-Activated Protein Kinases are Upregulated in T-Lymphocytes of Patients With Acute Coronary Syndromes

Ciro Indolfi, Annalisa Mongiardo, Carmen Spaccarotella, Daniela De Serio, Carla Vicinanza, Duino Boncompagni, Alessandro Ferraro, Angelo Leone, Valter Agosti, Daniele Torella, Antonio Curcio, Division of Cardiology, Magna Graecia University, Catanzaro, Italy

Background: Diagnosis of acute coronary syndromes (ACS) currently lacks of plaque instability markers. The aim was to estimate p-ERK1/2, p-JNK and p-p38 in T-cells of ACS patients.
Methods: Unstable angina (UA, N=22), acute myocardial infarction without ST elevation (NSTEMI, N=19) and MI with ST segment elevation (STEMI, N=19) patients underwent angiography and/or PCI. Healthy blood's donors (CTRL, N=8) and stable coronary disease patients (CTRL CAD, N=21), were analyzed as controls. CD3 and CD19 positive T-cells fraction was separated and incubated with antibodies against p-ERK1/2, p-JNK, p-p38. Fluorescence was analysed by flow cytometry and data confirmed by western blotting.
Results: FACS analysis showed a significantly increased p-ERK1/2 (mean of fluorescence 40±18) in UA patients, compared to CTRL (14±8; p<0.05, Figure). No change was found for p-JNK (UA, 12±7 vs. CTRL, 9±6). NSTEMI and STEMI groups showed a statistically significant increased phosphorylation of ERK1/2 (NSTEMI, 26±15; STEMI, 34±23), and JNK (NSTEMI, 36±19; STEMI, 40±28; p<0,05), compared to CTRL CAD. Diagnostic performance as determined by ROC curve analysis showed that 22.5 p-ERK intensity of fluorescence can significantly discriminate, with 78% sensitivity and 90% specificity, UA patients from stable angina patients.
Conclusions: Isolated T-cells from ACS patients demonstrated significant ERK, JNK and p38 activation. The identification of these distinct molecular clues could be useful for diagnosis of UA.



3:30 p.m.

1023-157 Necrotic Core Is a Major Component of Prolased Plaque and Is Associated With Post-Stenting Myonecrosis: Virtual Histology-Intravascular Ultrasound Analysis

Young Joon Hong1, Sang Wook Kim2, Myung Ho Jeong1, Yun Ha Choi1, Wang Soo Lee2, Kwang Je Lee2, Tae Ho Kim2, Doo Sun Sim1, Ju Han Kim1, Youngkeun Ahn1, Jeong Gwan Cho1, Jong Chun Park1, Chee Jung Kim2, Wang Seong Ryu2, Jung Chaee Kang1, 1The Heart Center of Chonnam National University Hospital, Gwangju, South Korea, 2Chung Ang University Hospital, Seoul, South Korea

Background: We used virtual histology-intravascular ultrasound (VH-IVUS) to evaluate the plaque components in prolapsed plaque.
Methods: The study group comprised 77 patients who underwent stent implantation and post-stenting VH-IVUS. Of these patients, 34 patients had plaque prolapse (PP) lesions (n=55) and 43 patients had no PP lesions (n=92). VH-IVUS classified the color-coded tissue into four major components: fibrotic (FT); fibro-fatty (FF); dense calcium (DC); and necrotic core (NC).
Results: Patients with PP had higher baseline creatine kinase-MB (6.4±7.7 U/l vs. 4.5±1.6 U/l, p=0.021), troponin-I (3.7±7.3 ng/ml vs. 0.02±0.02 ng/ml, p=0.001), and high-sensitivity C-reactive protein (1.8±2.7 mg/dl vs. 0.2±0.6 mg/dl, p<0.001). Cardiac enzyme was elevated more significantly after stenting in patients with PP compared with patients without PP [ΔCK-MB; +9.5±38.1 U/l vs. -4.0±26.1 U/l, p=0.008, and ΔcTnI; +5.0±16.6 ng/ml vs. -1.2±9.4 ng/ml, p=0.012, respectively]. Lesion site external membrane area (19.5±6.3 mm^2 vs. 15.6±5.6 mm^2, p<0.001), plaque area (15.1±5.6 mm^2 vs. 9.2±3.5 mm^2, p<0.001), and remodeling index (1.04±0.17 vs. 0.91±0.13, p<0.001) were significantly greater in PP lesions compared with non-PP lesions. In lesions with PP, PP area was 2.9±1.2 mm^2. In prolapsed plaque, FT component was greatest, however, NC component was also large (absolute plaque area: FT 0.44±0.43 mm^2, FF 0.07±0.09 mm^2, DC 0.04±0.08 mm^2, NC 0.10±0.22 mm^2, and relative plaque area: FT 68±19%, FF 14±13%, DC 5±9%, NC 13±16%, respectively). In patients with PP, although there were no correlations between % FT, % FF, % DC areas vs. Δcreatine-kinase MB and Δtroponin-I, % NC area in prolapsed plaque correlated with Δcreatine-kinase MB (r=0.311, p=0.026) and Δtroponin-I (r=0.388, p=0.005).

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 prolapsed plaque, and only NC component in prolapsed plaque is associated with post-stenting myonecrosis.

3:30 p.m.

1023-158 Thin Cap Fibroatheroma Is an Important Predictor for Rapid Plaque Progression; An Intravascular Ultrasound-virtual Histology Study

Jang-Ho Bae, Taek-Geun Kwon, Ki-Young Kim, Charanjit S. Rihal, Amir Lerman, Konyang University Hospital, Daejeon, South Korea, Mayo Clinic, Rochester, MN

Background: Vulnerable plaque (VP) is defined as a coronary plaque not only prone to thrombosis and/or rupture but also at risk for rapid progression. We sought to evaluate a lesion which shows rapid progression and to know clinical outcomes of intermediate lesion according to tissue type by intravascular ultrasound-virtual histology (IVUS-VH).
Methods: Study subjects consisted of 98 lesions in 94 patients (61.8±11.8 years old, 68 males) with intermediate coronary artery lesion (stenosed 30%~70%), who underwent IVUS-VH examination. Clinical follow up was done in 64 patients out of 65 eligible patients (98.5%) and follow up IVUS-VH were performed in 48 lesions/66 eligible lesions (72.7%).
Results: Mean minimal luminal diameter was 1.79±0.53mm and % diameter stenosis was 43.4±9.05% in total study subjects. Gray scale IVUS data showed that mean minimal luminal area was 5.4±2.1mm^2, number of lesion with minimal luminal area (MLA)<4.0mm^2 was 31 lesions (31.6%), and lesion length was 13.9±7.2mm. Fibrous cap atheroma was the most common lesion type (n=42, 42.9%), followed by thin cap fibroatheroma (TCFA, n=28, 28.6%), fibrocalcific atheroma (n=17, 17.3%), and pathological intimal thickening (n=7, 7.1%). The remaining 4 lesion could not be classified. There were 8 lesions in 7 patients showing rapid lesion progression, which required intervention during mean 8.7±2.9months follow up period. TCFA lesion type showed higher risk of rapid lesion progression (38.5% vs. 8.6%, p=0.014) than non-TCFA lesion and lesion MLA<4.0mm^2 showed also higher risk (35.3% vs. 6.5%, p=0.010) than lesion MLA ≥4.0mm^2. The risk of rapid lesion progression requiring PCI was highest (66.7%) in those presenting with MLA<4.0mm^2 and TCFA, followed by MLA<4.0mm^2 or TCFA (16.7%), and lowest (4.2%) in those without the above parameters.
Conclusions: This study suggests that TCFA is an important predictor for VP and IVUS-VH derived TCFA can be considered as MLA<4.0mm^2 by gray scale IVUS.

3:30 p.m.

1023-159 Prognostic Implications of the New Universal Definition of Myocardial Infarction

Rita Calé, Pedro Carmo, Nuno Santos, Jorge Ferreira, Carlos Aguiar, João Figueira, J. Aniceto Silva, Cardiology Department, Hospital Santa Cruz, CHLO, Lisbon, Portugal

Background: The clinical implications of the new ESC/ACCF/AHA/WHF universal definition of myocardial infarction (MI) are under debate.
Purpose: To evaluate the prognostic implications of the new diagnostic criteria -99th percentile of a normal reference population for cardiac troponin (cTn), as well as for the mass of CK-MB (MBm).
Methods: Prospective single centre registry of 444 consecutive patients (mean age 63±11 years, 20% female) admitted to an ICCU with non-ST-segment elevation acute coronary syndrome. We measured cTn I, MBm and CK-MB activity at admission and serially at 6, 12 and 24 hours. The peak value was used for analysis. We calculated the HR and 95% CI for death/MI at 1-year follow-up, adjusted for baseline demographic and clinical characteristics, between the presence or absence of MI using different criteria: 1) cTn I>99th percentile (0.04 ng/ml); 2) MBm>99th percentile (3.2 ng/ml); 3) MBm>2x ULN (12.2 ng/ml); 4) CK-MB activity>2x ULN (32U/L); 5) cTn I> best cut-off value (0.09 ng/ml).
Results: The new universal definition increased the incidence of MI in 86% for MBm >99th percentile but was not a predictor of death/MI at 1-year (see Table). Peak cTnI> 0.09 ng/ml was the only independent predictor of death/MI at 1 year.

Criteria of MI	MI, n (%)	Adjusted HR (95% CI) for death/MI at 1-year	p value
cTn I>99th percentile	294 (66.2)	1.52 (0.67-3.41)	0.32
MBm>99th percentile	221 (49.8)	1.77 (0.84-3.75)	0.14
MBm>2x ULN	119 (26.8)	1.30 (0.82-2.06)	0.26
CK-MB activity>2x ULN	94 (21.2)	1.08 (0.46-2.56)	0.86
cTn I>0.09	234 (52.7)	1.62 (1,05-2,51)	0.029

Conclusions: In a contemporary unselected population with non-ST-segment elevation acute coronary syndromes, the new universal definition of MI increased this diagnosis in 86% but was not an independent predictor of prognosis at 1-year.

3:30 p.m.

1023-160 Primary Percutaneous Coronary Interventions for Stent Thrombosis

Guido Parodi, Gentian Memisha, Benedetta Bellandi, Renato Valenti, Angela Migliorini, Ruben Vergara, Nazario Carrabba, 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 2,464 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 2,397 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%). Abciximab 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=0.034) 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=1843/2269), restenosis/reocclusion 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 reocclusion 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.

1023-161 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 de Werf, 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=5745), a randomized, placebo-controlled trial of pexelizumab in STEMI pts with primary PCI. Their pt/procedural 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=63) vs. native vessel (n=55) and their post-PCI TIMI 3 was 60.3% vs. 88.0% respectively (p=.043). 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=63) vs. native vessel (n=55) there was further discrimination of increased mortality (19.0% vs. 5.7%, p=0.05).
Conclusion: 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.

	No Prior CABG	Prior CABG	p
n	5617	128	
Age, yrs (median, IQR)	61(52-71)	69(58.3-76)	<0.001
Female, %	23.3	14.1	0.014
Hypertension, %	49.0	70.3	<0.001
Prior MI, %	10.9	64.1	<0.001
Prior PCI, %	9.2	36.7	<0.001
Prior HF, %	3.3	16.4	<0.001
Diabetes mellitus, %	15.7	25.0	0.004
Multivessel disease, %	40.2	81.9	<0.001
90-day death, %	4.6	11.9	0.001
Adj HR: 1.9, 95%CI(1.1-3.3) p=0.025			
90-day death, HF, shock, %	10.1	16.4	0.019
Adj HR: 1.1, 95%CI(0.7-1.7) p=0.816			

3:30 p.m.

1023-162 **Recombinant Human Interleukin-11 Has a Novel Role in the Mobilization of Endothelial Progenitor Cells and Reduction of Infarct Size in Mice**

Julius Aitsebaomo, 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 drug(s) to mobilize EPC in vivo.
Methods: In a preclinical study to evaluate the efficacy of mobilized EPC, saline or recombinant human interleukin-11 (rHIL-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 triphenyl-tetrazolium-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, and the infarct size was 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, this data shows that rHIL-11 has a novel role in reduction of infarct size and has a favorable effect on post-infarct remodeling suggesting a novel role of rHIL-11 as an adjunctive therapy for patients with AMI.

3:30 p.m.

1023-163 **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. Lopes, Hany Siha, 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 ≥ 1mm 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 can 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	LBBB with concordant ST-elevation	LBBB without concordant ST-elevation	P-value
CK-MB <=2x / troponin <=3x	13 (13.3%)	185 (3.3%)	<0.001	4 (7.7%)	9 (19.6%)	0.002
Pre-PCI TIMI flow 0-1	60 (61.3%)	4164(73.9%)	0.004	40 (76.9%)	20 (43.5%)	0.001
Pre-PCI TIMI flow 2-3	38 (38.8%)	1466(26.1%)	0.004	12 (23.1%)	26 (56.5%)	0.001
Primary PCI or in-hospital CABG	79 (80.6%)	5401(95.7%)	<0.001	46 (88.5%)	33 (71.7%)	0.037
"False Positive" STEMI	49(50.0%)	1639(29.0%)	<0.001	16(30.8%)	33(71.7%)	<0.001
90-Day mortality	5 (5.1%)	266(4.7%)	0.809	1 (1.9%)	4 (8.7%)	0.183
90-Day death/ heart failure/ shock	14 (14.3%)	572(10.1%)	0.179	7 (13.5%)	7 (15.2%)	0.804

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

3:30 p.m.

1023-164 **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^{SM} 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, 3,933 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 (18.8%) 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.

ACC.POSTER CONTRIBUTIONS

1032

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

9:30 a.m.

1032-125 **Fibrinolytic Therapy and Bleeding Complications: Risk Predictors From SWEDEHEART**

Jonas Oldgren, Lisa Wernroth, Ulf Stenestrand, 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 world-wide, 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 unselected Swedish STEMI patients.
Methods: The SWEDEHEART 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.

9:30 a.m.

1032-126 Predictors and Clinical Outcomes of Optimal Medical Therapy at Discharge in Patients With Acute Myocardial Infarction

Jang Hoon Lee, Shung Chull Chae, Hun Sik Park, Young-Jo Kim, Seung-Ho Hur, Chong-Jin Kim, Myeong-Chan Cho, Myung-Ho Jeong, Taek-Jong Hong, Doo-Il Kim, Kee-Sik Kim, Korean Acute Myocardial Infarction Registry Investigators, Kyungpook National University Hospital, Daegu, South Korea

Background: Only limited data are available for the recent trend of optimal evidence-based medical therapies (OMT) at discharge after acute myocardial infarction (AMI). We evaluated the predictors associated with OMT at discharge, and the association between the use of OMT at discharge and 6-month outcome. **Methods:** Between November 2005 and January 2008, we evaluated the discharge medications among 9474 post-MI survivors (6827 men and 2647 women; mean age=63.8±12.5 year-old) who did not have any contraindications to anti-platelet agents, beta-blockers (BB), angiotensin-converting enzyme inhibitors (ACE-I)/angiotensin II receptor blockers (ARB), or lipid-lowering drugs in the Korea Acute Myocardial Infarction Registry (KAMIR). OMT was defined as the use of all indicated medications. **Results:** Of the 9474 patients, 4735 (50%) received OMT at the time of discharge. The discharge prescription rates of anti-platelet agents, BB, ACE-I/ARB and lipid-lowering drugs were 98.8%, 72.2%, 81.2%, and 76.9%, respectively. In multivariate analysis, old age (age ≥65)(odds ratio [OR] 0.854, 95% confidence interval [CI] 0.738 to 0.987, p=0.032), history of dyslipidemia (OR 1.382, 95%CI 1.107 to 1.726, p=0.004), percutaneous coronary intervention (PCI) (OR 1.970, 95%CI 1.629 to 2.382, p<0.001), and serum creatinine levels (OR 0.586, 95%CI 0.461 to 0.745, p<0.001) were independent predictors of OMT. Overall, 6-month mortality was 1.3%. The OMT group had significantly lower 6-month mortality (0.9% vs. 1.7%, p=0.001). In multivariate analysis, OMT (OR 0.045, 95%CI 0.425 to 0.990, p=0.045), old age (OR 3.596, 95%CI 2.070 to 6.245, p<0.001), Killip class ≥2 (OR 2.142, 95%CI 1.405 to 3.264, p<0.001), PCI (OR 0.522, 95%CI 0.334 to 0.816, p=0.004), serum creatinine levels (OR 2.095, 95%CI 1.168 to 3.759, p=0.013), and body mass index (OR 0.921, 95%CI 0.861 to 0.986, p=0.018) were independent predictors of 6-month mortality after adjustment for confounding variables. **Conclusions:** Only half of post-MI patients are receiving OMT at the time of discharge despite current guidelines for management of AMI. The OMT is an independent predictor of 6-month mortality.

9:30 a.m.

1032-127 Worsening of Renal Function After Primary PCI in Patients With Acute Myocardial Infarction Is Not Determined by Radio-Contrast Dose but by Left Ventricular Dysfunction

Norihisa Ito, Hiroshi Ito, Katsuomi Iwakura, Atsunori Okamura, Yasushi Koyama, Motoo Date, Yoshiharu Higuchi, Koichi Inoue, Ryusuke Kimura, Hiroyuki Nagai, Yuko Toyoshima, Michio Imai, Makito Ozawa, Yukinori Okazaki, Masahiko Shibuya, Hidetaka Suenaga, Asuka Kubota, Kenshi Fujii, Sakurabashi Watanabe Hospital, Osaka, Japan

Background: It is well known that heart failure or use of radio-contrast worsen renal function and result poor clinical outcomes. However it remains unknown whether worsening of renal function is caused by pump failure or contrast-induced nephropathy in patients with acute myocardial infarction (MI) undergoing primary PCI.
Methods: Consecutive 237 patients with acute MI underwent primary PCI on the day of MI. We performed echocardiography to measure left ventricular ejection fraction (LVEF) and early peak mitral annulus velocity (e') at day-1 and day-14.
Results: Serum creatinine elevated by ≥0.3mg/dL after admission in 83 patients (35%), and we defined them as worsening group. There were no differences in baseline serum creatinine, estimated glomerular filtration rate or radio-contrast dose between two groups. LVEF (day-1 and day-14) and e'(day-14) were lower in worsening group. Incidence of proteinuria and peak CPK and CKMB were higher in the worsening group.
Conclusion. Worsening of renal function in acute MI patients is not determined by radio-contrast dose or baseline renal function but by left ventricular dysfunction, proteinuria and MI size.

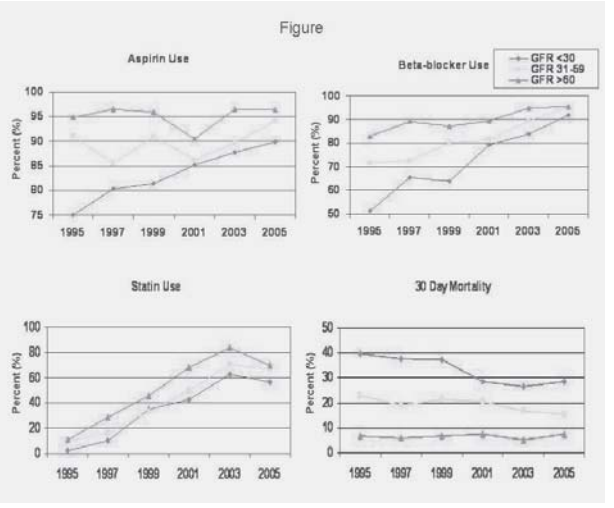
	Non-Worsening	Worsening	P value
Age, years	62±13	65±11	0.198
Male / Female	133/21	70/13	0.673
Hypertension, %	59	59	0.897
Dyslipidemia, %	61	41	<0.05
Diabetes mellitus, %	32	40	0.375
Proteinuria, %	32	46	<0.05
eGFR, ml/min/1.73m²	60.0±17.2	64.1±17.9	0.084
LVEF(day-1), %	54 ± 12	50 ± 10	<0.05
e' velocity(day-1), cm/s	6.18 ± 2.00	5.96 ± 2.33	0.456
E/e' ratio(day-1)	11.3 ± 4.16	11.5 ± 4.32	0.784
LVEF(day-14), %	59 ± 12	54 ± 14	<0.05
e' velocity(day-14), cm/s	5.81 ± 1.73	5.23 ± 1.41	<0.05
E/e' ratio(day-14)	10.2 ± 3.98	10.5 ± 4.15	0.637
Peak CPK, IU/L	2532 ± 2238	3844 ± 4030	<0.05
Peak CK-MB, IU/L	191 ± 164	273 ± 256	<0.05
Radio-contrast	208 ± 56	203 ± 50	0.466

9:30 a.m.

1032-128 Trends in the Medical Management and Thirty-Day Mortality Among Patients With Renal Dysfunction Admitted With Acute Myocardial Infarction

Paul A. Santolucito, Dennis A. Tighe, 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 disease admitted with AMI.
METHODS: Data from 6,219 hospitalized AMI patients (mean age= 70.7; 43.7% women) during 6 biannual 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.



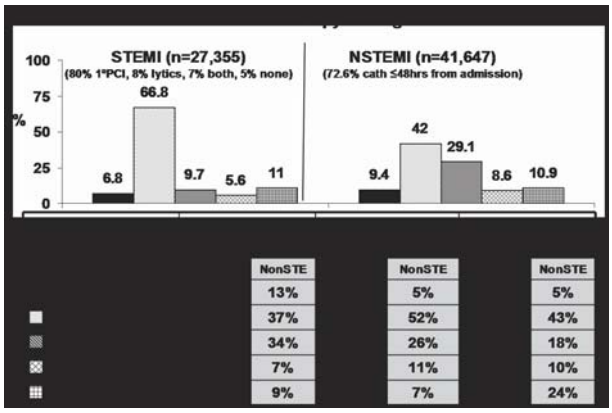
CONCLUSIONS: Data from this large population based study demonstrate favorable trends in the medical management and short-term outcomes among patients with renal disease admitted with AMI. Despite these trends, patients with renal disease remain at increased risk for adverse outcome after AMI.

9:30 a.m.

1032-129 Utilization of Antithrombotic Agents Among Patients Admitted With Myocardial Infarction in the ACTION Registry-GWTG

Mitul B. Kadakia, Nihar R. Desai, Karen P. Alexander, Anita Y. Chen, JoAnne M. Foody, Christopher P. Cannon, Stephen D. Wiviott, Benjamin M. Scirica, TIMI Study Group, Cardiovascular Division, Brigham & Women's Hospital and Harvard Medical School, Boston, MA, Duke Clinical Research Institute and Division of Cardiology, Duke University Medical Center, Durham, NC

Background:
Current practice guidelines, as well as recent trial data, support the use of unfractionated heparin (UFH), low molecular weight heparin (LMWH), bivalirudin, or fondaparinux in NSTEMI and STEMI. Little is known about how these agents are selected in current clinical practice.
Methods: Between January 2007 to June 2008, data for 41,647 patients with NSTEMI and 27,355 patients with STEMI were captured at 289 U.S. hospitals for the ACTION Registry-GWTG. Patients were stratified based on the antithrombin strategy selected during hospitalization to evaluate patterns associated with their use.
Results: 37,716 pts (90.6%) with NSTEMI and 25,493 pts (93.2%) with STEMI received at least one antithrombin agent. While LMWH was used more often in NSTEMI, UFH was the most commonly used agent in both NSTEMI and STEMI. The newer antithrombin bivalirudin was given to 11% while fondaparinux was given to <1% (Graph). There were significant differences in use of antithrombins by age (≥75), risk factors, concomitant medications and invasive care (Table). There were also significant differences in terms of unadjusted outcomes such as major bleeding, RBC transfusion, and in-hospital mortality.
Conclusions: While UFH remains the most often used antithrombin in patients with MI, key differences in antithrombin selection according to baseline characteristics and overall treatment strategies are evident. Further evaluation to clarify how antithrombin choice translates into clinical outcomes is warranted.



9:30 a.m.

1032-130 **Percutaneous Intramyocardial Stem Cell Injection and Electromechanical Mapping in Patients With Acute Myocardial Infarction: First-in-Man Study**

Korff 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 on 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(8) 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 periprocedural complications or major adverse events during the 12-month follow-up. EMM showed an improvement from baseline UV 45.5±14.3% to 59.3±19.2% of normal voltage (p=0.002) 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.

9:30 a.m.

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 "**F**X06 in **I**schemia/**RE**eperfusion 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 by late gadolinium enhanced (LGE) cardiac MRI. IS was measured both as total LGE zone and necrotic core (NC) zone. Patients were divided into early presenters (EP) and late presenters (LP) based on their pain-to-balloon-time of 0-3 hrs versus 3-6 hrs. The P-values were calculated using the Wilcoxon rank-sum test.
Results: The median pain-to-balloon time was ~3.1 hrs for the overall study population. A total of 96 patients were EP (n=44, FX06, n=52, placebo) and 99 patients were LP (n=49, FX06, n=50, placebo). The results are summarised below.

	IS at 5-7 days (NC) in grams	
	EP	LP
FX06	1.8 (0; 8.5)	1.42 (0; 9.1)
Placebo	4.9 (1.2; 10.9)	3.79 (0.1; 9.8)
	p=0.02	p=0.12
	IS at 5-7 days (LGE) in grams	
	EP	LP
FX06	19.1 (5.7; 45.6)	22.69 (12; 53.3)
Placebo	26.97 (12.6; 53)	27.39 (9.6; 39.1)
	p=0.12	p=0.94 (two-sided)
	IS at 4 months (NC) in grams	
	EP	LP
FX06	0.32 (0; 7.1)	4.04 (0.1; 13.6)
Placebo	3.14 (0.7; 7.2)	2.60 (0; 6.4)
	p=0.02	p=0.22 (two-sided)
	IS at 4 months (LGE) in grams	
	EP	LP
FX06	10.46 (4.7; 32.6)	23.29 (6.9; 44.2)
Placebo	22.93 (10.2; 38)	17.99 (6.5; 26.1)
	p=0.02	p=0.14 (two-sided)
Values are mean (IQR)		

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-balloon < 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.

9:30 a.m.

1032-132 **ST-Elevation Myocardial Infarction Care and Outcomes for the Oldest-Old**

Daniel E. Forman, Anita 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 years [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<0.0001). 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 (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 aged 75-84 and ≥85 only trended to benefit, suggesting differences persist related to reperfusion across age

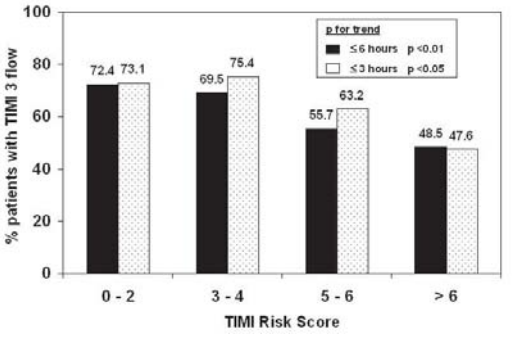
STEMI Patients	Age <75 (24,070)	Age 75-84 (4,273)	Age ≥85 (1,845)	P for trend
Reperfusion Contraindicated (%)	13	25	42	<.0001
Reperfusion Eligible	(20,121)	(3,099)	(1,038)	
Reperfusion (%)	96	90	85	<.0001
Reperfused	(19,686)	(2,863)	(900)	
Primary PCI (%)	81	78	78	<.0001
Door to ECG (median minutes, IQR)	6 (3-13)	8 (4-16)	10 (4-21)	<.0001
Door to Balloon (median minutes, IQR)	72 (55-91)	77 (59-98)	80 (63-103)	<.0001

9:30 a.m.

1032-133 **An Increased TIMI Risk Score Is Associated With a Decrease in TIMI Patency in Patients Treated With Thrombolytics 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 hours) 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 <0,0001) as well as TIMI 3 flow (p for trend 6), we could identify STEMI pts 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.



9:30 a.m.

1032-134 **Age and Outcomes After Myocardial Infarction With Persistent Total Occlusion of the Infarct Related Artery: An Analysis of the Occluded Artery Trial**

Adam H. Skolnick, Vladimir Dzavik, Venu Menon, Lea Liu, Aldo P. Maggioni, Antonio C. Carvalho, Luis Gruberg, Rudyney Eduardo Uchoa Azevedo, Erwin Schroeder, Camille A. Pearte, Harvey D. White, Gervasio A. Lamas, Judith S. Hochman, New York University School of Medicine, New York, NY

Background: OAT demonstrated that opening an occluded infarct-related artery in stable patients did not reduce events over 5 years. There was a trend toward interaction between age and treatment.
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 in either age group. Among younger patients MI rates tended to be higher in PCI vs. MED (HR 1.80 (CI:0.9-3.3), p=0.02), with no difference in older pts. During 5 year follow-up, younger patients more often had angina vs. older pts (H.R. 1.28, p=0.003), but rates were reduced with PCI vs. MED for both age groups (H.R. 0.77, p<0.0003).
Conclusion: Older OAT 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				
	Primary Outcome	Death	Fatal and Non Fatal MI	Class IV Heart Failure
Younger MED (%)	12.8	8.6	4.5	3.1
Younger PCI (%)	18.1	10.3	8.0	4.2
Older MED (%)	23.4	18.5	6.5	7.2
Older PCI (%)	20.9	14.9	4.6	6.7
Younger: PCI vs MED H.R. (99% CI)	1.4 (1.0-2.0) p=0.02	1.2 (0.7-2.0) p=0.40	1.8 (0.9-3.3) p=0.02	1.1 (0.5-2.3) p=0.73
Older: PCI vs MED H.R. (99% CI)	0.8 (0.5-1.4) p=0.37	0.8 (0.4-1.5) p=0.42	0.7 (0.3-1.9) p=0.38	0.9 (0.4-2.1) p=0.83
(The pre-specified significance was defined as p<0.01)				

9:30 a.m.

1032-135 **Impact of Pretreatment With Clopidogrel on Initial Patency and Outcome in Patients Treated With Primary Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction: A Systematic Review**

Pieter J. Vlaar, Tone Svilaas, Kevin Damman, Bart J. de Smet, Jan G. Tijssen, Hans L. Hillege, Felix Zijlstra, University Medical Center Groningen, Groningen, The Netherlands, Academic Medical Center, Amsterdam, The Netherlands

Background: The value of pretreatment with clopidogrel before primary percutaneous coronary intervention (pPCI) for ST elevation myocardial infarction (STEMI) is currently unclear.
Methods: Studies were retrieved through MEDLINE and Cochrane Register searches. Randomized trials were included when the research subjects were unselected patients with STEMI undergoing pPCI. Pilot trials, studies that enrolled patients undergoing rescue PCI, and studies with angiographic assessment not performed by core lab or 2 blinded investigators were excluded.
Treatment effect of clopidogrel was calculated using weighted logistic regression analyses. Jackknife estimation was used to establish the robustness of the multivariate model. A propensity score was calculated based on matching of alle baseline variables.
Results: 38 treatment groups (8429 pts) were included. Initial patency (TIMI 2/3 flow on initial angiogram) was higher in treatment groups in which patients received pretreatment with clopidogrel (34.3%; 95% confidence interval (CI), 32.9-35.8) compared with those in which patients did not receive clopidogrel before initial angiography (25.8%; 95%CI, 24.5-27.1). For extensive analyses see table.
Conclusions: Initial patency and clinical outcome were improved in treatment groups that received pretreatment with clopidogrel. These results in patients undergoing pPCI are in line with the experience of pretreatment with clopidogrel in elective patients, non-STEMI and thrombolytic studies.

Effect of pretreatment with clopidogrel on early reperfusion and adverse event rates.

		Multivariate-Adjusted Treatment Effect*			Jackknife Estimation*			Propensity Score-Adjusted Treatment Effect	
	Odds Ratio	95%CI	P	Odds Ratio	95%CI	P	Odds Ratio	95%CI	P
TIMI grade 2/3 flow	1.51	1.31-1.74	<0.0001	1.51	1.31-1.74	<0.0001	1.53	1.39-1.68	<0.0001
Mortality	0.57	0.38-0.85	0.0055	0.57	0.40-0.81	0.0019	0.52	0.41-0.67	<0.0001
Death/ reinfarction	0.54	0.38-0.75	0.0003	0.54	0.39-0.73	0.0001	0.50	0.40-0.62	<0.0001
*Adjusted for age, gender, history of diabetes mellitus, history of hypertension, heparin dose (high vs low dose), symptom duration, smoking, and year of publication.									

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. Umans, 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 emergency transferal to tertiary interventional 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, ^{99m}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). Multivariate analysis revealed that TIMI 0/1 flow grade at initial coronary angiography (OR 3.125, 95% CI 1.17-8.33, p=0.23), anterior wall localization of the myocardial infarction (OR 3.44, 95% CI 1.38-8.55, p<0.01), and development of pathological Q-waves (OR 5.07, 95% CI 2.10-12.25, p<0.01) were independent predictors of an infarct size > 12%.
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 TIMI 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 Tirofiban: Insights From the Facilitated Angioplasty with Tirofiban or Abciximab (FATA) Randomized Trial**

Nevio Taglieri, Francesco Saia, Cinzia Marrozzini, Vincenzo Guiducci, Guido Rocchi, Elena Biagini, 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 (PPCI) has shown to ameliorate left ventricular function recovery (LVFR). High-Dose Bolus (HDB) tirofiban 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 tirofiban or abciximab in ST elevated myocardial infarction (STEMI) patients treated with PPCI. 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; tirofiban, n=160) undergoing PPCI in the randomized Facilitated Angioplasty with Tirofiban or Abciximab trial. LVEF and wall-motion-score-index (WMSI) were assessed within 48-h post-PPCI and at 30-day. Among patients with left ventricular systolic dysfunction at baseline, LVFR was defined by one of the following: 1) increase of LVEF ≥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. tirofiban 49.3±10.1%, p=0.9) and at 30-day (abciximab 53.1±9.8% vs. tirofiban 52.5±10.2%, p=0.6). Likewise, there was no difference in WMSI post-procedure

(abciximab 1.56±0.34 vs. tirofiban 1.56±0.37; p=0.9) and at 30-day (abciximab 1.42±0.39 vs. tirofiban 1.42±49; p=0.9). Independent predictors of 30-day LVEF ≥50% were: pre-procedure TIMI-flow >0 (OR=2.4, 95% CI 1.32-4.34), anterior location (OR=0.25, 95% CI 0.15-0.42), and age (OR=0.97, 95% CI 0.95-0.99). Pre-procedure TIMI >0 was the only predictor of LVFR (OR=6.73, 95% CI 2.69-16.88).
Conclusions: This study showed no differences in terms of left ventricular function in patients undergoing PPCI treated either with abciximab or HDB tirofiban. Pre-procedure TIMI flow grade > 0 seems the most important predictor of favourable LVEF and LVFR at 30 days.

9:30 a.m.

1032-138 Lack of Change in Occurrence Rate and Long-Term Outcome of Patients With Post-Infarction Ventricular Septal Rupture: A 21-year Study

Abel E. Moreyra, Alan C. Wilson, Yingzi Deng, Nora M. Cosgrove, John B. Kostis, for the MIDAS Study Group, UMDNJ-Robert wood Johnson Medical School, New Brunswick, NJ

Background: Ventricular septal rupture (VSR) is a dreaded complication of acute myocardial infarction (AMI). The impact of recent improvements in therapy on the frequency and outcomes of post-infarction VSR is not well known.
Methods: We used MIDAS data of patients (pts) admitted with first AMI (n=399,491) for cases complicated with VSR (ICD9 429.71; n=367) in New Jersey between 1986 and 2006. Clinical characteristics, revascularization procedures and 30-day, 1 and 5 year mortality were analyzed in three seven-year time periods.
Results: 98% of all VSR cases occurred in the first AMI. Compared to pts without rupture, pts with VSR were older 71 vs 66 years (p=0.05), more likely to be female (53%, vs 43%, p<.0001), had more chronic renal disease (24 vs 9%), congestive heart failure (45 vs 32%) and had less diabetes (18 vs 25%) and hypertension (31 vs 44%); all p<.0001. By multivariate analysis, surgical repair significantly decreased 30-day mortality (O.R. 0.51, 0.31-0.84) but not 1-year mortality (O.R. 0.74, 0.46-1.19).

TRENDS IN VENTRICULAR SEPTAL RUPTURE AND SURVIVAL

Time Period	1986-1992	1993-1999	2000-2006	P value
VSR cases, n (%)	67 (0.05)	186 (0.15)	114 (0.06)	<.0001
Shock	31%	34%	39%	0.3
Anterior/Inferior MI	43% / 45%	43% / 44%	36% / 36%	0.008
Subendo. MI	1.5%	9.5%	16%	
PCI	3.0%	7.9%	16%	0.002
Surgical Repair	34%	45%	50%	0.02
Mortality - 30 days	40%	51%	40%	0.1
Mortality - 1 year	54%	60%	54%	0.47
Mortality - 5 year	61%	64%	60%	0.77

Conclusions: In this large series of pts with AMI complicated by VSR, the occurrence rate of rupture fluctuated but did not decrease over time. Significantly we observed an increase in the proportion of VSR occurring in subendocardial infarctions. Despite significant increases in the rate of PCI and surgery over time there were no improvements in associated mortality. Surgical repair was found to be associated with reduced short-term mortality, but the benefit was not maintained long-term.

9:30 a.m.

1032-139 CD34+ Cell Infusion after ST Elevation Myocardial Infarction is Associated with Improved Perfusion

Arshed A. Quyyumi, Jonathan R. Murrow, Fabio Esteves, James Galt, John Oshinski, Stamatios Lerakis, Salman Sher, Khan Pohlel, Edmund K. Waller, Douglas Vaughn, Emerson Perin, James Willerson, Dean Keriakis, Robert Preti, Andrew L. Pecora, Emory University School of Medicine, Atlanta, GA

Background: Cell therapy with intracoronary administration of unselected bone marrow cells has been shown to improve LV function in studies. The CD34+ bone marrow population is enriched for endothelial and other progenitors that may contribute to functional improvement by promoting neo-angiogensis and mitigating peri-infarct zone apoptosis. AMR-001 is an ongoing prospective, Phase I multicenter, escalating dose (5, 10, and 15 million CD34+ cells), cohort controlled study, designed primarily to assess the feasibility and safety of isolating autologous bone marrow derived CD34+ cells from patients after STEMI and infusing them into the infarct related artery. Secondary endpoints include assessment of cardiac function using MRI and quantitative resting LV perfusion with SPECT imaging. We hypothesize that CD34+ cell harvest and infusion will be safe and that the improvement in myocardial perfusion and function will be cell dose-dependent.
Methods: To date 31 patients (16 treated and 15 controls) have been enrolled and 6-month follow has been completed in the first 2 cohorts. Cell harvest using mini-bone marrow harvest (mean volume 409 ml) under conscious sedation was safe. Adequate numbers of viable Isolex selected CD34+ cells were safely infused via the infarct related artery, 7 to 10 days post STEMI following successful stenting.
Results: Compared to baseline, the change in SPECT total severity score and exercise tolerance were both improved in those receiving $10X10^6$ cells compared to patients receiving $5X10^6$ cells and controls; change in SPECT total severity score of -360, +8, and -62, respectively, p=0.01,$10X10^6$ vs. others; and change in exercise duration of +3.3, 0.6 and 1.9 minutes, respectively, p=0.05, $10X10^6$ vs. others. There was also a non-significant trend to a greater improvement in EF in the higher dose group; 5.8% in the $10X10^6$ compared to -0.8% and 2.6% in the $5X10^6$ cells and controls, respectively.
Conclusions: Intracoronary infusion of autologous bone marrow CD34+ cells administered during the repair phase after STEMI, at higher doses than previously given, is safe, and may be associated with improved functional recovery as a result of enhanced perfusion to the peri-infarct zone.

9:30 a.m.

1032-140 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 Francone, Iacopo Carbone, Emanuele Canali, Raffaele Scardala, Francesca Calabrese, Gennaro Sardella, Emanuela Algeri, 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 , patients were subcategorized into 4 quartiles on the basis of pain-to-balloon time distribution: <60 minutes (group A, n= 19), >60 to 150 minutes (group B, n= 17), >150 to 360 minutes (group C, n= 17), and >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 overtime in IS (8%, 11%, 12%, 18%, p=0.005, respectively), and MVO (0.5%, 1.5%, 3.7%, 6.6%, p=0.039, respectively) was observed, whereas salvaged myocardium at risk suddenly decreases 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?

Daniel Wiederkehr, Michelle Krukas, Lee Stern, Lois Lamerato, Dinara Makenbaeva, Essy Mozaffari, John Corbelli, Analytica International, Inc., New York, NY

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 2002-07. 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:1.28-2.65).
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.

1032-142 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 Lipiec, Maria Krzeminska - Pakula, Michal Plewka, Jacek Kusmierek, Anna Plachcinska, Remigiusz Szuminski, Tadeusz Robak, Anna Korycka, Jaroslaw D. Kasprzak, Medical University of Lodz, Lodz, Poland

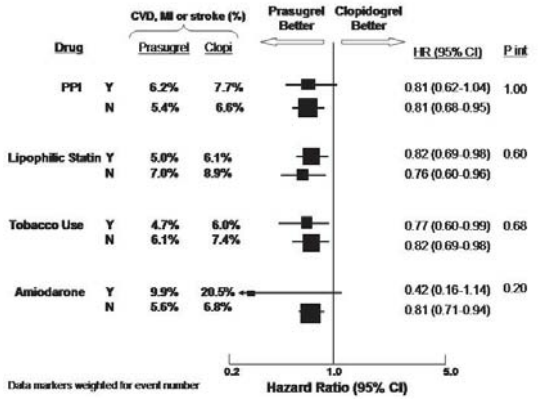
Background: We sought to investigate the impact of intracoronary injection of autologous mononuclear bone marrow cells (BMC) in patients with acute ST-elevation myocardial infarction (STEMI) on left ventricular volumes, global and regional systolic function and myocardial perfusion.
Methods: 39 patients 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 enhanced improvement in mean perfusion defect extent (p=0.02), left ventricular perfusion score index (p=0.03), infarct area perfusion score index (p=0.01) and 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.

9:30 a.m.

1032-143 Absence of an Interaction Between Drugs Metabolized by Cytochrome P450 Enzymes and the Benefit of Treatment With Prasugrel Versus Clopidogrel in Patients With Acute Coronary Syndromes Undergoing Percutaneous Intervention: A TRITON-TIMI 38 Analysis

Michelle O'Donoghue, Stephen D. Wiviott, Sabina A. Murphy, Eric R. Bates, Marc S. Sabatine, Jessica L. Mega, Nihar R. Desai, Carolyn H. McCabe, Elliott M. Antman, Eugene Braunwald, Brigham and Women's Hospital, Boston, MA

Background: Drugs that are metabolized by CYP P450 enzymes, including lipophilic statins and proton pump inhibitors (PPI), may alter the efficacy of clopidogrel by inhibiting its conversion to the active metabolite. Prasugrel is a novel thienopyridine that is more efficiently converted to its active form by the liver and improves outcomes in patients with ACS. It is unknown whether prasugrel offers comparable benefit over clopidogrel in patients who are or are not on P450-metabolized drugs.
Methods: TRITON-TIMI 38 randomized 13,608 subjects with ACS undergoing PCI to prasugrel or clopidogrel, in addition to standard therapy. The primary endpoint (EP) was CV death, MI or stroke. We performed a landmark post-hoc analysis from 3 days to capture medications at discharge.
Results: 9583 (70%) subjects were on a lipophilic statin and 3662 (27%)subjects were treated with a PPI. There was a consistent benefit of prasugrel over clopidogrel in reducing the primary EP in subjects who were on a lipophilic statin (HR 0.82, 95% CI 0.69-0.98) and those who were not (HR 0.76, 95% CI 0.60-0.96, P int=0.60). Similarly, prasugrel had a comparable benefit over clopidogrel in subjects treated with a PPI (HR 0.81, 0.62-1.04) and those who were not (HR 0.81, 0.68-0.95, P int=1.00). Significant treatment interactions were not observed for other relevant exposures, including tobacco or amiodarone.
Conclusion: Prasugrel improves outcomes after PCI in ACS, irrespective of use of many drugs hypothesized to alter clopidogrel metabolism.



9:30 a.m.

1032-144 Enoxaparin in Patients Not Undergoing Reperfusion for ST-Elevation Myocardial Infarction

Gabriel Tatu-Chitoiu, Dragos Vinereanu, Maria Dorobantu, Mircea Cinteza, Maria Udeanu, Olivia Manfrini, Crina Sinescu, Elvira Craiu, Marius Vintila, Mariana Radoi, Raffaele Bugiardini, Spitalul Clinic de Urgenta "Floreasca", Bucharest, Romania, University of Bologna, Bologna, Italy

Background: Enoxaparin therapy is beneficial in ST-elevation myocardial infarction (STEMI) patients receiving fibrinolytics 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 unfractioned heparin in the Romanian registry of ST-elevation 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 admission therapy with enoxaparin (no=1462) or unfractionated heparin (no=2350). Logistic regression was used to adjust the outcome of in-hospital death for baseline characteristics. Patients who were given enoxaparin were more likely to have history of hypertension (60.1% vs. 51.7%, p<.0001), lipid disorders (42.3% vs. 29.5%, p<.0001), and prior myocardial infarction (13.4% vs. 9.0%, p<.0001), and to present heart failure (48.6% vs. 34.3%, p<.0001). They were more likely to receive concomitant medication with aspirin and/or clopidogrel (93.7% vs. 83.5%, p<.0001). The rate of death was reduced by enoxaparin compared with unfractionated heparin (14.5% versus 16.9 %; OR, reference unfractioned heparin: 0.83; 95% CI 0.69-0.99, p<0.05). After adjustment for age, any clinical confounder and antiplatelet therapy with aspirin and/or clopidogrel, patients with enoxaparin had a 1.29-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 admission therapy.

9:30 a.m.

1032-145 The Classic Electrocardiographic Algorithm for Identification of the Right Coronary Artery as Infarct-Related Artery in Acute Inferior Myocardial Infarction Has Low Sensitivity in a Large Patient Cohort Undergoing Primary Percutaneous Coronary Intervention

Niels J. Verouden, Karel T. Koch, José P. Henriques, Jan Baan, René J. van der Schaaf, Marije M. Vis, Jan G. Tijssen, Jan J. Piek, Robbert J. de Winter, Academic Medical Center, Amsterdam, The Netherlands

Background: On the 12-lead electrocardiogram (ECG), ST-segment elevation (STE) in lead III exceeding that in lead II in combination with ST-segment depression (STD) in lead I or aVL is the generally accepted ECG algorithm for determination of the right coronary artery (RCA) as the infarct-related artery (IRA). However, this algorithm was derived from only few, small studies mainly from the thrombolytic era. We determined sensitivity and specificity of this ECG algorithm in a large cohort of patients undergoing primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI).
Methods: Between 2000 and 2007, 1131 patients with inferior STEMI underwent primary PCI. All 12-lead ECGs were recorded immediately prior to PCI and the IRA was determined during emergency angiography. ST-segment deviation was measured at the nearest 0.05 mV in all standard leads.
Results: Coronary angiography confirmed the RCA being the IRA in 895 patients (79%) with inferior STEMI. Application of the ECG algorithm resulted in 624 true positive cases of acute RCA obstruction (sensitivity 70%) and 170 cases with true negative result (specificity 72%). Current results deviate substantially from previously published data (**Table 1**).
Conclusions: The ECG algorithm of exceeding STE in lead III compared to lead II combined with STD in lead I or aVL shows a substantially lower sensitivity for the non-invasive diagnosis of acute RCA occlusion in a large cohort of inferior STEMI patients.

Table 1. Sensitivity, specificity, positive predictive value, and negative predictive value of ECG algorithm for prediction of the RCA being the IRA

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
ECG algorithm* by Zimetbaum PJ et al.† (N=255)	90	71	94	70
ECG algorithm in current cohort (N=1131)	70	72	90	39

* ECG algorithm for prediction of RCA occlusion: STE in lead III > lead II and STD in lead I and/or aVL > 1 mm.
† Extracted from: Zimetbaum PJ, Josephson ME. Use of the electrocardiogram in acute myocardial infarction. *N Engl J Med*. 2003;348(10):933-940.
RCA, right coronary artery; IRA, infarct-related artery; PPV, Positive Predictive Value; NPV, Negative Predictive Value.

9:30 a.m.

1032-146 Mitral Regurgitation Is an Independent Predictor of One-Year Mortality in ST-Elevation Myocardial infarction Patients Presenting in Cardiogenic Shock on Admission

Annemarie E. Engstrom, Krischan D. Sjauw, Marije M. Vis, Rene J. van der Schaaf, Jan Baan, Jr., Berto J. Bouma, Karel T. Koch, Robbert J. de Winter, Jan G. Tijssen, Jan J. Piek, José P. Henriques, Academic Medical Center, Amsterdam, The Netherlands

Background: Cardiogenic shock (CS) remains the most serious complication of acute ST-elevation myocardial infarction (STEMI). Mitral regurgitation (MR) is a frequent complication of STEMI and a well-known predictor of mortality in STEMI without CS. However, insight in the prognostic value of the presence and severity of MR is limited in

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 with 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.

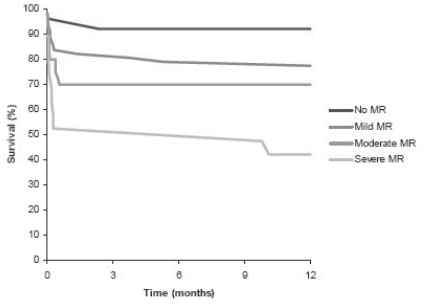


Figure 1 Kaplan-Meier estimates of 1-year survival according to grade of MR (log-rank test p<0.001). Total n=147; no MR n=26; mild MR n=62; moderate MR n=40; severe MR n=19.

9:30 a.m.

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

Rogerio Moura, Fernando Barreto, Marcus Costa, Carlos Barreto, Luciano Brasileiro, Fernando Tavares, Hospital Balbino, 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 (<6h).From them, 76 patients were submited 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 <0001) and Blush grade ≥2 (89.5% vs. 61 ,8% p = 0001). The need for IIb/IIIa inhibitors was lower in the TAC group (59% vs. 82% p <0005). 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

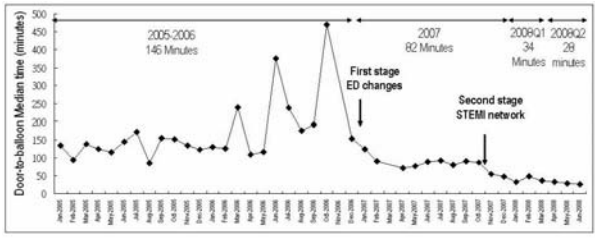
Background: Adipose tissue-derived stem cells (ASCs) show therapeutic value in the treatment of infarcted myocardium. However, there is little information about monitoring the fate of the injected ASCs in vivo. In this study, we used bioluminescence imaging for the first time to noninvasively evaluate the survival, proliferation and migration of human ASCs (hASCs) injected into the infarcted hearts of living mice.
Methods: hASCs were transducted with the lentiviral vector carrying luciferase gene. Half million hASCs were injected into the hearts of Scid mice (n=3) following the ligation of the left anterior descending coronary artery. Mice were imaged using the Xengene Imaging System to track the grafted hASCs at day 2, 7, 14, 21, 28 after cell injection, respectively. The intensity of in vivo bioluminescence signals (BLSs) was quantified by drawing the region of interest using Living Image Software v.3.0. Twenty-four days after surgery, the hearts were collected and the heart sections were subjected to immunofluorescence staining to detect injected hASCs using anti-lamin A/C antibody, which specifically binds to human cells.
Results: Our results show that the BLSs were detectable in the heart areas of 3 mice through 28 days of the experiment. During 2-14 days after cell injection, the intensity of BLSs was drastically reduced from $(2.33\pm0.93)\times10^6$ (mean±SD) to $(9.09\pm3.7)\times10^5$ in units of photons per second per centimeter squared per steradian. After that time, the BLSs gradually increased and arrived at $(1.40\pm1.2)\times10^6$ at day 28 after cell injection. No BLSs were observed in other organs. The immunofluorescence staining analysis showed 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 Chiou, 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 Univeristy, 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, morbidity and mortality.
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, two 24-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. STEMI 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 Thrombosuction in Patients With Acute Myocardial Infarction. Results of Long-Term Echocardiographic Follow-Up Study

Hyunmin Choe, Sung Yun Lee, Seung Hwan Lee, Min-Soo Ahn, Kyung Hoon Lee, Jang 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 thrombosuction 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 thrombosuction have never been evaluated.
Methods: From April 2005 to January 2008, we analyzed 111 patients who were underwent primary PCI with and without thrombosuction 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

(EF) were assessed at the baseline and the follow-up period. The wall motion score was analyzed and calculated according to the 16-segment model of the American Society of Echocardiography. Wall motion was visually assessed using endocardial motion and wall thickening and was quantitated using a 5-grade scoring system (1 = normal, 2 = hypokinesia, 3 = akinesia, 4 = dyskinesia, and 5 = aneurismal changes). LV Ejection fraction (EF) was measured by modified Simpson's method. To all patients, recovery of wall motion was defined as an improvement in wall motion of ≥ 2 contiguous segments in infarct-related segments between baseline and follow-up.

Results: Table

Conclusions: Our prospective randomized study shows that primary PCI with thrombosuction may be significant benefit to recovery of regional wall motion in patients with AMI.

	Suction Group (n=58)	Non-Suction Group (n=53)	P-value
Symptom to reperfusion time (min)	248.69 ± 154.73	233.17 ± 98.99	0.54
Peak CK-MB (ng/mL)	288.82 ± 206.08	278.21 ± 177.68	0.77
TIMI 3 flow after PCI (%)	52 (89.7)	48 (92.3)	0.63
Blush score ≥2 after PCI (%)	29 (50.0)	18 (34.6)	0.10
WMS Baseline	21.86 ± 4.99	22.08 ± 4.14	0.81
WMS Follow-up	20.47 ± 5.11	22.14 ± 4.92	0.09
LVEF Baseline (%)	51.75 ± 10.10	49.68 ± 6.65	0.22
LVEF Follow-up (%)	53.70 ± 9.84	51.75 ± 9.58	0.31
Recovery of regional wall motion (%)	28 (48.3)	14 (28.6)	0.03

9:30 a.m.

1032-151 Immediate ST-Segment Resolution Is Associated With Left Ventricular Function and Infarct Size Measured by Cardiovascular Magnetic Resonance in ST-Segment Elevation Myocardial Infarction Patients Treated With Primary Percutaneous Coronary Intervention

Joost D. Haeck, Niels J. Verouden, Wichert J. Kuijt, René J. Van der Schaaf, José P. Henriques, Marije M. Vis, Jan Baan, Jr., Jan J. Piek, Jan G. Tijssen, Robbert J. De Winter, Mitchell W. Krucoff, 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 left ventricular function and late enhancement to measure infarct size.

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 statistical significant (p<0.01).

	LVEDV (mL/m^2)	LVESV (mL/m^2)	EF (%)	Infarct size (% of LV mass)
Complete STR (N=110)	85.9 ± 18.8	40.2 ± 14.7	54.0 ± 8.1	8.8 ± 7.1
No complete STR (N=76)	95.2 ± 23.0	52.4 ± 21.6	46.5 ± 11.0	17.5 ± 12.0

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 moreover a clinical and simple tool for success of primary PCI.

9:30 a.m.

1032-152 Effect of Early Intensive Statin Therapy on Regression of Coronary Atherosclerosis in Patients With Acute Coronary Syndrome: Rationale for Lower Cholesterol Target in Diabetic Patients: Subanalysis of JAPAN-ACS Study

Hidenori Arai, Takeshi Kimura, Takeshi Morimoto, Takafumi Hiro, Katsumi Miyauchi, Hiroyuki Daida, Yoshihisa Nagkagawa, Yukio Ozaki, Tetsu Tamaguchi, Satoshi Saito, Kazuo Kimura, Masunori Matsuzaki, Japan-ACS investigators, Kyoto University Graduate School of Medicine, Kyoto, Japan, Yamaguchi University Graduate School of Medicine, Ube, Japan

Background: No study has been done to address the role of intensive lowering of LDL-cholesterol (LDL-C) with statins after acute coronary syndrome (ACS) in Japan.

Methods: A prospective, randomized open-label study with blinded endpoint evaluation was performed at 33 centers in Japan. Patients with ACS undergoing IVUS-guided PCI were randomly assigned to receive either 4 mg/day of pitavastatin or 20 mg/day of atorvastatin within 72 hours after PCI. The primary endpoint was % change in non-culprit coronary plaque volume (PV) by IVUS from baseline to 8-12 months follow-up. IVUS image was obtained in 252 patients. Out of 252, 74 patients were diabetic. LDL-C and non-HDL-C at the end of the study were divided into quartiles and the association with % PV change was assessed in total and diabetic patients by ANOVA.

Results: Decreasing LDL-C and non-HDL-C quartiles were associated with a progressively smaller plaque burden in total and diabetic patients (table). When the patients were divided into 2 groups according to their LDL-C (cutoff; 75 mg/dl in diabetes, 100 mg/dl in total) or non-HDL-C levels (cutoff; 100 mg/dl in diabetes, 130 mg/dl in total), each group of patients with lower LDL-C or non-HDL-C had a significantly greater reduction in PV.

Conclusions: Early intensive statin therapy in Japanese patients after ACS resulted in remarkable regression of coronary PV. Diabetic patients after ACS might have a benefit with intensive therapy to achieve the lower target level of LDL or non-HDL cholesterol in Japanese.

Table Association of % change in plaque volume with quartiles of lipid parameters

		quartile at follow up	1st	2nd	3rd	4th	P for trend
LDL-C	total	mean (range) [mg/dL]	53.2 (<66)	71.4 (66-79)	87.7 (79-98)	117.2 (98<)	
		% change in plaque volume (SD) [%]	-15.4 (12.7)	-20.3 (14.4)	-20 (13.0)	-14.2 (15.2)	0.025
	DM	mean (range) [mg/dL]	48.7 (<56.5)	69.1 (56.5-75)	88.6 (75-101.5)	119.4 (101.5<)	
		% change in plaque volume (SD) [%]	-16.5 (13.6)	-16.9 (14.5)	-10.6 (13.0)	-6.7 (15.2)	0.095
non HDL-C	total	mean (range) [mg/dL]	70.0 (<84)	90.1 (84-99)	109.6 (99-124)	143.9 (124<)	
		% change in plaque volume (SD) [%]	-15.6 (12.8)	-18.5 (12.7)	-21.4 (14.0)	-14.0 (15.6)	0.015
	DM	mean (range) [mg/dL]	63.9 (<82)	87.4 (82-95)	111.6 (95-125.5)	149.9 (125.5<)	
		% change in plaque volume (SD) [%]	-16.2 (14.0)	-15.3 (14.6)	-12.4 (13.3)	-6.9 (15.4)	0.217

9:30 a.m.

1032-153 The Effect of Pre-hospital Initiation of High Dose Bolus Tirofiban in ST-Segment Elevation Myocardial Infarction on the Incidence of Complete ST-Segment Resolution Before Primary Percutaneous Coronary Intervention: A Sub-analysis of the On-TIME 2 Trial

A.A.C.M. Heestermans, J.W. van Werkum, J.M. ten Berg, A. Mosterd, M.J. de Boer, A.T. Gosselink, T. Dill, G. van Houwelingen, C. Hamm, A.W.J. van 't Hof, Department of Cardiology, Isala Klinieken, locatie Weezenlanden, Zwolle, The Netherlands

Background: In patients with ST-segment elevation myocardial infarction (STEMI), complete ST-segment resolution (STR) might occur during transportation, before primary percutaneous coronary intervention (PCI). In a sub-study of the On-TIME 2 trial we looked for predictors of complete STR during transportation and evaluated whether pre-hospital initiation of High Dose Bolus Tirofiban (HDT) will increase the number of patients with complete STR before primary PCI.

Methods: Patients with STEMI were randomized to HDT or no HDT in the ambulance on top of 600 mg clopidogrel, 500 mg aspirin and 5000 IU unfractionated heparin and were referred for primary PCI. Complete STR before primary PCI was defined as ≥70% STR on the electrocardiogram (ECG) obtained pre-angiography as compared to the inclusion ECG.

Results: In a total of 1121 out of 1398 patients (80.2%) an interpretable ECG was obtained at inclusion and at pre-angiography. The incidence of complete STR pre-angiography was 16.8% (188/1121).

Patients with complete STR pre-angiography were younger (58.8 ± 11.0 yrs. vs. 62.2 ± 12.0 yrs, P< 0.001), were more often smokers (55.7% vs. 45.0%, P=0.008), had a shorter symptom-onset (SO) to diagnosis time-interval (91.9 ± 93.3 min. vs. 135.3 ± 170.3 min, P< 0.001) and more often were treated with HDT (55.9% vs. 48.0%, P=0.05). Patients who received HDT within 75 minutes after SO had the largest effect on resolution of ST segment deviation during transportation (24.6% vs. 17.0%, p=0.03). Patients with complete STR during transportation, before primary PCI had a significantly smaller enzymatic infarct size (650 ± 851 IU/L vs. 2139 ± 1816 IU/L, p<0.0001) and a significantly lower 30 day mortality (0.5% vs. 2.8%, p=0.045).

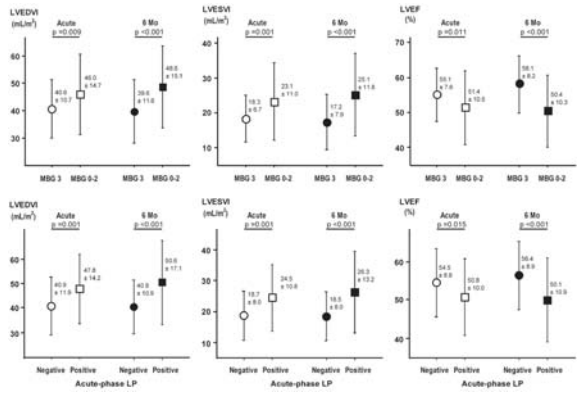
Conclusions: In patients with STEMI, pre-hospital initiation of high dose bolus tirofiban significantly increased the number of patients with complete ST-segment resolution before primary PCI. This was particularly seen in patients who received high dose tirofiban shortly after the onset of symptoms. Complete ST-segment resolution before primary PCI was associated with a small infarct size and a low mortality.

9:30 a.m.

1032-154 Impact of Myocardial Perfusion After Primary Angioplasty on Ventricular Conduction Delay and Left Ventricular Remodeling in Patients With ST-Segment Elevation Myocardial Infarction

Shinichi Okino, Shigeru Fukuzawa, Juji Sugioka, Atsushi Ikeda, Jumpei Maekawa, Soichiro Ichikawa, Takashi Uchiyama, Masayuki Inagaki, Funabashi Municipal Medical Center, Funabashi, Japan

Background: The aim was to assess the impact of myocardial perfusion after primary angioplasty on ST-segment elevation myocardial infarction (STEMI) on ventricular conduction delay and remodeling. **Methods:** Myocardial blush grade (MBG) was assessed at the end of primary angioplasty in 159 STEMI patients. Signal-averaged electrocardiography to detect late potentials (LP) and echocardiography were examined during the acute phase and six months later. **Results:** Seventy-seven patients obtained MBG 3 and 57 had positive LP in the acute phase. LP was less found in MBG 3 (23.4% v.s. 47.6%, p=0.001). Indexed left ventricular end-diastolic volume (LVEDVI) and end-systolic volume (LVESVI) were larger and left ventricular ejection fraction (LVEF) was lower in MBG 0-2 patients in the acute phase and at six months. LVEDVI and LVESVI were larger and LVEF was lower in positive-LP in the acute phase and at six months. Multivariable analysis revealed MBG 0-2 and positive LP were independent predictors of LVESVI>30 mL/m^2 (odds ratio (OR) 3.13 [95%CI 1.14-8.62], p=0.027, OR 4.36 [1.76-10.8], p=0.001, respectively) and LVEF <45% (OR 3.25 [1.11-9.50], p=0.031, OR 5.18 [1.86-14.5], p=0.002, respectively) at six months. **Conclusions:** MBG was associated with LP in the acute phase. Furthermore, both MBG and LP had an impact on LV remodeling.



9:30 a.m.

1032-155 **Treatments and Prognosis of Acute Myocardial Infarction Due to the Occlusion of the Left Main Coronary Artery in the Contemporary Coronary Reperfusion Era**

Masaya Usami, Yasuhiko Sakata, Masahiko Shimizu, Shinichiro Suna, Sen Matsumoto, Hiroshi Sato, The OACIS Investigators, Osaka University Graduated School of Medicine, Suita-city, Japan

Background: Previous studies have shown that acute myocardial infarction due to the occlusion of the left main coronary artery (LMCAMI) is associated with poor prognosis. Due to the limited number of the sample size in these studies, however, the results including mortality varies with respect to each study. Accordingly, a study to investigate the prevalence, management and outcome of LMCAMI with a large cohort is required. **Methods:** Among consecutive 8,025 patients registered in the Osaka Acute Coronary Insufficiency Study (OACIS) between 1998 and 2007 (74.7% male, age 65.9±11.8 y.o.), 178 patients (2.2%) had LMCAMI (75.3% male, age 67.6±11.8 y.o.).We sought to observationally assess treatments and prognosis of LMCAMI using the database of the OACIS. **Results:** Among them, 132 patients (age 67.5±12.2 y.o.) received primary PCI for LMCAMI lesion and remaining 40 patients (age 68.1±10.8 y.o.) received emergent CABG. Subjects received PCI had higher prevalence of cardiogenic shock, and PCPS use (53.8% vs 25.0%, p=0.004, 52.3% vs 17.5%, p<0.001). The 30-day mortality of LMCAMI was significantly higher than that of non-LMCAMI (37.6 % vs 4.6 %, p<0.001), and it was particularly high when treated with PCI, compared with when treated with CABG (42.4% vs 17.5%, p=0.005). In addition, even after discharge, the long term mortality (mean follow-up, 803 days) after discharge in LMCAMI was higher than in non-LMCAMI (14.0%, 8.3%, 7.1%, 4.6% for LMCAMI, AMI with 3-vessel disease, 2-vessel disease, and 1-vessel disease, respectively, p<0.001). However, there was no difference in major adverse cardiac events between those who survived LMCAMI with PCI and CABG (21.1% vs 23.3%, p=0.66). **Conclusions:** The present investigation with a relatively large cohort showed that prognosis after LMCAMI is still poor even in the contemporary reperfusion era. In-hospital mortality of LMCAMI patients treated with PCI was worse than those with CABG, possibly reflecting the patients' background, whereas mortality after discharge was similar between patients treated with PCI and CABG. Further efforts to improve survival after LMCAMI may be needed.

9:30 a.m.

1032-156 **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, Loic Belle, Guilaume 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

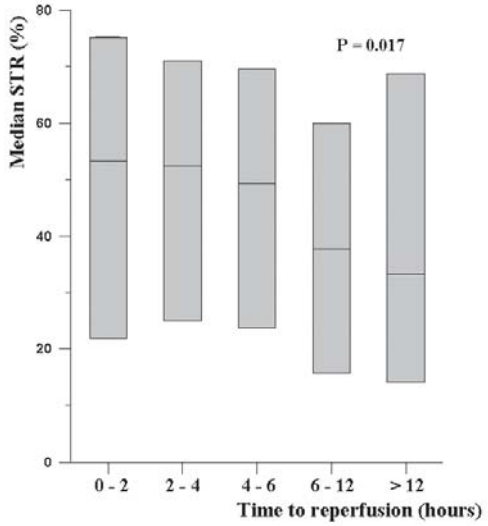
Background: Prehospital treatment with a high dose of tirofiban brings benefits in patients with STEMI who undergo primary angioplasty. In these patients, prehospital high dose of tirofiban had not been directly compared to the administration of a high dose of tirofiban in the cath-lab.
Methods: The 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 serum troponin I and management delays were secondary end-points.
Results: On september 25th, all 300 patients had been included in the AGIR2 study. The data are being processed for analysis.
Results will be available by the end of december 2008.
Conclusions: This randomized controlled trial will bring important evidence regarding the timing of initiation of a GPIIb/IIIa inhibition in patients managed in the prehospital setting for an acute myocardial infarction.

9:30 a.m.

1032-157 **ST-Segment Deviation Resolution After Primary Percutaneous Coronary Intervention Is Inversely Associated With Time to Reperfusion in Patients With Acute Myocardial Infarction**

Niels J. Verouden, Wichert J. Kuijt, Joost D. Haeck, Karel T. Koch, José P. Henriques, Jan Baan, René J. van der Schaaf, Marije M. Vis, Jan G. Tijssen, Jan J. Piek, Robbert 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, 1900 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.



9:30 a.m.

1032-158 **Association Between Heart Rate Variability and Platelet Reactivity After Acute Myocardial Infarction**

Giancarla Scalone, Ilaria Coviello, Pasquale Santangeli, 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 by 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^{-7} M). Cardiac autonomic function was assessed by heart rate variability (HRV) on 24-hour ECG Holter recordings.
Results. An inverse correlation was found between HRV variables and both PFA-100 aggregation time and basal and post-ADP MPA formation (Table).
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.

Correlation between HRV parameters and platelet reactivity variables

	SDNN	HF
AT (PFA-100)	R=0.6, P=0.025	R=0.4, P=0.19
MPA Baseline	R=-0.7, P=0.008	R=-0.6, =0.015
MPA ADP	R=-0.6, P=0.012	R=-0.6, P=0.017

9:30 a.m.

1032-159 **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**

Demosthenes B. Panagiotakos, Christina Chrysohoou, Panagiotis Aggelopoulos, 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 had an acute coronary syndrome (ACS). **Methods**: During 2006-2007, 351 post ACS patients (66±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: 0.552±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:0.598±0.036, p=0.05), men (AUC:0.551±0.03, p=0.09) and diabetic patients (AUC:0.591±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.

1032-160 **How Serum Levels of Glucose and Inflammatory Biomarkers Upon Presentation Affect 1-Year Mortality in Non-diabetics With Acute Coronary Syndromes**

Stefanos G. Foussas, Michael N. Zairis, Stamatis Makrygiannis, Dimitrios Mytas, Georgios Z. Tsiaousis, Nikolaos Patsourakos, Joseph Papadopoulos, Andreas Melidonis, Anastasios Koutsovasilis, Stylianos Handanis, Tzanio State Hospital, Piraeus, Greece

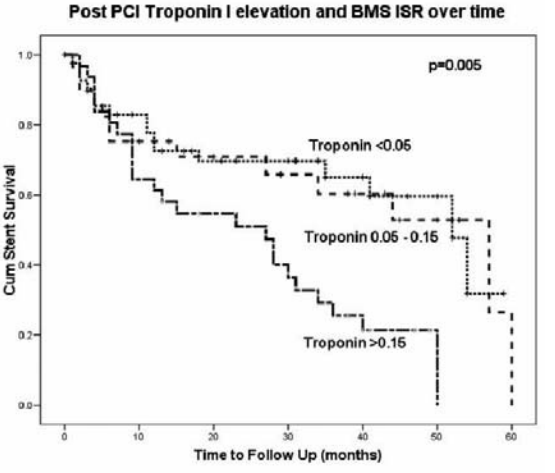
Background: Serum levels of glucose and inflammatory biomarkers upon presentation seem to confer incremental predictive value for no-diabetics (and diabetics) with acute coronary syndromes (ACS). We sought to investigate the possible interrelation of serum levels of glucose and inflammatory biomarkers 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 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 NSTE-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 NSTE-ACS (p=0.002) pts respectively. Inflammatory biomarkers were significantly related to the incidence of 1-year mortality in pts with STEMI and NSTE-ACS. Particularly, hs-CRP (p<0.001 and p<0.001), IL-6 (p=0.004 and p=0.008) and FIB (p=0.03 κα p=0.02) were significantly related to 1-year death in STEMI and NSTE-ACS pts respectively. By 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.

1032-161 **Percutaneous Coronary Intervention Related Infarction Is a Predictor of Late In-Stent Restenosis in Bare Metal Stents**

Andrew G. Dickerson, Ian J. Neeland, Ayushi Ahuja, Riyaz Patel, Muhiddin Ozkor, Jonathan Murrow, Saurabh Dhawan, Habib Samady, S. Tanveer Rab, John Douglas, Douglas Morris, A. Maziar Zafari, Arshed A. Quyyumi, Emory University School of Medicine, Atlanta, GA

Background: Several clinical and angiographic variables are known to be predictors of in-stent restenosis (ISR). The impact of peri-procedural ischemia on ISR is unknown. We hypothesized that myocardial ischemia/infarction during PCI leads to elevated risk of late ISR requiring further intervention.
Methods: We conducted a retrospective analysis of 1150 subjects in the Emory Genebank Registry. Of these, we identified 104 patient episodes of a successful elective PCI with a bare metal stent (BMS), subsequent angiographic follow up, and cardiac biomarker data. Mean follow-up time was 23 months. Peri-procedural ischemia/infarction were defined as next day Troponin I measures >0.05 and >0.15ng/mL, respectively, based on institutional assays.
Results: At 5 years of follow-up, there were 53 ISR events. Peri-procedural infarction at the time of first BMS placement was associated with a significantly higher risk of developing ISR requiring re-intervention (OR= 5.57, 95% CI [1.95, 15.87], p=0.001). The observed risk remained significant after adjusting for age, gender, treated risk factors and smoking (OR= 6.3, 95% CI [1.99-19.9], p=0.002). Kaplan Meier analysis revealed median time to re-intervention was 27 vs. 52 months, log-rank p= 0.005, Figure. We did not find a similar association with peri-procedural ischemia.
Conclusions: Peri-procedural infarction as assessed by Troponin I after BMS placement independently predicts a higher risk of developing late ISR requiring re-intervention at 5 years.

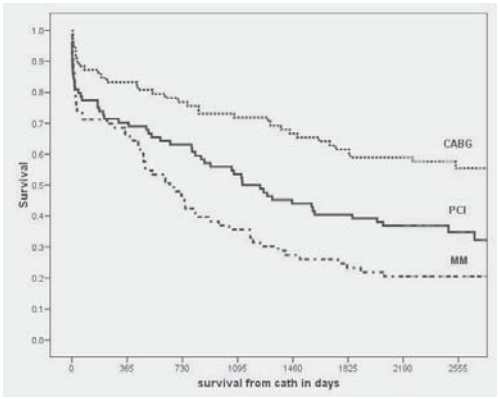


9:30 a.m.

1032-162 **Survival in Patients With Multivessel Coronary Artery Disease and Chronic Kidney Disease Presenting With Acute Coronary Syndromes**

Shayibu Harruna, Brenda Brownell, P Diane Galbraith, Jean F. Legare, William A. Ghali, Merril L. Knudtson, Michael P. Love, Jaroslav Hubacek, Divisions of Cardiology/Cardiac Surgery Queen Elizabeth II Health Sciences Centre and Dalhousie Univ, Halifax, NS, Canada, Department of Medicine, University of Calgary, Calgary, AB, Canada

Background: Data regarding the optimal mode of revascularization for patients with chronic kidney disease (CKD) and multivessel coronary artery disease (MVCAD) who present with acute coronary syndromes (ACS) are conflicting. We examined the long-term survival of a large cohort of ACS patients with CKD and MVCAD according to treatment strategy.
Methods: We identified 235 consecutive ACS patients with CKD and MVCAD hospitalized between January 1998 and December 2000 using two registries in the Canadian provinces of Nova Scotia and Alberta. Our primary end-point was 7-year survival from index catheterization according to chosen therapeutic strategy: percutaneous coronary intervention (PCI), coronary artery bypass surgery (CABG), or medical management alone (MM).
Results: Baseline characteristics were similar in all three groups. The figure shows the crude 7-year survival according to treatment strategy. Risk-adjusted hazard ratio analysis suggests increased mortality risk with MM as compared to CABG (HR 2.44; 95% CI 1.58-3.76) but not to PCI (HR 0.83; 95% CI 0.57-1.22). CABG compared to PCI was associated with reduced mortality risk (HR 0.48; 95% CI 0.31-0.74).
Conclusions: This registry-based observational study demonstrates a survival benefit of CABG relative to MM and PCI in CKD patients with ACS and MVCAD. CABG appears to be the optimal revascularization option for these patients.

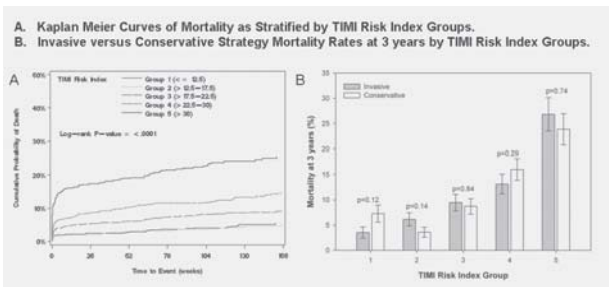


9:30 a.m.

1032-163 **TIMI Risk Index Predicts Long-Term Mortality in Patients With ST-Elevation Myocardial Infarction in the TIMI-II Clinical Trial**

Quynh A. Truong, Christopher P. Cannon, Neil A. Zakai, Ian S. Rogers, Robert P. Giugliano, 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 $[age/10]^2$ /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, 82% 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% (97/397) in Group 5 as compared to 5.1% (63/1368) in Group 1 and 2 (Figure A). 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=0.002) (c statistic 0.69). After controlling for multiple cardiovascular mortality risk factors, adjusted HR remained significant: Group 5 (HR 4.2, p<0.0001), Group 4 (HR 2.2, p=0.0005), Group 3 (HR 1.7, p=0.02). No difference was seen between Group 2 and 1. When stratified by TRI groups, no difference in mortality between treatment strategies was found (Figure B).
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.

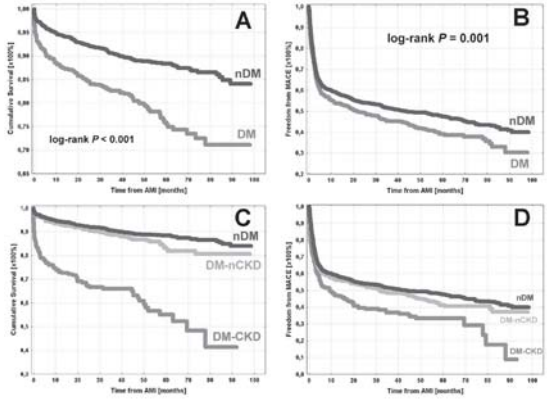


9:30 a.m.

1032-164 **Prognosis in Diabetic Patients With Acute Myocardial Infarction Is Related to Renal Function**

Jacek Kowalczyk, Radoslaw Lenarczyk, Krzysztof Strojek, Janusz Gumprecht, Agnieszka Sedkowska, 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 and 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.
All diabetics were divided with respect to their renal status into: diabetics with CKD (DM-CKD; n=264) and without (DM-nCKD; n=735). Independent predictors of death and major adverse cardiovascular events (MACE) were selected with multivariate Cox-regression model.
Results: Mortality rates were significantly higher in DM group compared to nDM in all observation periods. DM-CKD was associated with excessive total mortality (35.6%) when compared to DM-nCKD (11.6%, P<0.001) and to nDM (9.8%, P<0.001). Mortality and MACE rates did not differ significantly between DM-nCKD and nDM group. Diabetes coexisting with CKD was one of the strongest independent risk factors for death (hazard ratio 1.93; confidence interval 1.79-2.07; P<0.001).



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.

ACC.ORAL CONTRIBUTIONS

906

Therapeutic Consideration In the Patient Undergoing CABG

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

0906-3 **The Effect of Angiotensin-Converting Enzyme Therapy on Early Outcomes in Patients Undergoing Coronary Artery Bypass Grafting Surgery**

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 10,023 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%, OR 1.21, 95%CI 1.1 - 1.35, p<0.001) respectively. Neither ACE inhibitors nor control group was associated with increased risk of postoperative myocardial infarction and cerebral events. In a multivariate analysis, preoperative Ace inhibitors treatment was an independent predictor of mortality (OR 2.02, 95% CI 1.2 - 3.38, p=0.007), PRD (OR 1.42, 95% CI 1.12 - 1.75, p=0.001), use of inotropic support (OR 1.17, 95% CI 1.07 - 1.29, p=0.001) and AF (OR 1.41, 95% CI 1.26 - 1.57, p<0.001).
Conclusions: Preoperative therapy with ACE inhibitors is associated with an increased risk of mortality, post operative renal dysfunction and use of inotropic support. In addition, ACE inhibitors therapy was also a risk factor for new onset of postoperative atrial fibrillation. 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.

0906-4 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, Rhondalyn C. McLean, Jason B. Thompson, David R. Thiemann, Katherine Laws, Jodi B. Segal, John V. Conte, Kathleen W. McNicholas, Todd C. Villines, Edward P. Shapiro, Steven P. Schulman, Thomas S. Kickler, 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 multidetector CT coronary angiography. At the time of angiography, tests of aspirin responsiveness and global platelet function were performed as indicated.
Results: Complete inhibition of AA-induced platelet aggregation was present in 256/258 (99.2%) patients on ASA monotherapy. VG occlusion was associated with low PFA-100 C/ADP CT and elevated levels of $UTXB_2$. By multivariate analysis, a PFA-100 C/ADP CT <88 sec and $UTXB_2$ 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 (28.8%) patients at highest risk, defined by low PFA-100 C/ADP CT and high $UTXB_2$ level, had 6.5 times the odds of occlusion (p =0.003) compared to VGs in 67 (26.1%) patients at lowest risk, defined by a high PFA-100 C/ADP CT and low $UTXB_2$ level.
Conclusion: Despite suppression of platelet COX-1 activity by ASA, global platelet hyper-reactivity (defined by low PFA-100 C/ADP CT) and persistent thromboxane generation (defined by an elevated $UTXB_2$ level) are common 6 months after CABG surgery and are independent risk factors for early VG occlusion.

	Per Patient			Per Graft		
	≥ 1 Occluded SVG	No Occluded SVG	p-value	Occluded SVG	Patent SVG	p-value
Platelet Aggregometry (Ohms)						
Arachidonic Acid (AA; 0.5 mM)**	0	0	NS	0	0	NS
ADP (5μM)*	17.7	17.7	NS	17.7	17.5	NS
ADP (20μM)*	16.5	16.8	NS	16.6	16.7	NS
Epinephrine (50μM)*	5.5	5.4	NS	6.14	5.12	NS
Collagen (1 μg/mL)*	14.8	14.6	NS	14.7	14.7	NS
PFA-100™ Closure Time (CT; sec)						
Collagen/Epinephrine (C/Epi)**	288	299	NS	288	292	NS
Collagen/ADP (C/ADP) **	81	92	<0.001	81	89	<0.001
Log Urine 11-dehydro-TXB_2 ($UTXB_2$; pg/mg creatinine)*	5.85	5.77	NS	5.97	5.79	0.002
VerifyNow-ASA™ (ASA Resistance Units)*	449	457	NS	454	456	NS
*t test (mean), ** Mann Whitney (median)						

0906-5 New Onset Postcoronary Artery Bypass Graft Atrial Fibrillation and Long-Term Survival

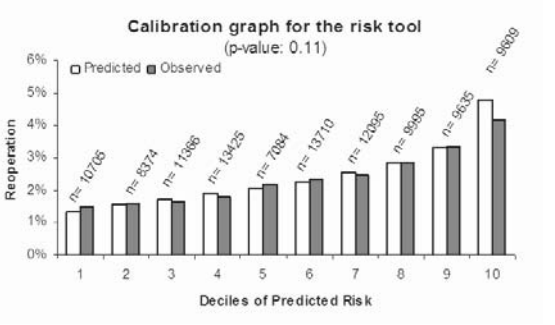
Giovanni Filardo, Cody Hamilton, Robert F. Hebeler, Jr., Baron Hamman, Paul Grayburn, Institute for Health Care Research and Improvement, Baylor Research Institute, Dallas, TX, Department of Statistical Science, Southern Methodist University, Dallas, TX

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 and other clinical/non-clinical details was used to investigate the association between new-onset AFIB post-CABG and long-term survival. After adjustment, new-onset AFIB post-CABG was strongly associated (Hazard Ratio: 1.31; 95%CI: 1.17, 1.45) with increased risk of death.
Conclusions: This study provides strong evidence that new-onset post-CABG AFIB is strongly associated with increased long-term risk of mortality independent of patient pre-operative severity. After controlling for a comprehensive array of risk factors associated with post-CABG adverse outcomes, risk of long-term mortality in patients that developed new-onset post-CABG AFIB was 31% higher than in patients without it.

0906-6 Identifying Patients at Risk for Reoperation for Bleeding After Coronary Artery Bypass Surgery

Rajendra H. Mehta, Shubin Sheng, Sean O.Brien, Frederick L. Grover, James S. Gammie, T Bruce Ferguson, Eric D. Peterson, Duke Clinical Research Institute, Durham, NC

Background: Patients (pts) undergoing CABG are at risk for reoperation for bleeding (RFB) that is associated with high morbidity and mortality. Rapid, accurate estimation of pts risk for RFB may help in clinical decision making.
Methods: We evaluated 528,279 pts from STS database undergoing CABG (2004-2007). Logistic regression was used to identify major predictors of RFB in 80% of the sample. The model coefficients were converted to an additive risk score that was then validated in remaining 20% sample.
Results: Reoperation for bleeding was required in 12644 pts after CABG (2.4%). Independent preoperative risk factors associated with risk of RFB were age >/=60 yrs, male sex, lower body surface area, non-white race, surgery status (highest for emergent salvage), baseline creatinine or dialysis, clopidogrel <24 hrs, clopidogrel + GpIIbIIIa <24 hrs, IABP, prior cardiac surgery, nondiabetic pts and 3 vessel CAD (c-index 0.60). Individual pt risk scores ranged from 0 to 98. The risk score tool performed well in the validation set with good concordance between predicted values and the observed risk in this sample (Hosmer-Lemeshow p=0.11) and had good ability to identify pts at low, moderate and high-risk for RFB (Figure).
Conclusions: We have identified the major risk factors for RFB in pts undergoing CABG. These factors have been converted into a simple, accurate bedside risk tool. This tool should promote preventive measures when feasible in this at-risk group.



0906-7 Timing of In-Hospital Coronary Artery Bypass Graft in Relationship to Mortality for Acute Coronary Syndrome Patients: Results From the NCDR ACTION Registry

Shailja V. Parikh, James A. de Lemos, Michael Jessen, Emmanouil Brilakis, Anita Y. Chen, Tracy Wang, Matthew Roe, Elizabeth Holper, University of Texas - Southwestern, Dallas, TX, Duke University, Durham, NC

Background: 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 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 1.39, 95% CI 0.88 - 2.19; composite: OR 1.10, 95% CI 0.76 - 1.58).
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

	NSTEMI (n=2784)			STEMI (n=974)		
	Early (n=870) 31.3%	Delayed (n=1914) 68.8%	p-value	Early (n=511) 52.5%	Delayed (n=463) 47.5%	p-value
Age (yrs)*	62.0 (55.0,72.0)	65.0 (57.0,75.0)	0.04	63.0 (54.0,71.0)	62.0 (54.0,73.0)	0.63
Diabetes (%)	30.8	39.1	<0.0001	25.8	28.3	0.35
Prior MI (%)	17.1	21.8	0.01	16.6	19.7	0.48
Prior Revascularization (%)	17.6	21.2	0.01	17.8	22.0	0.30
Prior CHF (%)	3.9	9.8	<0.0001	1.8	4.8	0.03
Prior Stroke (%)	5.6	8.7	0.04	4.1	6.9	0.26
Arrival to catheterization (hrs)*	8.4 (2.9,17.5)	26.5 (15.5,49.0)	<0.0001	1.0 (0.7,1.4)	1.2 (0.8,3.0)	<.0001
Clopidogrel within 24 hours of arrival (%)	27.9	38.1	0.002	39.5	61.2	0.001
* 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

3:30 p.m.

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. Tsiaousis, Michael N. Zairis, Nikolaos Patsourakos, Stamatis Makrygiannis, Konstantinos Vogiatzidis, Evridiki Gougourela, Stylianos Karvounaris, Konstantinos Ritsatos, Konstantinos Fakiolas, Stefanos G. Foussas, Tzanio 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 P-450 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, including treatment with PPIs, during the first year of follow-up was prospectively collected. For the purpose of the present analysis the pts were divided into those with (365/612; 59.6%) or without PPIs (247/612; 40.4%) drug therapy during the follow-up.
Results: By the 1-year 21 (3.4%) pts died and 39 (6.4%) pts had a new myocardial infarction. There were not significant differences in baseline clinical, angiographic and coronary stenting related data among the 2 groups. There was any difference in the other drug therapy between the 2 groups during the follow-up, and pts who received PPIs during the follow-up have similar incidence of death (3.6% vs 3.2; RR; 95%CI=1.1; 0.7-1.4; p=0.8) and myocardial infarction (6.3% vs 6.5; RR; 95%CI=1; 0.8-1.3; p=0.9) than those who did not receive such therapy during the first year.
Conclusions: 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.

3:30 p.m.

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

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

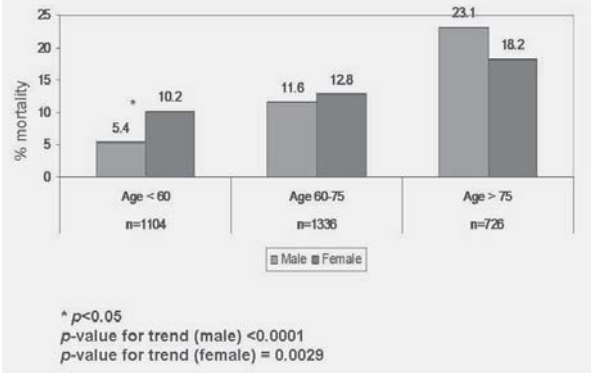
Background: Bleeding is a risk of dual antiplatelet therapy. There is an association between bleeding and cardiovascular mortality. However, the potential link of bleeding risk and inhibition of platelet aggregation (IPA) is not established.
Methods: We conducted secondary post-hoc analyses of 5μM ADP-induced 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) (n=117) treated with ASA (81 mg/daily) and clopidogrel for a median of 6 months.
Results: Demographic characteristic differed substantially depending on the underlying vascular disease, however IPA and bleeding risks were similar between CAD and IS. All three bleeding scales adequately captured serious hemorrhagic events, where the TIMI scale was the most exclusive, while BleedScore™ was the most inclusive. Over half of all patients experienced superficial event(s), most commonly occurring during 2-3 distinct bleeding episodes. There was no correlation between IPA and duration of antiplatelet therapy. IPA above 50% strongly predicts minor (r2 =0.583), but not severe (r2 =0.109) bleeding events.
Conclusions: Chronic treatment with dual antiplatelet therapy is associated with a very high (56.5-60.7%) incidence of bleeding. We postulate that in trials and registries, these hemorrhages are grossly underestimated due to the bleeding definitions that are used. IPA is well suited for defining the risk of minor complications, but more serious bleeding events cannot be predicted, suggesting that factors other than IPA may play a role.

3:30 p.m.

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

Dharam J. Kumbhani, Mehdi H. Shishehbor, Anthony A. Bavry, 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 (Tn) negative (p=0.005), but not Tn + (p=0.26) women <60 years.
Conclusions: Low-risk women (Tn 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.



3:30 p.m.

1041-128 The Significance of Clopidogrel Low-Responsiveness Assessed by a Point-of-Care Assay in Acute Coronary Syndrome Patients Undergoing Coronary Stenting

kyounghoon Lee, Seung-Hwan Lee, Jun-won Lee, Young-Jin Youn, Seong-Yoon Kim, Jang-Young Kim, Byung-Su Yoo, Junghan Yoon, Kyung-Hoon Choe, Wonju Christian Hospital, Wonju, South Korea

Background: To prevent atherothrombotic events, clopidogrel and aspirin is currently routinely used in treatment of patients undergoing percutaneous coronary intervention (PCI). Despite clopidogrel therapy, patients undergoing PCI are at risk of recurrent coronary events. Therefore, we sought to prospectively evaluate the death and myocardial infarction (MI) of acute coronary syndrome patients and their responsiveness to clopidogrel.
Methods: We enrolled consecutive 610 patients (pts, 160 males, 65.2±10.3 years) who received percutaneous coronary intervention (PCI) with acute coronary syndrome (Unstable angina, non-ST elevation MI and ST elevation MI) from Jan. 2006 to Jun. 2008. Endpoint was defined by cardiac death and stent thrombosis (ST) by definitions of the Academic Research Consortium (ARC). Aspirin and clopidogrel responsiveness were evaluated by VerifyNow™ tests (Accumetrics Inc, CA). Clopidogrel low-responsiveness was defined as the less than 20% inhibition of P2Y12 receptor.
Results: Baseline demographic characteristics were similar between normal group (370

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 definit 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 multivariable 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.

3:30 p.m.

1041-129 Outcomes After Acute Coronary Syndromes in Patients With Rheumatoid Arthritis

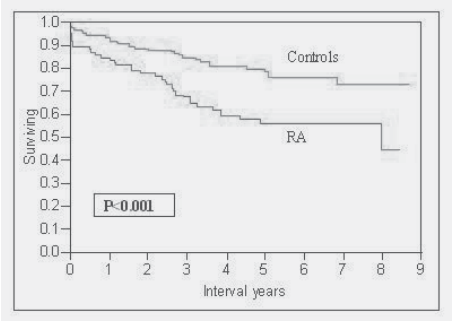
Anbazhagan Prabhakaran, Anitha Rajamanickam, Henri Roukoz, Anil Jain, Deepak L. Bhatt, Cleveland Clinic, Cleveland, OH

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 (36.5% males, 70.4±12.4yrs, 74% were on anti-rheumatic drugs), and 172 control subjects (38.4% male, age 72.1±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 (RR=1.66, CI: 1.13-2.45, p=0.01) and peripheral arterial disease related re-hospitalizations (RR=2.23, CI: 1.02-6.08, p=0.038). RA was not associated with significant cardiac related re-hospitalizations.

Conclusions: After MI, 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.



3:30 p.m.

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 Lourenco, Rogerio Teixeira, Elisabete Jorge, Rui Baptista, Fatima Saraiva, Francisco Goncalves, Pedro Monteiro, Mario Freitas, Luis A. Providencia, 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=112); C - CC<60 mL/min and GLY<180 mg/dL (n=316) and D - CC<60 mL/min and GLY>=180 mg/dL (n=124).

Results: After univariate analysis, in-hospital morbidity (1.7% vs 5.4% 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 killip 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

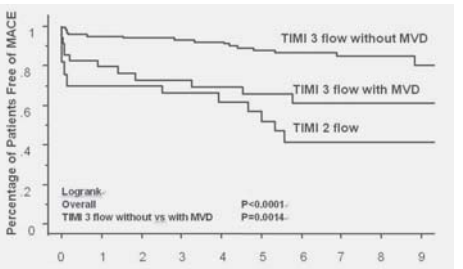
Koichi Tamita, Atsushi Yamamuro, Shuichiro Kaji, Minako Katayama, Takeshi Kitai, Takafumi Yamane, Makoto Kinoshita, Natsuhiko Ehara, Yutaka Furukawa, Takashi Akasaka, Kobe General Hospital, Kobe, Japan, Wakayama Medical College, Wakayama, Japan

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 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

Bimmer E. Claessen, Rene J. van der Schaaf, 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 noninfarct-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 a CTO in a noninfarct-related artery on long-term mortality after STEMI.

Methods: Between 1997 and 2005, we admitted 3277 patients with STEMI treated with primary PCI. We categorized patients as having single vessel disease (SVD), 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: SVD was present in 2115 patients (65%), 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 SVD 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)

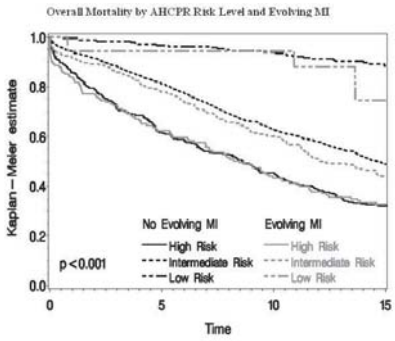
Conclusion: In STEMI patients without CTO, only patients with 3-vessel disease and not patients with 2-vessel disease have a significantly higher risk for mortality. Even after correction for the number of diseased vessels, a CTO in a noninfarct-related artery represents the patient category with the worst prognosis after STEMI.

3:30 p.m.

1041-133 **A Clinical Risk Stratification Model Provides Accurate Long-Term Risk Stratification For ACS Patients: The Olmsted County Acute Chest Pain Study**

Louai Razzouk, Verghese Mathew, Guy S. Reeder, Peter A. Smars, Sameer Bansilal, Ryan J. Lennon, Heather J. Wiste, David R. Holmes, Jr., Michael E. Farkouh, Mount Sinai School of Medicine, New York, NY, Mayo Clinic College of Medicine, Rochester, MN

Background: The long-term outcomes of patients presenting with an index episode of acute chest pain (ACP) and classified by clinical risk stratification remains unknown.
Methods: We identified all residents of Olmsted County (OC), Minnesota presenting to the county's 3 emergency departments (ED) with non-ST elevation acute coronary syndrome (NSTE-ACS) over an 8-year period. The medical records of the study population were abstracted using the Rochester Epidemiology Project. Patients were classified into high (HR), intermediate (IR), and low-risk (LR) groups using the AHCPR criteria, a clinical, non-biomarker based risk model. Patients with an elevated CK-MB biomarker were classified as evolving myocardial infarction (MI). Cox models were used to estimate the adjusted association between AHCPR risk and mortality.
Results: Of the 2271 patients (mean age 63 yrs, 57.5% males), 436 patients (19.2%) were classified as HR, 1,557 (68.6%) as IR and 278 (12.2%) as LR. At median follow-up of 16.6 years, HR patients had a 1.68 fold (p = 0.011) and IR 1.38 fold (p =0.09) increased mortality compared to LR patients. Survival was similar, whether or not the patient presented initially with an evolving MI (see figure).
Conclusions: A non-biomarker based clinical tool can reliably stratify long-term mortality in a community-based cohort with NSTE-ACS. More emphasis should be placed on the initial clinical risk stratification which can be accomplished almost immediately upon presentation to an ED.

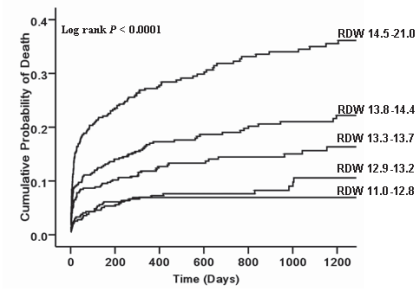


3:30 p.m.

1041-134 **Relation Between Red Blood Cell Distribution Width and Mortality in Patients With Acute Myocardial Infarction**

Salim Dabbah, Haim Hammerman, Michael Kapeliovich, Rafael Beyar, Walter Markiewicz, Doron Aronson, Rambam Medical Center, Haifa, Israel

Background: Increased red blood cell distribution width (RDW), a measure of the variability in size of the circulating erythrocytes, has been shown to be associated with adverse outcomes in patients (pts) with heart failure and with coronary disease. However, there is no information regarding the prognostic significance of RDW in the acute phase of acute myocardial infarction (AMI).
Methods: We performed a post hoc analysis of data from a prospective study. Baseline RDW was measured in 2095 pts admitted with AMI and followed for a median of 19 months. We used Cox proportional hazards models to examine the association between quintiles of RDW and all-cause mortality, adjusting for the Global Registry of Acute Coronary Events (GRACE) risk score and baseline hemoglobin.
Results: During the follow period 362 pts died. There was a graded positive association between increased RDW and mortality across quintiles of RDW (Figure). In a Cox model, the adjusted HRs of pts with RDW in the 2nd, 3rd, 4th, and 5th RDW quintile compared with pts in the 1st quintile were 1.0 [95% CI, 0.6 to 1.7], 1.5 [95% CI, 1.0-2.3], 1.9 [95% CI, 1.2 to 2.9] and 2.7 [95% CI, 1.8 to 4.0], respectively (P for trend < 0.0001). The association between increased RDW and mortality remained highly significant in sensitivity analyses that excluded pts with anemia (Hb < 12 g/dl) and pts with abnormally low (<82 μm3) or high (>98 μm3) mean corpuscular volume.
Conclusions: There is a graded independent relation between increased RDW and the risk of death in pts with AMI.



3:30 p.m.

1041-135 **A Novel Risk Score System for the Assessment of Clinical Outcomes in Patients With Acute Non-ST-Segment Elevation Acute Coronary Syndrome**

Hyun 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

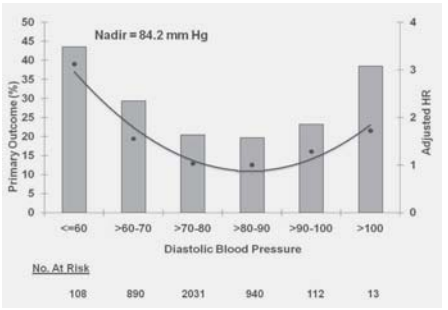
Background : Prognostic variables of Thrombolysis In Myocardial Infarction (TIMI) risk score have some limitations predicting short- and long- term clinical outcomes in patients with non-ST elevation acute coronary syndrome (NSTE-ACS). Utilizing a multivariable Cox regression analysis, multiple risk 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 Nov 2005 and Aug 2007, 5,409 patients with NSTE-ACS (64.6± 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 : 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).
For 6-month post discharge mortality rates, new risk score (AUC : 0.768;CI : 0.742 - 0.794) demonstrated a significant differences in predictive accuracy when compared with GRACE (0.768 vs 0.658, p<0.0001) and TIMI risk score(0.768 vs 0.651, 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.

3:30 p.m.

1041-136 **How Low Is Low Enough? Relationship of Blood Pressure and Cardiovascular Events in Patients With Acute Coronary Syndromes: An Analysis From the PROVE-IT TIMI 22 Trial**

Sripal Bangalore, Jie Qin, Sabina A. Murphy, Christopher P. Cannon, PROVE-IT TIMI 22 Trial Investigators, Brigham and Women's Hospital, Boston, MA

Background: Aggressive blood pressure control has been advocated as an important measure to reduce recurrent cardiovascular events in patients with acute coronary syndromes (ACS). However, how low is low enough?
Methods: We evaluated 4162 patients enrolled in the PROVE-IT TIMI 22 trial [ACS patients randomized to Pravastatin 40 mg vs. Atorvastatin 80 mg]. The mean post baseline blood pressure (systolic and diastolic) was recorded and categorized into 10-mm Hg increments. Primary endpoint was a composite of death from any cause, myocardial infarction, unstable angina requiring rehospitalization, revascularization and stroke through an average of 2 years follow-up.
Results: The relationship between blood pressure (systolic or diastolic) followed a J-curve association with primary endpoint with increased events rates at both low and high blood pressure values, both unadjusted and after adjusting for baseline variables (Figure). Non-linear Cox proportional hazard model showed a nadir of 135.8 mm Hg for systolic and 84.2 mm Hg for diastolic pressure where the event rate was lowest. Similar J-curve association was found between blood pressure and the risk of all-cause mortality and myocardial infarction.



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.

3:30 p.m.

1041-137 High Clopidogrel Maintenance Dose Does Not Increase Platelet Aggregation Time in Patients With Acute Coronary Syndromes

Eleftheria Tsagalou, Charris Matsouka, Evangelos Repasos, Eleni Tseliou, Panagiotis Zotos, John Kanakakis, Anastasia Leonti, Vasiliki Kontopidi, John Nanas, 3rd Department of Cardiology, University of Athens School of Medicine, Athens, Greece

Background_After treatment with clopidogrel, a significant portion of patients present reduced platelet inhibition. This could be of particular importance in the setting of acute coronary syndromes (ACS) since those patients present increased rates of reccurent ischemic events .
Purpose: The aim of this pilot study was to assess the functional impact of a high maintenance dose of clopidogrel in patients with ACS and suboptimal clopidogrel-induced antiplatelet effects.
Methods: Consecutive patients with recent (<1month) ACS, on dual antiplatelet therapy, were screened to identify suboptimal clopidogrel responders. The latter were treated with a standard (75 mg x 1, n=12 ,Group A) or high (75x2, n=16, Group B) daily maintenance dose. Platelet function was assessed at 2 time points baseline and at 30 days using PFA-100.
Results: A total of 67 patients were screened to identify 28 suboptimal responders. Baseline aggregation identified by PFA-100 was similar in the two treatment groups (72±12 vs 71±10 for Group A and B respectively, p=0.938). Thirty days after treatment, platelet aggregation time was similarly increased in both treatment groups (126±79 for Group A , p=0.029 vs baseline and 155±100 for Group B, p=0.006 vs baseline, p=0.411 for Group A vs Group B)). Suboptimal clopidogrel response was still present in 4 (31%) patients of the 75mg regimen and 7(44%) patients on the 150 mg regimen (p=0.702).
Conclusions: Ex vivo platelet reactivity decreases with time in a significant percentage of patients with ACS and clopidogrel resistanse. A 150-mg maintenance dose of clopidogrel was not associated with enhanced antiplatelet effects compared with 75 mg in this high risk patient population

3:30 p.m.

1041-138 Impact of Statin on the Regression of Coronary Atherosclerotic Plaque in Women; An Intracoronary Ultrasound (IVUS) Subanalysis of Japanese Acute Coronary Syndrome (JAPAN-ACS) Study

Yukio Ozaki, Shino C. Kan, Hirouki Naruse, Masanori Okumura, Kousuke Hattori, Makoto Ishikawa, Tomoko Kawai, Hiroto Harigaya, Shigeru Matsui, Sadako Motoyama, Masayoshi Sarai, Junichi Ishii, Hitoshi Hishida, Masunori Matsuzaki, JAPAN-ACS Study Group, Fujita Health University Hospital, Toyoake, Japan, Yamaguchi University Graduate School of Medicine, Ube, Japan

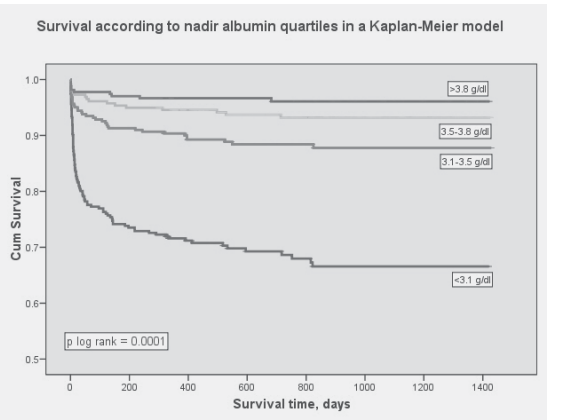
Background: Although cardiovascular disease is a major cause of death in women, it has not yet been well established whether the degree of atherosclerotic plaque regression derived from statin is similar between women and men.
Methods: We performed a prospective multicenter randomized study to assess 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 (pitavastatin; 4mg/day) or atorvastatin (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 (-18.1±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 the two. While baseline total cholesterol (TC, mg/dl) level was significantly higher in women than in men (211±35 vs. 194±35, p<0.01) and baseline low-density lipoprotein cholesterol (LDL-C) level was greater in women than in men (144±33 vs. 129±31, p<0.01), smoking habits were more common in men than in women (52% vs. 23%, p<0.01). While statin significantly reduced TC and LDL-C in both groups during follow-up, the degree of TC reduction and LDL-C reduction were similar between women and men (TC; -48±44 vs. -45±33, p=ns, LDL-C; -56±39 vs. 48±29, p=ns). However, %PV changes derived from statin treatment were significantly greater in women than in men (-21±14% vs. -16±13%, 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.

3:30 p.m.

1041-139 The Impact of In-Hospital Metabolic Changes on Long Term Mortality in Patients with Acute Myocardial Infarction

Robert Dragu, Michael Kapeliovich, Haim Hammerman, Rambam Health Care Campus, Haifa, Israel

Background: To assess the prevalence and long term prognostic significance of changes in serum albumin levels during hospitalization in patients with acute myocardial infarction (AMI).
Methods: We prospectively studied 1418 consecutive patients admitted with AMI and normal synthetic liver function. Serum albumin concentration was tested daily during hospitalization. The mean follow-up period was 24 months. Multivariate Cox models were used to assess the relationship between nadir albumin level and long term survival.
Results: During hospitalization 54.5% of study population developed hypoalbuminemia (<3.5 g/dl). The mean nadir albumin was 3.38±0.58 g/dl (median 3.5, IQR 3.1-3.8 g/dl), 0.31 g/dl lower then admission levels (p<0.0001). The long term mortality according to nadir albumin quartiles (from lowest to highest) was: 30.2%, 10.1%, 5.5%, 3.9% respectively (p<0.0001). After adjusting for age, gender, diabetes mellitus, hypertension, ST-elevation AMI, anterior wall involvement, left ventricular systolic function and creatinine clearance, the nadir albumin in lowest quartile (<3.1 g/dl) remained a strong predictor for mortality (HR 3.23, 95% CI [1.24-8.40], p<0.016). Figure 1 depicts the Kaplan-Meier cumulative probability for mortality curves for each group.
Conclusions: The development of hypoalbuminemia is frequent during hospitalization of patients with AMI and is strongly related to high long term mortality.

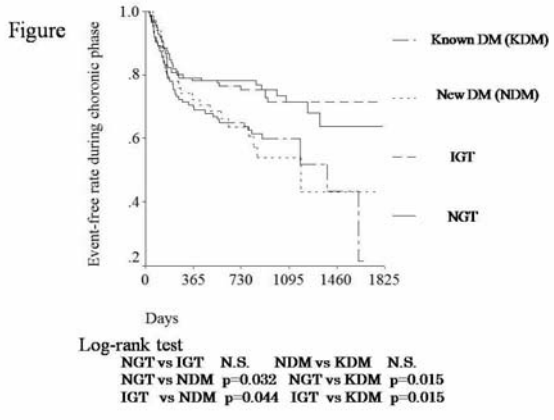


3:30 p.m.

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 Kataoka, Mitsuru Abe, Yoichi Goto, Genjirou Kimura, Hiroshi Nonogi, 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±1.32 years). **Results:** There was no significant difference in clinical backgrounds excluding body mass index and the state of glucose tolerance. The level of HbA1c of NDM was normal range but significantly lower than those of KDM. (HbA1c: 5.69mg/dl for NDM vs 7.81mg/dl for KDM, p<0.001). For long-term periods, patients with NDM and KDM after AMI had similarly increased risk of MACE and had a significant higher incidence of MACE compared to IGT and NGT (p<0.05). **Conclusions:** These date demonstrated that patients with newly diagnosed DM are at high risk of MACE after AMI 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.



3:30 p.m.

1041-141 **Persistent Elevated Levels of Plasma Myeloperoxidase as an Independent Predictorof Recurrent Cardiovascular Events in Patients With Unstable Angina Pectoris**

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

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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 admission), 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, 18.3±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 > 16.0ng/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.

3:30 p.m.

1041-142 **Enhanced Monocyte Expression of Adiponectin Receptors Is Related to Increased Carotid Intima-Media Thickness and Arterial Stiffness in Patients With Chronic Coronary Artery Disease**

Ignatios Ikonomidis, A. Kollias, John Lekakis, Ioannis Palios, P. Tsiotra, E. Maratou, Katerina Fountoulaki, G. Dimitriadis, Sotirios A. Raptis, Dimitrios Th Kremastinos, 2nd Cardiology Department, 'Attikon' Hospital, University of Athens, Athens, Greece, 2nd Department of Internal Medicine, Research Institute and Diabetes Center, Attikon' Hospital, Univ, Athens, Greece

Background:Adiponectin is reduced in patients with CAD. Adiponectin receptors 1 (ADR1) and 2 (ADR2) are expressed on cells within atheromatic lesions and on monocytes transformed to macrophages and are activated by PPAR-receptor agonists. Carotid intima-media thickness and arterial stiffness are markers of subclinical atherosclerosis with prognostic significance. We investigated whether ADR1 and 2 are associated with carotid intima-media thickness and arterial stiffness in patients with angiographically documented chronicCAD.
Methods: We studied 60 patients with suspected CAD who underwent coronary angiography (mean age: 59±7 years 39 male and 5 females). We measured a) expression of ADR1 and 2 on blood monocytes [mean fluorescence intensity arbitary units -MFI-AU] by flow-cytometry b) carotid to femoral artery pulse wave velocity (PWV), as an estimate of arterial stiffness using the Complior apparatus c)mean intima-media thickness (IMT) in common carotids and carotid bulbs using ultrasound imaging.
Results: ADR1 and 2 expression was lower in patients with coronary stenosis >50% in at least one vessel (n=40) than in those with no significant stenosis (63±25 vs. 84±27 and 82±37 vs.111±46 MFI-AU respectively, p<0.05). Both groups had similar atherosclerotic risk factors. Within patients with significant CAD, increased expression of ADR2 was related to increased PWV (rs=0.67, p=0.01), carotid bulb IMT (rs=0.43, p=0.03) and presence of carotid plaques (IMT>1.5mm) (rs=0.39, p=0.04). Increased expression of ADR1 was also related to increased PWV (rs=0.46, p=0.03). These associations were not observed in patients without significant CAD.
Conclusions: Expression of adiponectin receptors is reduced in patients with significant CAD. Increased expression of ADR2 receptors on monocytes is related to peripheral vascular atherosclerosis in vivo. This increased expression of ADR in patients with more extensive atherosclerosis may reflect a compensatory mechanism for the low circulating adiponectin levels and may offer a potential therapeutic target for the use of PPAR-receptor agonists to activate the anti-inflammatory and anti-atherogenic action of these receptors.

3:30 p.m.

1041-143 **Interrelationships of Impaired Erectile Function, Increased Arterial Stiffness and Coronary Artery Disease**

Charalambos Vlachopoulos, Nikolaos Ioakeimidis, Konstantinos Rokkas, Dimitrios Terentes-Printzios, Konstantinos Aznaouridis, Konstandina Aggeli, Katerina Baou, Thanos Askitis, Christodoulos Stefanadis, 1st Cardiology Department, Athens Medical School, Athens, Greece

Background : Accumulating evidence suggests that erectile dysfunction (ED) may be an early manifestation of generalized vascular disease. Arterial stiffness is an independent marker and prognosticator of cardiovascular risk. Aim of this study was to determine arterial stiffness and its predictive value for the presence of underlying cardiovascular pathology in men with ED.
Methods: Carotid-femoral Pulse Wave Velocity (PWV) as an index of aortic stiffness and radial Augmentation Index (AIx) as a measure of wave reflections were measured in 344 consecutive men with ED of vascular origin. ED was diagnosed according to history and score of the 5-item Sexual Health Inventory for Men (SHIM, cut-off value <21). Lower scores indicate poorer erectile function and vice versa.
Results: Subjects were categorized according to tertiles of SHIM score [Group 1: first tertile (SHIM score: 15-20, n=117), Group 2: second tertile (SHIM score: 10-14, n=115), Group 3: third tertile (SHIM score: <9, n=112)]. The patients with lower SHIM score were older (p <0.01) and have higher central pulse pressure (p <0.05) and greater proportion of diabetes (p<0.01). PWV and AIx were significantly different between Groups 2 and 3 (p <0.001 and p = 0.02) and between Groups 1 and 3 (p <0.001 and p < 0.01), respectively. The proportion of ED patients with angiographically documented coronary artery disease (CAD) and presence of multi-vessel CAD was significantly higher in Group 3 (p <0.01 and p<0.001, respectively). In multivariable logistic regression analysis adjusting for age, mean blood pressure, metabolic profile, C-reactive protein, arterial function parameters, use of statins 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.

3:30 p.m.

1041-144 **Different Contributors to Thrombus Formation Between Sirolimus-Eluting Stents and Paclitaxel-Eluting Stents: Serial Angioscopic Observations**

Tomoaki Higo, Shinichi Hirotani, 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 angioscopic 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 angioscopic examinations of stent-implanted lesions were serially performed immediate (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 of stent and prevalence of thrombus were angioscopically evaluated.
Results: Baseline clinical and angiographic characteristics were similar between two groups. Max color grade in SES-implanted lesions was significantly increased from baseline to follow-up (1.4 ± 1.1 vs 1.9 ± 0.6, p<0.001), although that in PES-implanted lesions did not change (1.8 ± 0.4 vs 1.4 ± 0.6, p=0.76). Especially in the area yellow plaques were not detected at baseline, newly formed yellow neiontima was observed at follow-up in 85% of SES-implanted lesions, but not in PES-implanted lesions. On the other hand, prevalence of thrombus in the area stent was not covered by neointima was significantly higher in PES-implanted lesions than in SES-implanted lesions (64% vs 26%, p=0.029). Stent struts were not covered by neointima, at least in part, in approximately all lesions, and prevalence of yellow plaques in the area was not different between two groups.
Conclusions: SES promoted atherosclerotic change in the stent-implanted lesions. Thrombogenic potential of stented lesions with incomplete neointimal coverage was higher in PES than in SES. Our data suggest that contributors to thrombus formation are

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.

3:30 p.m.

1041-145 **Intramyocardial Autologous Bone Marrow Cell Injection In No-option Patients With Refractory Angina Pectoris and Documented Ischemia: A Randomized, Double Blinded, Placebo-Controlled Trial**

Jan van Ramshorst, Jeroen J. Bax, Saskia L. Beeres, Stijntje D. Roes, Petra Dibbets, Albert de Roos, Marcel PM Stokkel, Ernst E. van der Wall, Martin J. Schalij, Douwe E. Atsma, Leiden University Medical Center, Leiden, The Netherlands

Background: Several non-randomized clinical studies have demonstrated that intramyocardial bone marrow-derived mononuclear cell (BMC) injection is safe and feasible in no-option patients with angina pectoris. In this randomized, double blinded and placebo-controlled trial, we investigated the efficacy of intramyocardial BMC injection in no-option patients with angina pectoris and documented ischemia.
Methods: In 50 patients, bone marrow was aspirated from the iliac crest. After cell isolation, patients were randomly assigned to injection of autologous BMC or placebo solution. Using the NOGA system (Biosense-Webster, Belgium), injection of $98\pm7x10^6$ BMC or placebo solution was performed.
Anginal symptoms and quality of life were evaluated at baseline and at 3 and 6 months. Gated single-photon emission computed tomography and magnetic resonance imaging were performed at baseline and at 3 months follow-up to assess myocardial perfusion and left ventricular function.
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 2.2±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, P=NS). Moreover, quality of life improved from 56±9% 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 3.9±1.8 to 1.5±1.5 (p<0.01) in the BMC group, compared to a modest decrease from 3.1±1.5 to 2.4±1.8 (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%, P=NS).
Conclusion: In no-option patients with angina pectoris, intramyocardial BMC injection has a beneficial effect on anginal symptoms, myocardial perfusion and left ventricular function.

3:30 p.m.

1041-146 **Patient Perceptions Regarding Benefits of Elective Coronary Revascularization for Stable Coronary Artery Disease in the Current Era**

Apurva Motivala, 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) over 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 61 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%), 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 catheterization 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 of risks, benefits, alternatives and findings of current literature to patients prior to referring them for an elective PCI.

3:30 p.m.

1041-147 **Prevalence of Extra Coronary Arterial Disease in Patients With Coronary Artery Disease Undergoing Coronary Intervention**

Yoshimitsu Soga, Hiroaki Kobayashi, Tatsuki Doijiri, Tomoko Urakawa, Kenji Ando, Hiroyoshi Yokoi, Masashi Iwabuch, Hideyuki Nosaka, Masakiyo Nobuyoshi, kokura memorial hospital, Kitakyushu, Japan

Background: The prevalence of carotid stenosis (CS), renal artery stenosis (RAS), peripheral artery disease (PAD) of lower extremities and abdominal aortic aneurysm (AAA) in patients with coronary artery disease (CAD) remains unclear.
Methods: Patients who underwent percutaneous coronary intervention (PCI) at our institution between November 2007 and July 2008 were prospectively studied. All patients gave informed consent for this investigation. The coexistence of CS, RAS, PAD and AAA were evaluated in all patients by carotid and aortorenal duplex ultrasound and an ankle-brachial index (ABI).
Results: In total, consecutive 802 patients underwent elective PCI, with a mean age of 69 ± 10 years (range, 39-92), 76% of male gender, 41% with diabetes mellitus (DM), 71% with hypertension, 5% with renal failure, 22% with smoking, and 11% with stroke. Of them, 190 patients (23.7%) suffered from coexsistence of arterial disease. Frequency of CS, RAS, PAD and AAA was 3.6%, 5.4%, 17.2%, and 3.4%, respectively. Frequency of triple and double vascular disease was 6 (0.7 %) and 35 (4.4%), respectively. On multivariate analysis, age, history of coronary artery bypass surgery (CABG), hemodyalysis, HDL<40mg/dl, prior stroke and acute coronary syndrome was independent predictors for extra-coronary artery disease.
Conclusions: Prevalence of extra-coronary arterial disease (CS, RAS, PAD and AAA) is high in patients with CAD undergoing PCI. Initial screening for them by duplex ultrasound and ABI is useful.

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.

1041-148 **Endogenous Plasma Levels of VEGF Are Associated With Late Lumen Loss in Drug Eluting Stents**

Walter S. Speidl, Katharina M. Katsaros, Stefan P. Kastl, Gerlinde Zorn, Kurt Huber, Gerald Maurer, Dietmar Glogar, Johann Wojta, Günter Christ, Medical University of Vienna, Vienna, Austria, Wilhelminenhospital, Vienna, Austria

Background: Drug eluting stents (DES) reduce the rate of instent restenosis (ISR) compared to bare metal stents (BMS) through inhibition of migration and proliferation of coronary smooth muscle cells. However, recent studies suggest that DES also inhibit endothelial cell proliferation leading to delayed healing of the endothelium. VEGF may reduce neointima formation through accelerated reendothelialization. The aim of this study was to evaluate whether endogenous plasma levels of VEGF are associated with development of ISR after implantation of DES.
Methods: We studied 85 patients that were treated with 159 DES. Blood samples for measurement of VEGF antigen were taken directly before and 24 hours after implantation of DES. Late lumen loss (LL) was evaluated at 6 to 8 months by coronary angiography.
Results: During the follow up period, 2 patients died of cardiovascular causes and 12 patients developed ISR. High baseline VEGF levels were protective for ISR and restenosis rates declined according increasing tertiles of VEGF (25.9%, 14.3% and 3.6%; p<0.05). In contrast, the increase of VEGF after PCI correlated with LL (R=0.33, p<0.0001) independently from clinical and angiographic risk factors.
Conclusion: High endogenous plasma levels of VEGF before PCI are protective for ISR, however, the increase of VEGF after PCI was associated with LL. This dual role of VEGF in neointima formation after implantation of DES needs further studies.

3:30 p.m.

1041-149 **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 pathological studies have revealed that lack of neointimal strut coverage and

heterogeneous neointimal coverage over drug-eluting stents greatly increase thrombotic risk. The aim of this study is to compare by using angioscopy heterogeneity of neointimal coverage and thrombus formation between PES and SES.
Methods: We examined 30 PES-implanted lesions (29 patients) and 78 SES-implanted lesions (77 patients). Angiographic and angioscopic examinations at stent-implanted lesions were performed 1 year (11.1±3.5 months) after implantation. Maximum and Minimum neointimal coverage grade of the stent (Max coverage, Min coverage; 0, not covered; 1, covered by thin layer or 2, buried under neointima) and prevalence of thrombus were angioscopically evaluated. We also evaluated whether the neointimal coverage of stent was heterogeneous or not. Neointimal coverage was defined as 'heterogeneous' when the stented lesion had multiple coverage grades.
Results: Baseline clinical and angiographic characteristics were similar between two groups. Max coverage was significantly higher in PES-implanted lesions than in SES-implanted lesions (1.8 ± 0.4 vs 1.4 ± 0.6, p<0.001). Min coverage was lower in PES-implanted lesions, though it was not statistically different (0.5 ± 0.6 vs 0.7 ± 0.5, p=0.14). Neointimal coverage was heterogeneous in 93% of PES-implanted lesions and 68% of SES-implanted lesions (p=0.006). Prevalence of thrombus was significantly higher in PES-implanted lesions than that in SES-implanted lesions (53% vs 36%, p=0.01), especially at the site struts were not covered (27% vs 3%, p<0.001).
Conclusions: Max coverage was greater, neointimal coverage was more heterogeneous and prevalence of thrombus was higher in PES-implanted lesions than in SES-implanted lesions. These angioscopic findings may explain larger late loss and higher risk of LST in patients with PES than those with SES.

3:30 p.m.

1041-150 The Strategy of High Pressure Balloon Predilatation May Lead Better Long-Term (Two-Year) Outcomes in Patients of Bare-Metal Stents Restenosis Treated With Silorimus-Eluting Stent

Katsuo Noda, Shuichi Oshima, Shinichi Nakamura, Kumamoto Chuo hospital, Kumamoto, Japan

Background: Silorimus-eluting stent (SES) has been shown to reduce restenosis, even in bare-metal stents restenosis (ISR). However, some reports have been shown the late catch-up beyond one-year. In de-novo cases, it has been reported that SES under-expansion became one of the predictors associated with long-term outcomes, but few reports existed in the association between SES under-expansion and long-term outcomes in ISR treated with SES. We performed a high-pressure pre-dilatation for ISR prior to SES implantation, and to evaluate the efficacy of that strategy for the long-term outcomes. **Methods:**Between August 2004 and August 2006, a consecutive 138 ISR patients were treated. We divided into 2 groups, one was H (high-pressure pre-dilatation; n=80) and the other was N (no high-pressure pre-dilatation; n=58). High-pressure pre-dilatation was performed >= 12-atmosphere pressure with non-compliant balloon before SES implantation. Pre-dilatation balloon size was decided at least the same size of prior implanted BMS. We investigated the 2-year outcomes in each group, and the predictors of MACEs were evaluated with multivariate analysis. **Results:** There were no significant differences of clinical and angiographic characteristics in both groups. The 30-day MACEs were 2.5% in H, and 1.7% in N (p=NS). 1-year and 2-year MACEs were lower rate in H than N, significantly (7.5% vs. 27.6%, p=0.002; 12.5% vs. 43.1%, p<0.0001). Stent thrombosis occurred one in each group. 2-year late loss was smaller in H, significantly (0.6+/-0.7 mm vs. 0.9+/-1.0 mm, p=0.02). Multivariate analysis showed that ejection fraction (p=0.025, HR=1.03) and SES minimum stent area (MSA) with IVUS <5.0 mm² (p=0.003, HR=3.47) were positive predictors, and high-pressure balloon pre-dilatation (p=0.008, HR=0.33) was a negative independent predictors of 2-year MACEs. A subgroup of SES-MSA>=5.0 mm² and high-pressure balloon pre-dilatation showed especially lower MACEs rate than the other group (3.7% vs. 38.6%, p<0.0001). **Conclusions:**These results lead that the high-pressure balloon pre-dilatation may change the 2-year long-term outcomes in patients with SES implantation for BMS-ISR.

3:30 p.m.

1041-151 Sleep Disordered Breathing in Patients With Coronary Artery Disease: A Prevalence Study

Christian Prinz, Thomas Bitter, Cornelia Piper, Dieter Horstkotte, Olaf Oldenburg, Department of Cardiology, Heart Center North Rhine- Westphalia, Ruhr University Bochum, Bad Oeynhausen, Germany

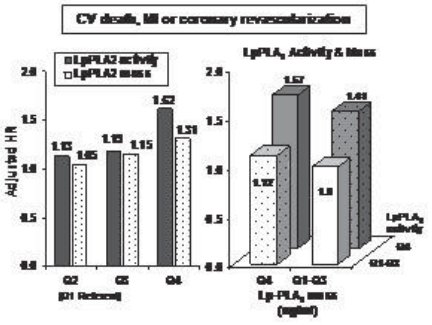
Background: Sleep disordered breathing (SDB) has a high prevalence and prognostic impact in patients (pts) with various cardiac diseases. Aim of this study was to investigate the prevalence of SDB in pts with coronary artery disease (CAD).
Methods: We consecutively included 257 pts (212 men; age 67.5 ± 1.0 years; CCS 1.4 ± 0.2; body mass index (BMI) 28.4 ± 0.5 kg/m²) with relevant CAD (at least one stenosis ≥ 70 %) and left ventricular ejection fraction (LVEF) ≥ 50%. All pts underwent echocardiography, cardiac catheterisation and in-hospital unattended cardiorespiratory polygraphy (Embletta, Embla, NL). In case the apnea-hypopnea-index (AHI) was > 5/h pts were considered to have SDB. If thoracic and abdominal inspiration efforts were documented, SDB was considered to be obstructive (OSA), otherwise central sleep apnea (CSA) was diagnosed.
Results: SDB was documented in 188 pts (74 %) with an AHI of 16.4 ± 1.9 /h. 58 pts (23.3 %) had CSA (AHI 29.7 ± 4.5 /h) and 130 pts (50.6 %) OSA (AHI 16.9 ± 2.2 /h). Only 69 pts (26.8 %) demonstrated no relevant SDB. Severity of SDB measured by AHI was higher in pts with CSA than in pts with OSA (AHI 29.7 vs. 16.9 /h; p < 0.01). As expected severity of SDB was significant lower in pts with BMI ≤ 25 kg/m² (AHI 9.9 ± 3.4 /h) than in pts with BMI > 25 kg/m² (AHI 17.8 ± 2.2 /h; p = 0.002). Pts with OSA (BMI 29.0 ± 0.8 kg/m²) had a significant higher BMI than pts with noSDB (BMI 26.7 ± 0.8 kg/m²; p = 0.0002). Interestingly pts with CSA (BMI 28.9 ± 1.0 kg/m²) had also a higher BMI (p = 0.0006).
Conclusions: SDB has a high prevalence in pts with CAD. OSA was found more often (50.6 % vs. 23.3 %). AHI was higher in pts with CSA and in pts with higher BMI. Pts with SDB had a higher BMI than pts with noSDB.

3:30 p.m.

1041-152 The Prognostic Utility of Lipoprotein-Associated Phospholipase A_2 Activity Versus Mass in Patients With Stable Coronary Artery Disease

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

Background: Lipoprotein-associated phospholipase A_2 ($LpPLA_2$) is believed to contribute to atherogenesis. The relative prognostic utility of $LpPLA_2$ measured as enzyme activity versus mass remains undefined.
Methods: $LpPLA_2$ activity and mass (diaDexus) were measured at baseline in 3743 subjects in PEACE, a randomized trial of trandolapril 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 $LpPLA_2$ activity versus 1.12 (95% CI 1.04-1.19, P=0.002) for $LpPLA_2$ mass. Analyses by quartile are shown in Figure (left). In ROC analyses, $LpPLA_2$ activity (P=0.035), but not mass (P=0.16), significantly improved the C-statistic over traditional predictors. $LpPLA_2$ 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 analysis, elevated $LpPLA_2$ activity was predictive of risk regardless of mass (Fig, right).
Conclusion: $LpPLA_2$ activity and mass each independently predict outcomes in patients with stable CAD. The two markers are moderately correlated, and $LpPLA_2$ activity appears to be the stronger independent predictor of outcomes.



3:30 p.m.

1041-153 Diastolic Dysfunction by Cardiac Magnetic Resonance Imaging in Women With Open Coronary Arteries and Microvascular Dysfunction

Janet Wei, Louise Thomson, Chrisandra Shufelt, YuChing Yang, Edward Gill, Margo Minissian, Saibal Kar, Daniel Berman, C. Noel Bairey Merz, Cedars-Sinai Medical Center, Los Angeles, CA

Background: Coronary microvascular dysfunction is an etiological mechanism of ischemia in women with persistent angina, open coronary arteries and clinical evidence of ischemia. The relationship between microvascular dysfunction and left ventricular diastolic dysfunction is unexplored.
Methods: Coronary reactivity testing and resting cardiac magnetic resonance (CMR) of 41 women with suspected microvascular dysfunction were analyzed. Left ventricular end-diastolic pressure at rest, coronary flow reserve (CFR) and coronary blood flow (CBF) were measured during cardiac catheterization. Cine CMR images of the entire left ventricle were obtained in consecutive short-axis planes and used to measure septal wall thickness, left ventricular ejection fraction, peak filling rate (PFR) and time to peak filling rate from end-systole (tPFR). Univariate correlations and logistic regression were examined.
Results: All women had evidence of ischemia, nonobstructed epicardial coronary arteries, mean age 55 ± 8.3 years, and mean left ventricular ejection fraction 65 ± 13%. Mean left ventricular end-diastolic pressure was 15 ± 4.5 mmHg. Microvascular dysfunction (CFR<2.5 or CBF<50%) was present in 35/41 (85%) women. Mean tPFR was 178 ± 110 msec; mean PFR was 3.2 ± 0.64 end-diastolic volume/sec. CMR evidence of diastolic dysfunction (tPFR>127 or PFR<3.2) was present in 36/41 (88%) women and in 33/35 (94%) women with microvascular dysfunction. tPFR increased with age (r= 0.37, p= 0.017) and septal wall thickness (r= 0.47, p= 0.002), while PFR decreased with age (r= -0.45, p= 0.003). There was an inverse relationship between CFR and tPFR (r= -0.3, p= 0.058) and between CBF and PFR (r= -0.28, p= 0.08). Univariate logistic regression analysis was nonsignificant, but a trend toward significance was found between PFR and age (β= 0.07, p= 0.072).
Conclusion: CMR indices of diastolic filling correlate inversely with CFR and CBF, both trending toward statistical significance. The majority of women with microvascular dysfunction had resting diastolic dysfunction by CMR. This observation suggests a relationship between microvascular dysfunction and diastolic dysfunction, and may have therapeutic implications.

3:30 p.m.

1041-154 **Withdrawn**.

3:30 p.m.

1041-155 Defective Recovery of QT Dispersion Predicts Late Cardiac Mortality After Percutaneous Coronary Interventions

Marco Zimarino, Alessandro Corazzini, Alfonso Tatasciore, Marcello Caputo, Nicola Maddestra, Cesare Di Iorio, Raffaele 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 testing the association between rapidly occurring changes in corrected QTD (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 the 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=0.001). 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 (2.5%, P<0.001).
Conclusions: cQTD 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.

1041-156 Neopterin Predicts Left Ventricular Function in Patients With Chronic Stable Angina Pectoris

Rodrigo Estevez-Loureiro, Alejandro Recio-Mayoral, Juan A. Sieira-Rodriguez-Moret, Ernesto Trallero-Araguas, Juan Carlos Kaski, St. George's Hospital, London, United Kingdom

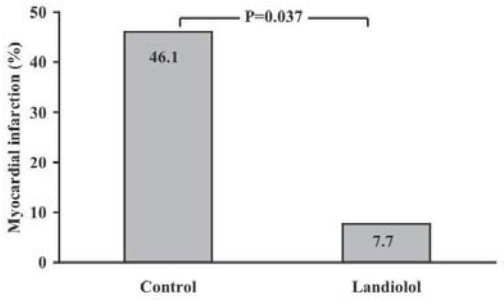
Background: Left ventricular ejection fraction (LVEF) is the strongest predictor of survival in patients with CSA. Inflammation plays a pathogenic role in atherosclerosis, and an enhanced inflammatory status is known to impair patient outcome. A link exists between inflammation and LV dysfunction. Neopterin, 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; 78% 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.

1041-157 Intravenous Administration of Subdepressor 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 subdepressor dose of short-acting beta-blocker Landiolol before coronary artery occulusion 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=13) 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 to >2 times the upper limit of normal within 24 hours of PCI.
Results: Intravenous administration of subdepressor 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 subdepressor dose of short-acting beta-blocker Landiolol before coronary artery occulusion may reduce the incidence of post-PCI MI in stable angina.

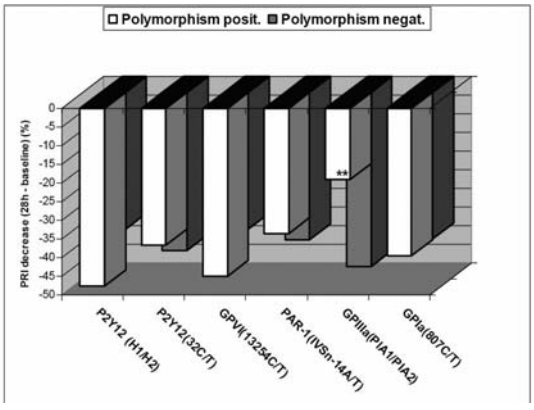


3:30 p.m.

1041-158 High Loading Dose of Clopidogrel Is Unable to Satisfactorily Inhibit Platelet Reactivity in Patients With Glycoprotein IIIA Gene Polymorphism : A Genetic Substudy of PRAGUE-8 Trial

Zuzana Motovska, Petr Widimsky, Jan Kvasnicka, Robert Petr, Dana Bilkova, Jaroslava Hajkova, Iuri Marinov, Stanislav Simek, Petr Kala, on behalf of the PRAGUE 8 study investigators, Third Medical Faculty Charles University and University Hospital Kralovske Vinohrady, Prague, Czech Republic

Background: The study aimed to assess the impact of 9 platelet receptors, enzymes, and haemostatic factor polymorphisms on clopidogrel efficacy in patients with stable CAD undergoing elective coronary angiography ±ad hoc PCI.
Methods: The study was performed as a genetic substudy of the PRAGUE-8 trial. 95 patients pretreated with 600mg clopidogrel >6h prior to coronary angiography were tested. Baseline platelet reactivity to ADP was assessed before the drug use. Clopidogrel efficacy was tested again at 12 and 28h after administration. Polymorphisms of 6 platelet receptors (Figure), gene variations of COX-1, Leiden and factor II mutations were studied. Flow cytometric tests of VASP phosphorylation states were used as a measure of drug efficacy.
Results: None of gene polymorphisms influenced baseline ADP-induced platelet reactivity significantly. 28h after drug administration, differences in suppression of ADP-induced platelet reactivity were observed between polymorphism positive and polymorphism negative patients. Inhibition of platelet reactivity, after 600mg of clopidogrel, was significantly less in carriers of PIA2 (p=0.009 for mean decrease in platelet reactivity index (PRI)). The proportion of clopidogrel non-responders (PRI>50%) was apparently higher in PIA2 carriers in comparison to PIA1/PIA1 patients (54% vs. 24%, p = 0.082).
Conclusions:A 600mg loading dose of clopidogrel failed to acceptably inhibit platelet reactivity in patients who were positive for the PIA2 polymorphism.



3:30 p.m.

1041-159 Long-Term Prognosis of Patients With Cardiac Syndrome X: Data From the Italian Registry of Syndrome X (RISX)

Isabella Tritto, Gaetano A. Lanza, Fausto Rigo, Stefano Favale, Oberdan Parodi, M. Lorenza Muiesan, Salvatore Novo, Irma Porchetta, M. Giovanna Conti, Giuseppe Ambrosio, Cardiology, University of Perugia, Perugia, Italy

Background: 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 identifing patients at higher risk of cardiovascular events. As this condition is rare, most information comes from single center studies, recruiting a small number of patients. The Italian Registry of Syndrome X (RISX) 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 [61±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 anginal 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 of 5.43; 95% C.I. 2.33-12.65; p<0.0005), and family history of coronary heart disease (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 anginal episodes. 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.

3:30 p.m.

1041-160 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.
OBJECTIVE: To compare results of IC and DC of bivalirudin (Bv) vs heparin (Hep) alone on ischemic and bleeding complications in low-risk PCI.
METHODS: Relevant studies chosen for IC included a common comparator (abciximab + Hep): REPLACE-2 (Bv vs abciximab + Hep) and ISAR REACT (abciximab + Hep vs Hep). The IC was performed according to the formula:
$RR_{Bv\ vs\ Hep}$ = ($RR_{Bv\ vs\ abciximab\ +\ Hep}$) x ($RR_{abciximab\ +\ Hep\ vs\ Hep}$); RR = relative risk. The results of IC were compared with a DC of Bv vs Hep based on ISAR REACT-3. The studies were comparable in terms of patient population, outcomes, and concomitant therapies (>85% thienopyridine pretreatment). An interaction test was conducted to assess whether treatment outcomes differed between IC and DC.
RESULTS (Table): Compared with Hep alone, IC yielded a nonsignificant 27% increase in ischemic composite endpoint (death/MI/TVR) compared with a nonsignificant 16% increase with Bv in the DC (between-comparison P = 0.75). While the point estimates for bleeding were in opposite directions, the IC and DC results did not differ significantly (interaction P value >0.05).
CONCLUSION: The results of IC accurately predicted the findings observed in a direct head-to-head comparison that Bv does not provide superior efficacy or safety compared with Hep alone during low-risk PCI. .

Bivalirudin vs Heparin Alone in Low-risk PCI

30-day Outcome	Bivalirudin vs Abcix + heparin (REPLACE-2)	Abcix+heparin vs heparin (ISAR REACT)	Bivalirudin vs heparin (Indirect Comparison)	Bivalirudin vs heparin (ISAR REACT-3)	Interaction P value
Death/MI/ urgent TVR	1.21 (0.93-1.58)	1.05 (0.69-1.59)	1.27 (0.77-2.08)	1.16 (0.91-1.49)	0.75
TIMI major bleeding	0.73 (0.41-1.32)	1.50 (0.62-3.66)	1.10 (0.38-3.17)	0.48 (0.23-0.98)	0.21
Transfusion rate	0.66 (0.46-0.94)	2.60 (1.25-5.37)	1.72 (0.76-3.85)	0.73 (0.46-1.16)	0.07

Data are shown as RR and 95% CI. Abcix: abciximab; TVR = target vessel revascularization; MI = myocardial infarction

3:30 p.m.

1041-161 Diabetes Mellitus and Adiponectin Synthesis at Different Types of Adipose Tissue in Patients With Coronary Atherosclerosis

Constantinos Bakogiannis, Charalambos Antoniades, Dimitris Tousoulis, Alexios S. Antonopoulos, Antigoni Miliou, Costas Triantafyllou, Constantinos Psarros, Robin Choudhury, Janet Digby, Ilias Kylintireas, George Ekonomopoulos, Christodoulos Stefanadis, 1st Cardiology Department, Hippokration Hospital, Athens Medical School, Athens, Greece, Department of Cardiac Surgery, Hippokration Hospital, Athens, Greece

Background: Adiponectin is an adipokine with antiatherogenic properties, but it is still unclear which sites of adipose tissue (AT) are mainly responsible for its synthesis in patients with atherosclerosis. We examined the association between circulating adiponectin and its synthesis in human subcutaneous, pericardial and femoral AT in patients with advanced atherosclerosis, and we examined the effect of diabetes mellitus (DM) on its synthesis.
Methods: The study population consisted of 75 patients with advanced atherosclerosis undergoing elective CABG, 22 with type 2 DM and 53 without DM. Serum adiponectin was measured preoperatively by ELISA, while the following types of AT were collected intraoperatively: (a) Subcutaneous from the site of insertion (b) pericardial (surrounding the pericardium) (c) femoral, around saphenous vein (perivascular). Adipose tissue was cultured ex-vivo for 4 hours, and adiponectin was measured in the AT culture supernatants by ELISA.
Results: Adiponectin synthesis was lower in subcutaneous AT (152.9±10.8 pg/mg) compared to femoral (185.5±15.2pg/mg p<0.05) or pericardial (214.8±18.4pg/mg, p<0.05) AT. Circulating adiponectin was significantly correlated with subcutaneous (r=0.416, p=0.005) and pericardial (r=0.828, p=0.002) but not with femoral (r=-0.251, p=ns) AT. Importantly, patients with DM had significantly lower serum adiponectin (9.6±2.1 vs 31.2±4.9 ug/mL p<0.001) as well as lower adiponectin synthesis in subcutaneous (126.6±16.8 vs 194.5±17.7pg/mg) and pericardial AT (152.7±25.5pg/mg vs 231.1±25.0pg/mg p<0.05) but not in femoral AT (209.2±52.1 vs 183.7±22.6pg/mg p=NS).
Conclusions: Circulating adiponectin levels are mainly driven by its release from subcutaneous and pericardial AT, while adiponectin synthesis in femoral AT is regulated by different mechanisms. Type 2 DM decreases adiponectin synthesis in subcutaneous and pericardial AT, leading to a respective effect on its circulating levels, while it has no impact on adiponectin synthesis in femoral AT. These findings provide new insights into the mechanisms regulating adiponectin synthesis in human atherosclerosis.

3:30 p.m.

1041-162 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. Pesaro, Carlos V. Serrano, Jr., Herlon Saraiva Martins, James De Lemos, Paulo R. Parra, Juliano L. Fernandes, Renata T. Ladeira, Roberto Rocha C.V. Giraldez, José Carlos 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 efficacy (25.8% vs 3.5%, respectively; 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.

Changes of lipid parameters, CRP and PFA

	S 80 (n=25)			E 10 / S 20 (n=22)		
	Baseline	After 6 weeks	p	Baseline	After 6 weeks	p
LDL-C (mg/dl)	93 (84.5-133.5)	75 (58.0-91.5)	<0.001*	96 (89.0-115.0)	71 (62.0-79.0)	<0.001*
HDL-C (mg/dl)	43 (38.5-48.5)	42 (38.0-48.0)	0.5**	41 (37.0-47.0)	41 (38.0-46.0)	0.90**
TG (mg/dl)	128 (90.0-172.5)	102 (85.0-141.0)	0.06**	142 (113.0-216.0)	121 (82.0-164.0)	0.02**
CRP (µg/ml)	2.1 (0.6-3.8)	0.9 (0.3-3.0)	0.01**	1.9 (0.3-3.0)	1.2 (0.7-3.3)	0.85**
PFA (seconds)	151.0+79.6	157.1+78.9	0.02*	168.7+70.1	203.4+67.5	0.02*

LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; PFA, platelet function aggregation; *ANOVA test; **Wilcoxon test; Data expressed in median (25th and 75th percentil); PFA expressed in average+SD.

ACC.ORAL CONTRIBUTIONS

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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.

0912-3 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 Zalewski, Patrick W. Serruys, Thoraxcenter Erasmus MC, Rotterdam, The Netherlands, GlaxoSmithKline, 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 L(p)PLA2 levels were observed to decrease in patients with acute coronary syndromes over time. With the exception of CRP and IL-6, the expression of classical biomarkers did not correlate with the presence of echogenic plaque on IVUS gray scale imaging or palpography. Proteomic 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 differences between baseline and a time point post-procedure 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, FGF-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 MIP-1d, TGF-b RIII 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.

0912-4 Growth-Differentiation Factor-15 for Risk Assessment in Patients With an Ongoing Non-ST-Elevation Acute Coronary Syndrome and After Clinical Stabilization

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

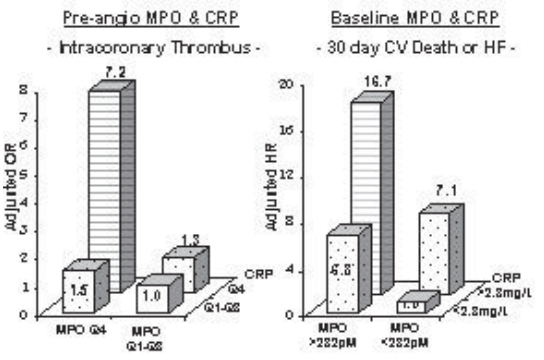
Background: Growth-differentiation factor-15 (GDF-15) is a stress-responsive TGF-β cytokine family member that has emerged as a prognostic biomarker in patients with a non-ST-elevation acute coronary syndrome (NSTE-ACS). The aim of the present study was to assess the time course and the prognostic relevance 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 1236 ng/L; p<0.001) as compared to patients randomized to a conservative strategy (1305 to 1268 ng/L; p=0.11). GDF-15 was consistently related 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 [1.1-3.9]; 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 (n=39/469 [8.3%]).
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.

5:00 p.m.

0912-5 Serial Inflammatory Biomarkers to Predict Angiographic and Clinical Outcomes in Patients With STEMI Undergoing Fibrinolysis: A CLARITY-TIMI 28 Substudy

Michelle O'Donoghue, David A. Morrow, Songtao Jiang, Nader Rifai, Christoph Bode, C. Michael Gibson, Robert E. Gerszten, Christopher P. Cannon, Marc S. Sabatine, Brigham and Women's Hospital, Boston, MA, Massachusetts General Hospital, Boston, MA

Background: Inflammation contributes to atherothrombosis. The utility of serial inflammatory biomarkers for predicting angiographic and clinical outcomes in ST-elevation myocardial infarction (STEMI) remains unknown.
Methods: C-reactive protein (CRP) and myeloperoxidase (MPO) were measured at baseline and prior to angiography (CRP cohort n=1250; MPO case-cohort n=701) in CLARITY-TIMI 28, a randomized trial of clopidogrel vs placebo in STEMI and fibrinolysis. Angiography was performed at 2-8 d; events followed to 30 d. Analyses were adjusted for cardiac risk factors, timing and type of lytic therapy, Killip class, and peak CK-MB.
Results: Patients with a baseline CRP >2.8 mg/L (median) compared with those below had a higher risk of CV death or heart failure (CVD/HF) (adj HR 2.1, 1.2-3.8, P=0.02). Pre-angiographic CRP in the top quartile was associated with a higher odds of intracoronary thrombus at angiography (adj Q4:Q1 OR 1.6, 1.03-2.6, P=0.04). MPO levels >232 pM were associated with a higher risk of CVD/HF (adj HR 3.0, 1.1-8.2, P=0.03). Pre-angiographic MPO in the top quartile was associated with higher odds of intracoronary thrombus (adj OR 2.3, 1.1-5.1, P=0.03). The combination of CRP and MPO provided incremental information for predicting CVD/HF and the presence of intracoronary thrombus (Figure).
Conclusions: In STEMI, serial measurement of CRP and MPO provide significant and complementary predictive ability for clinical and angiographic outcomes independent of traditional risk factors.



5:15 p.m.

0912-6 Cytochrome P450 2C19 Polymorphism in Young Post-Myocardial Infarction Patients Treated With Clopidogrel

Jean-Philippe Collet, Jean-Sebastien Hulot, Ana Pena, Eric Villard, Jean-Baptiste Esteve, Johanne Silvain, Laurent Payot, Guillaume Cayla, Farzin Beygui, Delphine Brugier, Christian Funck-Brentano, Gilles Montalescot, Hopital Pitie-Salpetriere Institut de Cardiologie, Paris, France, Hopital Pitié-Salpetriere Unite de Pharmacologie, Paris, France

Background: The frequent genetic functional variant 681 G>A (also called *2) of cytochrome P450 2C19 is an important contributor to the wide interindividual variability of the antiplatelet effect of clopidogrel. We evaluated whether the CYP2C19*2 polymorphism has an impact on the long-term clinical prognosis of young patients (< 45years) who survived a first myocardial infarction and were chronically treated with clopidogrel.
Methods: 259 patients underwent CYP2C19*2 determination and had a median [25th-75th] clopidogrel exposure time of 1.07 [0.28-3.0] years. The primary endpoint was a composite of death, myocardial infarction and urgent coronary revascularization occurring during exposure to clopidogrel. The key secondary endpoint was angiographically proven stent thrombosis.
Results: Baseline characteristics were balanced between carriers (heterozygous *1/*2, n=64; homozygous *2/*2, n=9) and non carriers (n=189) of the CYP2C19*2 genetic variant. The primary end point occurred more frequently in carriers than in non carriers of the CYP2C19*2 genetic variant (HR, 3.69; 95% CI, 1.69 to 8.05; p=0.0005). Stent thrombosis was also significantly more frequent in carriers than in non carriers (HR 6.02; 95%CI 1.81 to 20.04, p=0.0009). The detrimental effect of the CYP2C19*2 genetic variant persisted from 6 month after clopidogrel initiation up to the end of follow-up (HR 3.0; 95%CI, 1.27 to 7.10; p=0.009). Following multivariable analysis, the CYP2C19*2 genetic variant was the unique independent predictor of cardiovascular events (HR 4.04; 95% CI 1.81-9.02, p=0.0006).
Conclusion: The CYP2C19*2 genetic variant is a major determinant of prognosis in young post-MI patients on clopidogrel treatment.

5:30 p.m.

0912-7 **CRP1444, CD14 and MMP3 Polymorphisms Correlate With Coronary Plaque Volume in Patients With Coronary Artery Disease: IVUS Data From the ENCORE Trials**

Matthias Hermann, Dieter Fischer, Michael M. Hoffmann, Theo Gasser, Kurt Quitzau, Thomas Meinertz, Thomas Munzel, Thomas F. Luscher, University Hospital Zurich, Zurich, Switzerland

Background: Several single-nucleotide polymorphisms (SNPs) have been linked to progression of atherosclerosis, coronary plaque size and incidence of acute coronary 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 promotor 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.

	Plaque volume / vessel size	p-value
CD14 (n=33) CC	0.285 ± 0.103	
CD14 (n=78) CT	0.294 ± 0.113	
CD14 (n=62) TT	0.335 ± 0.128	0.026
CRP1444 (n=11) CC	0.286 ± 0.123	
CRP1444 (n=78) CT	0.284 ± 0.110	
CRP1444 (n=84) TT	0.331 ± 0.122	0.002
MMP3 (n=50) 6A/6A	0.268 ± 0.126	
MMP3 (n=75) 5A/6A	0.310 ± 0.108	
MMP3 (n=48) 5A/5A	0.344 ± 0.114	0.016

ACC.POSTER CONTRIBUTIONS

1050

Stable Ischemic Syndrome; Cardiopulmonary Resuscitation/ Emergency Cardiac Care/Shock; Coronary Artery Bypass Surgery/ Innovative Techniques

Tuesday, March 31, 2009, 9:30 a.m.-12:30 p.m.
Orange County Convention Center, West Hall D

9:30 a.m.

1050-125 **Albuminuria, the Glomerular Filtration Rate, and Angiographically Determined Coronary Atherosclerosis**

Philipp Rein, Christoph H. Saely, Lorenz Risch, Stefan Beer, Alexander Vonbank, Christian Boehnel, Vlado Jankovic, Ulrich Neyer, Heinz Drexel, Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria, Private University in the Principality of Liechtenstein, Triesen, Liechtenstein

Background: We aimed at investigating the association of albuminuria and of the glomerular filtration rate (eGFR) with angiographically determined coronary atherosclerosis.
Methods: Urinary albumin and creatinine concentrations were measured in 856 consecutive patients undergoing coronary angiography for the evaluation of suspected or established stable coronary artery disease (CAD); the eGFR was calculated by the Mayo clinic quadratic equation.
Results: From our patients, 278 had an eGFR <90ml/min/1.73m², and 204 had albuminuria (ACR ≥30 mg/g). When compared to subjects with both normal eGFR and normal urinary albumin excretion (n = 467), the prevalence of significant coronary stenoses (i.e. stenoses with lumen narrowing ≥50%) was significantly higher in patients with normal eGFR and albuminuria (n = 111) and in those with decreased eGFR and albuminuria (n = 93), but similar in those (n = 185) who had decreased eGFR but not albuminuria (51.8 vs. 64.0%, p = 0.021; 51.8 vs. 65.8%, p = 0.015; and 51.8 vs. 49.2%.; p = 0.545, respectively). Concordantly, in logistic regression analysis the ACR but not the eGFR proved predictive of significant coronary stenoses after adjustment for age, gender, diabetes, body mass index, LDL cholesterol, HDL cholesterol, blood pressure and smoking, with odds ratios (OR) of 1.26 [95% CI 1.02 - 1.56]; p = 0.032 and 1.05 [0.86 - 1.28]; p = 0.63, respectively. Further, in line with our results from univariate analyses, the association between the ACR and significant coronary stenoses remained significant after further adjustment for eGFR (OR = 1.28 [1.03 - 1.60]; p = 0.025).
Conclusion: Albuminuria is strongly associated with angiographically determined coronary atherosclerosis, independent of conventional cardiovascular risk factors and of the eGFR.

9:30 a.m.

1050-126 **Promotion of Coronary Collateral Growth by External Counterpulsation in Patients With Coronary Artery Disease**

Steffen Gloekler, Stefano F. de Marchi, Tobias Rutz, Pascal Meier, Kerstin Wustmann, Stefano F. Rimoldi, Mario Togni, Christian Seiler, University Hospital, Bern, Switzerland

Background: Arteriogenesis is a promising therapeutic option for patients with extensive coronary artery disease (CAD). External Counterpulsation (ECP) augments diastolic arterial pressure by sequential leg cuff compressions with increase in coronary perfusion. Augmented coronary perfusion with elevated laminar shear stress at the endothelial cell layer has been shown to induce arterial remodelling and collateral growth (arteriogenesis). It is unclear yet whether the clinical benefit of ECP is related to its hypothesized effect of collateral growth. The purpose of the present study is to evaluate the effects of ECP on coronary collateral function.
Methods: Fifteen patients with stable CAD were included in this single-blind, sham-controlled study. They were randomly assigned to 30 hours of ECP treatment (n=9: cuff inflation pressure 300mmHg in 8 patients and 120mmHg in 1 patient.) or 30 hours of sham-ECP treatment (n=6: cuff inflation pressure 80mmHg) over three weeks, i.e., 2 hours per session. Invasive coronary collateral assessment was performed at baseline and after ECP. Collateral Flow Index (CFI) was determined invasively during balloon occlusion by means of a pressure guide wire distal to the balloon-occluded artery and was calculated as: (Poccl-CVP)/(Pao-CVP); Poccl=mean coronary occlusive pressure; Pao=mean aortic pressure; CVP=central venous pressure.
Results: In the ECP group, CFI changed from 0.122 +- 0.06 to 0.210 +-0.07 (p= 0.0002) and in the sham-ECP group from 0.165 +-0.08 to 0.130 +-0.06 (p=0.04). The treatment-induced difference in CFI was +0.088 +-0.07 in the ECP group and -0.044 +- 0.07 in the sham-ECP group (p=0.00005).
Conclusions: This first clinical study investigating the effect of ECP on coronary collateral function in patients with CAD clearly documents efficacy. The clinical benefit of ECP for CAD patients may be at least partly explained by its arteriogenetic effect.

9:30 a.m.

1050-127 **Significant Association of Left Mammary Arterial Wall Thickness With Arterial Stiffness in Hypertensive Patients With Coronary Artery Disease**

Maria Marketou, Anastassios Koutsopoulos, Theoxaris Xenikakis, George Kochiadakis, Konstantina Dambaki, Polichronis Malliotakis, John Hassoulas, Efstathios Stathopoulos, Panos Vardas, Heraklion University Hospital, Heraklion, Greece

Background: Pulse wave velocity (PWV) measurements are useful for evaluating arterial stiffness, which reflects the overall opposition of large arteries to the pulsatile effects of ventricular ejection, and has independent predictive value for cardiovascular events. However, there is lack of data regarding the structural changes of the arterial wall in humans with increased PWV. We investigated the relation of PWV with the left mammary arterial wall thickness and fibrosis in hypertensive patients with coronary artery disease (CAD).
Methods: Segments of the left mammary artery were obtained from 11 hypertensive patients (7 men, aged 67 ± 10 years) who underwent coronary artery bypass surgery because of 3-vessel stable CAD. A day before, PWV was measured noninvasively by Complior in all patients. Five μm tissue sections were cut and stained with hematoxylin and eosin for the evaluation of artery wall thickness and with Picrosirius Red for the evaluation of fibrosis. In each artery, we determined the percentage of total and media fibrosis, the wall thickness/lumen ratio, the media thickness and the media/lumen ratio.
Results: The carotid-femoral PWV showed a strong correlation with the left mammary arterial wall thickness/lumen ratio and the media thickness in patients with CAD (r=0.72, p <0.01, and r=0.62, p=0.02, respectively). No significant association was found between the percentage of total and media fibrosis with PWV.
Conclusions: Left mammary arterial wall and media thickness were significantly associated with pulse wave velocity in hypertensive patients with CAD. Our data contribute to the understanding of the structural changes of the arterial wall that underlie the increased arterial stiffness in those patients.

9:30 a.m.

1050-128 **Noninvasive Pressure Waveform Analysis in Women With Chest Pain and Nonobstructive Coronary Artery Disease**

Wilmer W. Nichols, Scott J. Denardo, B. Delia Johnson, Barry L. Sharaf, Carl J. Pepine, University of Florida, Gainesville, FL

Background: Early return of reflected blood pressure (BP) waves from the lower body augments aortic systolic BP and increases systolic pressure-time index (SPTI) and wasted LV energy which increase left ventricular (LV) afterload and myocardial O_2 demand. Such changes are due to increased arterial stiffness and pulse wave velocity (PWV) and can contribute to myocardial ischemia and angina pectoris, especially when coronary artery (CA) perfusion pressure is jeopardized. We sought to determine wave reflection characteristics and diastolic BP timing in a subgroup of Women's Ischemia Syndrome Evatuation (WISE) participants referred for coronary angiography for suspected myocardial ischemia but without obstructive CAD.
Methods: Radial artery BP waveforms were recorded by applanation tonometry and central aortic BP waveforms derived. Data were collected from 63 WISE participants and compared to an asymptomatic reference group of 65 women matched for age, height, BMI, mean arterial BP and heart rate.
Results: Compared to the reference group, WISE participants had higher aortic systolic

(121±16 vs 115±14 mmHg, P<0.03) and pulse (40±12 vs 36±7.9 mmHg, P<0.04) BP. These differences were associated with an increase in augmented BP (12±5.1 vs 9.5±4.3 mmHg, P<0.003), augmentation index (30±7.6 vs 25±8.9%, P<0.001) and reflected wave duration (194±21 vs 173±24 msec, P<0.001). These modifications in WISE participants were associated with an increase in ejection duration (330±23 vs 309±23 msec, P<0.001), SPTI (2562±398 vs 2344±408 units, P<0.003) and wasted LV energy (4806±2330 vs 3534±1818 dyne-sec-cm^{-2}, P<0.001) and a decrease in pulse BP amplification (1.2±0.12 vs 1.3±0.13, P<0.04), the myocardial viability ratio (1.3±0.25 vs 1.5±0.20, P<0.01) and the diastolic BP time fraction (DPTF) (0.61±0.04 vs 0.64±0.04, P<0.01).

Conclusions: WISE participants have changes in wave reflection characteristics and diastolic timing that increase LV afterload, myocardial O_2 demand and wasted LV energy and reduce coronary perfusion. These alterations in cardiovascular function contribute to an undesirable mismatch in the myocardial O_2 supply/demand ratio that favors ischemia and angina pectoris.

9:30 a.m.

1050-129 Incident Diabetes Mellitus in Patients With Stable Coronary Artery Disease

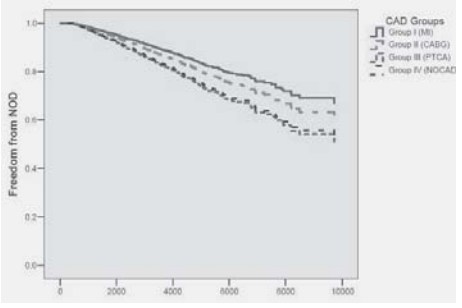
Apurva Badheka, Neha Garg, Mohammad A. Kizilbash, Samrat Bhat, Ankit Rathod, Sony Jacob, Luis Afonso, Wayne State University, Detroit, MI

Background: Predictors and significance of new onset diabetes (NOD) in patients with stable coronary arterial 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=3856). Groups II (n=1408) and III (n=994) comprised patients post revascularization (CABG 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 blocker (0.66, 0.55-0.80), trandolapril (0.74, 0.62-0.87) and BMI (1.11, 1.09-1.12). Groups III and IV were at significantly higher risk of NOD (1.62, 1.30-2.02 and 1.58, 1.22-2.04) as compared to Group I (figure). NOD was associated with increased composite outcome of cardiovascular death, MI, PTCA or CABG (1.25, 1.07-1.46).

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 portends poor prognosis in stable CAD.



9:30 a.m.

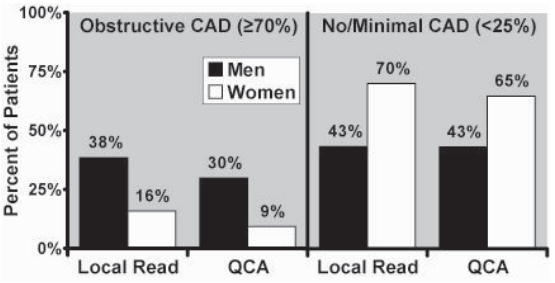
1050-130 Differential Prevalence of Clinically Significant Coronary Artery Disease Among Symptomatic Men and Women Referred for Coronary Artery Catheterization

Whittemore G. Tingley, Eric J. Topol, Szilard Voros, Alexandra J. Lansky, Robert S. Schwartz, William E. Kraus, Amy J. Sehnert, May Yau, Michael R. Elashoff , Steven Rosenberg, Philip Sager, CardioDx, Palo Alto, CA

Background - The evaluation of coronary artery disease (CAD) in symptomatic women is often considered more challenging than in men. Despite advances in non-invasive diagnostic testing, the prevalence of significant CAD is little studied in women and men referred for coronary catheterization (CATH).

Methods - We addressed this issue in 875 pts enrolled at 31 US centers in the PREDICT trial, which is prospectively evaluating the ability of peripheral blood gene expression to identify CAD. All pts were referred for CATH based on local practice criteria and were symptomatic but not previously known to have CAD or myocardial infarction. CAD severity was evaluated by local site reads and by a blinded quantitative coronary angiography (QCA) core lab.

Results - The mean age was 58 (±12) yrs, 412 (47%) were women and 210 (24%) had diabetes. Stable or unstable symptoms were present in 78% and 22% of pts and 675 (77%) had at least one non-invasive test (including 609 stress nuclear tests or echos). Based on local CATH reads, only 243 (28%) of pts had obstructive CAD (at least one lesion >70% diameter stenosis or a left main lesion >50%): 38% of men and 16% of women (P<0.0001), despite similar clinical variables. 490 (56%) pts had no or minimal disease (<25% lesion). QCA analysis yielded lower numbers with obstructive CAD (men vs women P<0.0001; figure).



Conclusions - Despite widely used non-invasive testing, only a minority of new, symptomatic pts referred for CATH have clinically significant CAD. The rate is particularly low in women.

9:30 a.m.

1050-131 Association Between Genetic Variants on the Chromosomal Loci 9p21.3, 6q25.1, and 2q36.3 and Angiographically Determined Coronary Artery Disease

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

Background: Recently, the chromosomal loci 9p21.3, 6q25.1, and 2q36.3, represented by their respective leading single nucleotide polymorphisms (SNPs) rs1333049, rs6922269 and rs2943634 have been linked with a history of coronary artery disease (CAD) by genome-wide association studies. Whereas the association of variant rs1333049 with CAD was analysed in several subsequent studies, replication studies of SNPs rs6922269 and rs2943634 are still missing.

Methods: Therefore, to further elucidate the role of variants rs1333049, rs6922269, and rs2943634 on the molecular genetics of CAD, we performed genotyping of these SNPs in two large cohorts of consecutive Caucasian patients undergoing coronary angiography for the evaluation of suspected or established stable CAD, comprising 671 and 940 subjects, respectively; coronary stenoses with lumen narrowing ≥50% were considered significant.

Results: In models of dominant inheritance SNP rs1333049 was significantly associated with an increased risk of significant coronary stenoses in both study cohorts, with adjusted odds ratios (OR) of 1.71 [1.15-2.52]; p = 0.007 and 1.55 [1.10-2.18]; p=0.012, respectively. A significant association of variant rs6922269 with an increased susceptibility for CAD could be observed in neither cohort. Carriers of the A allele of variant rs2943634 showed a significant association with an increased risk of significant coronary stenoses in the second cohort (OR=1.41 [1.06-1.86]; p=0.018), but not in the first cohort (OR=0.85 [0.57-1.26]; p=0.420).

Conclusion: We conclude that variant rs1333049 is significantly associated with angiographically determined CAD. By contrast, SNP rs6922269 did not show any impact on the presence of significant stenoses. The association between variant rs2943634 and CAD warrants further investigation.

9:30 a.m.

1050-132 Use of Pulsed Electromagnetic Fields For Ischemic Cardiomyopathy Therapy (EFFECT Trial): A Randomized, Double-Blind, Parallel, Placebo-Controlled, Prospective Trial

Michael Y. H. Shen, Craig R. Asher, Mary Chandy, Tudor Scridon, Eric Dandes, Eduardo Vargas, Adrian Hernandez, Howard S. Bush, Kenneth R. Fromkin, Louis Ignarro, Arthur Pilla, Gian M. Novaro, Cleveland Clinic Florida, Weston, FL, Columbia University, New York, NY

Many studies have shown that pulsed electromagnetic fields (PEMF) are effective in treating chronic wounds, avascular necrosis & chronic pain by improving blood flow/angiogenesis via NO/cGMP pathway. This is the 1st pilot trial to evaluate PEMF safety & efficacy in pts with chronic angina and ischemic heart disease (IHD). **Methods:** Pts (n=33) with severe IHD (≥70% stenosis) & angina, on max medical therapy & not amenable to revascularization, were randomized into sham (S, n=17) or treatment (T, n=16) groups. A PEMF device was put over the left chest (4msec, 27.12MHz, 50mG at 2Hz, Ivivi Technologies) 30 min BID for 3 mon. Vital signs (VS), labs (C24), Seattle Angina Questionnaire, Echo & SPECT (17 segment summed stress score, SSS) were performed at baseline, 1, 3 & 5 mon. Continuous home telemetry performed 1 wk pre & post PEMF. **Results:** Two pts in S and 1 pt in T group were withdrawn due to adverse events. No significant differences in VS, labs, tele or LVEF were found between the groups. Anginal score & physical capacity were significantly improved with PEMF. **Conclusions:** This is the first study using PEMF in pts with IHD. The trial shows that PEMF is safe to use and effective improving symptoms in pts with IHD and failed medical & revascularization options. This unique device is non-invasive, non-pharmacological & self-operable at home. Future studies are needed to investigate mechanistic effects, perfusion changes and clinical outcomes in large trials.

	n=30	Baseline	1 mon	3 mon	5 mon
Angina Score (100 highest stability)	S n=15	63±31	53±16	62±23	63±16
	T n=15	57±18	69±25*	78±21*	87±16*
Physical Capacity (100 highest function)	S n=15	57±26	56± 24	54±24	49±25
	T n=15	62±24	69±22	68±24	75±18*
Stress SSS	S n=15	19±11	19±11	19±11	19±12
	T n=15	16±9	14±8	15±8	14±8

P<0.01 S vs. T group, Kruskal-Wallis rank test & Wilcoxon rank sum test

9:30 a.m.

1050-133 **Granulocyte-ColonyStimulatingFactor (G-CSF) Promotes Coronary Collateral Growth and Myocardial Microvascular Function in Patients With Coronary Artery Disease: A Randomized, Double-Blind, Placebo-Controlled Study**

Steffen Gloekler, Pascal Meier, Rainer Zbinden, Stefano F. de Marchi, Tobias Rutz, Andreas Indermuehle, Rolf Vogel, Stephan Windecker, Christian Seiler, University Hospital, Bern, Switzerland

Background: Coronary artery disease (CAD) is one of the leading causes of death in industrialized countries. About 1/5 to 1/3 of CAD patients are not suitable for the traditional revascularization therapies. Therefore, alternative strategies, like collateral growth promotion (arteriogenesis), are warranted. Since the amount of collateral flow is directly related to survival, prognosis of CAD may be improved by arteriogenesis. Monocytes play a pivotal role in arteriogenesis. The purpose of the present study was to investigate the efficacy and safety of G-CSF as a monocyte-stimulating factor with regard to collateral growth.
Methods:52 patients (age 63 +- 10 years) with CAD were prospectively included in the study, and they received G-CSF (5 micrograms/Kg per day, s.c.) or placebo during 14 days. The study protocol comprised invasive measurement of functional collateral flow and fractional flow reserve (FFR) at baseline and follow-up. Collateral Flow Index (CFI) was determined during balloon occlusion by a pressure guide wire distal to the balloon-occluded artery, and was calculated as: (Poccl-CVP)/(Pao-CVP); Poccl=mean coronary occlusive pressure; Pao=mean aortic pressure; CVP=central venous pressure. Of the 26 G-CSF patients, 3 aborted the study prematurely because of side effects, and 1 due to a short episode of angina pectoris. Intention-to-treat-analysis.
Results:CFI changed from 0.116 +- 0.08 to 0.164 +-0.09 in the G-CSF group (p=0.0000012), and from 0.152 +-0.08 to 0.132 +-0.07 (p=0.02) in the placebo group (figure). FFR changed from 0.84 +- 0.11 to 0.86 +-0.10 in the verum group (p=0.03), and from 0.87 +-0.11 to 0.84 +-0.12 (p=ns) in the placebo group. In the intracoronary and external ECG, G-CSF patients had less signs of myocardial ischemia during coronary occlusion in comparison to placebo patients after therapy (p= 0.0002 and 0.007). Angina pectoris during coronary occlusion was also reduced in G-CSF patients after therapy (p= 0.009).
Conclusions: This study shows for the first time that G-CSF is both efficient and safe for the promotion of coronary collateral growth in patients with CAD.

9:30 a.m.

1050-134 **Postload Reduced Insulin Level Is Associated With High Mortality Rates in Patients With no Previous Diagnosis of Diabetes Mellitus**

Shin Kadota, Mitsuo Matsuda, Masayasu Izuhara, Osamu Baba, Hirokazu Mitsuoka, Keisuke Shioji, Takashi Uegaito, Kishiwada City Hospital, Kishiwada, Japan

Background: Hyperinsulinemia and insulin resistance have been proposed for having a causal role in pathogenesis of atherosclerosis; however, the relation between post-load insulin levels and long-term survival is not clear. We sought to test the hypothesis that post-load insulin response is a predictor of outcome in patients with no previous diagnosis of diabetes mellitus (DM).
Methods: The data of 933 Japanese patients (621 males and 312 females) who were admitted to the hospital between 2002 and 2007 with suspected coronary artery disease and who underwent both coronary angiography and a 75g oral glucose tolerance test was analyzed. Various metabolic factors were measured including fasting, post-load plasma glucose and insulin levels. The determinant factors in association with major adverse cardiovascular events (MACE), including all-cause death, reinfarction, heart failure or angina requiring re-hospitalization, coronary artery bypass grafting, and percutaneous coronary intervention were examined by multivariate Cox regression analysis.
Results: The numbers of patients with normal, impaired and diabetic glucose tolerance were 326, 408 and 199, respectively. The differences of insulin levels in glucose tolerance status were significant by one-way analysis of variance (fasting P=0.0004, 1-hour P<0.0001, 2-hour P<0.0001). During the follow-up period (mean 1162 ± 688 days), MACE occurred for 230 patients including 24 non-cardiac and 13 cardiac deaths. There were no significant differences on MACE incidence or mortality between glucose tolerance statuses. Kaplan-Meier curves indicated that the lower response group of 2-hour insulin levels (<75.3 μU/ml; median) was associated with higher mortality (Logrank P=0.006). Multivariate Cox regression analysis revealed that 2-hour insulin levels were an independent predictor of all-cause death (P=0.026), and 1-hour insulin levels were that of cardiac death (P=0.005), after adjustment for age, gender, number of stenosed vessels, ejection fraction, metabolic factors, and treatment.
Conclusions: Post-load reduced insulin response is seen as a predictor of long-term mortality for patients with no previous diagnosis of DM.

9:30 a.m.

1050-135 **Significant Impact of Genetic Variants on Chromosomal Locus 1p13.3 on Serum LDL-Cholesterol and on Angiographically Characterized Coronary Artery Disease**

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

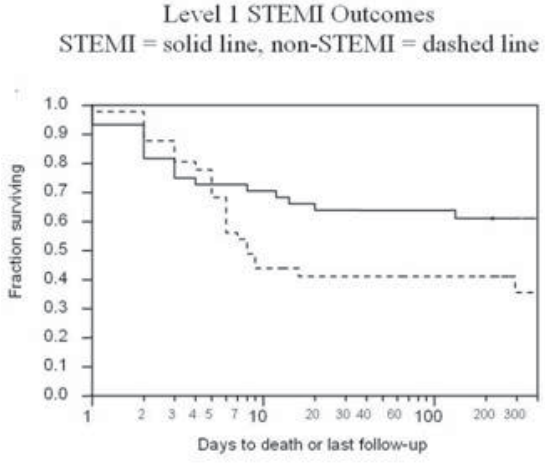
Background: Recently, genome-wide association studies identified a significant impact of a novel locus on chromosome 1p13.3 on serum LDL-cholesterol, which is causally linked to coronary artery disease (CAD). Potential associations between variants on this locus and angiographically characterized coronary 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 [0.63-0.96]; 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.

1050-136 **Cool It: Therapeutic Hypothermia for Cardiac Arrest in Patients With ST-Elevation Myocardial Infarction and Unique Benefits With Combined Treatment**

Leah A. Swanson, Kalie M. Edelstein, William M. Parham, Christopher E. Kapsner, Barbara T. Unger, Mary E. Kalb, James Hodges, M. Nicholas Burke, Anil K. Poulose, Timothy D. Henry, Michael R. Mooney, Minneapolis Heart Institute Foundation at Abbott Northwestern Hospital, Minneapolis, MN

Background: Out-of-hospital cardiac arrest (OOHCA) with ST elevation myocardial infarction (STEMI) leads to poor neurologic outcome. Therapeutic hypothermia (TH) has been shown to improve survival and neurologic outcome following OOHCA but has not been performed simultaneously with STEMI percutaneous coronary intervention (PCI).
Methods: Following the Level 1 transfer program for STEMI, the Cool It program established a regional TH system. OOHCA pts with STEMI are transferred to the cath lab for PCI. TH is implemented in the cath lab before PCI, and TH at 33ºC is continued for 24 hrs. Cerebral function after TH was measured by the five point Pittsburgh Cerebral Performance Category (CPC) scale. CPC 1 and 2 are favorable neurologic outcomes.
Results: From 2/06 to 5/08, 85 pts were treated with TH, 44 were Level 1 STEMI pts with 59% of STEMI pts in cardiogenic shock. TH was initiated within 150 minutes in Level 1 STEMI pts and 153 minutes in non-STEMI pts (p=0.88). For each hour TH was delayed, the relative risk of death increased by 20%. Compared to non-STEMI pts, STEMI pts had a higher survival rate (64% vs. 41%, p=0.052) and neurologic outcome (100% vs. 82%, p=0.048).
Conclusions: OOHCA pts with STEMI displayed unique benefits from TH with high survival rates and positive cognitive outcomes. Our results indicate the need for simultaneous execution of TH and STEMI protocols in OOHCA patients with acute MI. Given these positive outcomes, TH should be included as a part of acute MI programs that function as tertiary centers.



9:30 a.m.

1050-137 Incidence of Infection in Patients With Sudden Cardiac Death Treated With Therapeutic Hypothermia Versus Conventional Care

Brian E. Gulbis, Andrea C. Hall, James Constable, Punit S. Parasher, Christopher Y. Kim, Raghavendri Moturi, Tayyab Mohyuddin, Saurab Sanon, Santiago Segurola, Ramal Weragoda, H. V. Anderson, Stefano Sdringola, 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 144 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.

1050-138 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 age 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). Etiology of death with exertion was cardiac (124, 68.0%), non-cardiac (2, 1.0%), or idiopathic (61, 31.0%); non-exertional death was cardiac (134, 67.4%), non-cardiac (2, 1.1%), or idiopathic (58, 31.5%, p=0.99). Of exertional cardiac death, the most common cause of death was atherosclerosis (64, 51.6%), concentric LV hypertrophy without disarray (19, 15.3%), anomalous coronary artery (10, 8.1%), and hypertrophic cardiomyopathy (10, 8.1%). The activity associated with sudden death was most commonly physical fitness training (45.1%), recreational sports (45.1%), or military training (3.8%). 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 (139, 75.6%) while hypertrophic CM (10, 5.4%) and concentric 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 provide clues as to etiology. Hypertrophic cardiomyopathy is much less common that previously reported in a population undergoing active surveillance and autopsy.

9:30 a.m.

1050-139 Etiology of Sudden Death Among Younger Adults in the Community: Results of Anatomic Metabolic and Genetic Evaluation

A. Selcuk 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 autopsy, laboratory testing 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%) but inadequately treated. 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 SCN5A.
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. Analgesic 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.

1050-140 The Significance of ST Elevation in Right Precordial Leads in Acute Anterior Myocardial Infarction

Alon Barsheshet, Hanoch Hod, Dan Oiero, Athanasios Michailidis, Ilan Goldenberg, Michael Glikson, Michael Eldar, Shlomi Matetzky, 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 anterior acute myocardial infarction (AMI) are unknown.
We aimed to asses the clinical utility of ST-segment elevation in leads V3R and V4R in anterior AMI.
Methods: This study comprised 120 consecutive patients who were admitted within 12 hours of symptoms onset of anterior ST elevation AMI. All had 18 leads electrocardiograms with right precordial leads. Patients were stratified into two groups based on whether they had ST elevation ≥ 1 mV in V3R and V4R (group A) or not (group B). Early primary ventricular fibrillation (VF) was defined as VF occurring within 12 hours of symptoms onset and before coronary catheterization.
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=.0019, for HF 15/39 (38%) vs. 14/81(17%), p=.021]. Patients in group A compared with group B had a trend towards less spontaneous reperfusion (14% vs. 32%, p=.063) and had higher incidence of multivessel coronary artery disease [median (interquartile range) of 2 (1-3) vs. 1 (1-2), p=.097 respectively]. 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.

1050-141 Association of Body Mass Index on Survival After In-Hospital Cardiac Arrest.

Renuka Jain, Brahmajee K. Nallamouthu, 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 (18.5-24.9), overweight (25.0-29.9), obese (30.0-34.9), and very obese (>35.0), 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 (p for trend=0.001) (Table 1). In contrast, of 17,267 patients with arrests due to asystole or pulseless electrical activity, 2,773 (15.6%) survived. Cardiac arrest in patients who were underweight was associated with markedly 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.

VF and Pulseless VT

BMI	N	Survived to Discharge no.(%)	Adjusted OR	p-value
<18.5	221	61 (27.6)	0.57 (0.40, 0.82)	0.002
18.5 to 25	1,369	500 (36.5)	0.75 (0.63, 0.88)	0.0007
>25 to 30	1,328	605 (45.6)	Reference	Reference
>30 to 35	817	357 (43.7)	0.88 (0.72, 1.07)	0.20
>35	764	302 (39.5)	0.80 (0.65, 0.98)	0.03
			p-value for trend	0.001

Asystole and PEA

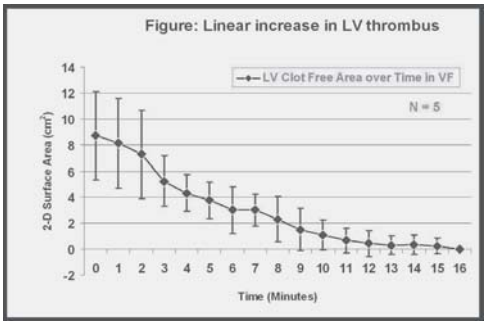
BMI	N	Survived to Discharge no.(%)	Adjusted OR	p-value
<18.5	1,277	61 (27.6)	0.63 (0.51, 0.77)	<.0001
18.5 to 25	5,897	500 (36.5)	0.93 (0.83, 1.03	0.17
>25 to 30	4,876	605 (45.6)	Reference	Reference
>30 to 35	2,772	357 (43.7)	1.10 (0.97, 1.25)	0.14
>35	2945	302 (39.5)	0.96 (0.84, 1.09)	0.53
			p-value for trend	<.0001

9:30 a.m.

1050-142 **Linear Increase in Left Ventricular Thrombus Over Time in Ventricular Fibrillation Confirmed by Intra-cardiac Echocardiography**

Martin C. Burke, Carmen Jaramillo, Thomas H. Freeman, Matthew Smelley, Dipak Shah, Ian Weisberg, John F. Beshai, Susan S. Kim, Albert C. Lin, Bradley P. Knight, University of Chicago, Chicago, IL

Mortality increases 10% every minute in cardiac arrest. To understand the poor outcome, we studied thrombus formation using direct imaging of the cardiac chambers with an intracardiac echocardiography (ICE) (Accuson, Mountain View, CA) probe during induced VF in pigs. Methods: Six adult pigs were anesthetized and ventilated. Vascular access was obtained by cut-down of the femoral and internal jugular veins. An ICE probe was placed in the right atrium and positioned to view the left ventricle (LV). A pacing wire was positioned into the right ventricle. VF was then induced with alternate-current energy. ICE images of the LV were stored at baseline (pre -VF), and at one minute increments in VF out to 20 minutes. Image analysis measured 2-dimensional area of LV thrombus over time in VF and was then compared to baseline chamber area. Results: Data from five pigs was analyzable. One pig suffered from asystole early in the experiment and was excluded from analysis. The entire study group maintained atrial electromechanical activity during VF. The mean baseline area of the left ventricles viewed by ICE was 8.7 ± 3.4 centimeters^2. The LV chambers were completely filled with thrombus within 16 minutes. A linear increase in thrombus burden is demonstrated in the figure. Conclusions: ICE images provide real-time evidence of progressive thrombus burden in the LV during VF. The contribution of the thrombus burden to the mortality and morbidity following cardiac arrest needs more evaluation.



9:30 a.m.

1050-143 **Hospital Variation in Time to Defibrillation After In-Hospital Cardiac Arrest**

Paul S. Chan, Graham Nichol, Harlan M. Krumholz, John A. Spertus, Brahmajee K. Nallamothu, Saint Luke's Mid America Heart Institute, Kansas City, MO, University of Washington - Harborview Center for Prehospital Emergency Care, Seattle, WA

Background: Delays to defibrillation are associated with worse survival after in-hospital cardiac arrests. We determined the extent of variation in delayed defibrillation among hospitals and factors that may explain this variation.
Methods: Adult inpatients with cardiac arrests amenable to defibrillation (n=7,479) at 200 hospitals from 2000 to 2008 were identified from the National Registry of Cardiopulmonary Resuscitation. Hospital rates of delayed defibrillation, defined as greater than 2 minutes, were assessed using hierarchical models, after adjusting for demographic, clinical, and cardiac arrest variables.
Results: Adjusted rates of delayed defibrillation varied substantially among hospitals (range, 2.4% to 50.9%), with hospital differences accounting for a significant amount of the total variation across institutions after adjusting for patient factors (median odds ratio [OR] of 1.49 for overall hospital-level effects). Among hospital factors evaluated, bed volume (reference: <200 beds; 200-500 beds: odds ratio [OR] of 0.62 [95% Confidence Interval (CI) 0.48 to 0.80]; >500 beds: OR of 0.74 [0.53 to 1.04]; p for trend <.001) and arrest location (reference: ICU; telemetry unit: OR of 1.92 [1.65 to 2.22]; nonmonitored unit: OR of 1.90 [1.61 to 2.24]; p <.001) were associated with differences in rates of delayed defibrillation. 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.

9:30 a.m.

1050-144 **Association Between Waveform Characteristics of Ventricular Fibrillation and Survival in Out-of-Hospital Cardiac Arrest**

Esther M. ter Braack, Wessel Keuper, Marc A. Brouwer, Freek WA Verheugt, Joep LRM Smeets, University of Twente, Enschede, The Netherlands, Radboud University Medical Centre Nijmegen, Nijmegen, The Netherlands

Background: Early defibrillation in patients with ventricular fibrillation (VF) in out-of-hospital cardiac arrests (OHCA) is associated with a higher defibrillation success rate and a better survival. Whether waveform characteristics of VF are associated with survival to discharge is the purpose of this study.
Methods: Patients with VF as initial rhythm and digital ECG recordings were selected from a prospective registry of OHCA between 2006 and 2008 in the Nijmegen area. Frequency and amplitude characteristics were calculated from the first 4 seconds of digital VF signal. Complete follow-up was an additional entry criterium.
Results: In 155 patients a 4 seconds digital ECG recording was available and in 39 patients complete follow-up was present. From 39 analyzed patients, there were 8 patients who survived to discharge. Baseline characteristics between survivors and non-survivors did not differ: age (years) 66.2 and 64.0 (p=NS); witnessed arrest (%) 100 and 81.3 (p=NS); call to arrival (minutes) 8 and 7 (p=NS). Survivors showed significantly higher frequency, amplitude and slope measures than non-survivors (see table, results displayed as median and 25-75 interquartile range).
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.

	Survival to discharge (n=8)	No survival to discharge (n=31)	p-value (Wilcoxon)
Median Frequency (Hz)	5.47 (4.62-7.17)	4.13 (3.16-4.86)	0.01
Dominant Frequency (Hz)	5.49 (4.39-7.02)	4.15 (2.69-5.37)	0.03
Mean Frequency (Hz)	5.81 (4.76-7.04)	4.58 (3.52-5.42)	0.02
Mean Peak-to-trough amplitude (mV)	0.38 (0.33-0.47)	0.25 (0.18-0.35)	0.03
Mean slope (mV/s)	10.03 (9.21-10.90)	6.37 (3.65-8.76)	0.001
Median slope (mV/s)	4.38 (3.90-4.86)	2.72 (1.60-3.85)	0.003

9:30 a.m.

1050-145 **Outcomes of Therapeutic Hypothermia With Iced Saline and Endovascular Cooling in Shockable and Nonshockable Rhythms**

Vinod S. Kudagi, Nitesh Sood, Jeffery Kluger, Joseph Taliercio, Justin Lundbye, 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 Thermoregulation system. The target temperature was 33 ± 1 °C. The primary endpoints were time to reach target temperature from initiation of hypothermia, feasibility of maintaining hypothermia and neurological recovery assessed by Pittsburgh cerebral performance category (PCPC) of 1 (good performance), 4 (vegetative state), and 5 (death).
Results: Out of 29 pts, 17 (58.6%) had VF and 12 (41.4%) had non- shockable rhythms with either pulseless electrical activity (PEA n=8) or asystole (n=4) at presentation. The mean age was 60 (±13) yrs with 86% males. The target temperature was reached in all patients (100%) with a mean time to target temperature of 220 (± 130) minutes. Temperature was effectively maintained at 33.6 ± 0.6 °C during 18 hrs of hypothermia.
Out of the 29 patients 15 had complete neurological recovery (CNR) (51.7%) (PCPC=1), 13 patients died (PCPC=5) (44.8%) and 1 patient (3%) had persistent vegetative state (PCPC=4). There were 10/17 pts with VF that had CNR (58.4%) compared to 5/12 (41.6%) with either PEA or asystole (p =0.3). There were no Alseus catheter or hypothermia related complications in any patient.
Conclusions: Therapeutic hypothermia using a protocol of cold normal saline infusion prior to endovascular cooling achieves target temperatures quickly in 100% of patients without complications. Complete neurological recovery occurs in a majority of patients irrespective of the rhythm at presentation.

9:30 a.m.

1050-146 **Influence in Female Patients With Stable Multivessel Coronary Disease Submitted to Off-Pump and On-Pump Coronary Surgery**

Felipe Paulitsch, Neuza Lopes, Fernando Costa, Cibele Garzillo, Alexandre Pereira, Noedir Stolf, Luiz Cesar, Whady Hueb, Heart Institute University of Sao Paulo, Sao Paulo, Brazil

Background: Female patients experience greater events compared with males regarding coronary bypass surgery with the on-pump technique. We sought to determine whether the off-pump technique changes outcomes between genders.
Methods: This was a prospective study that included 279 patients with stable coronary artery disease, preserved left ventricular function, and the possibility of surgery by either the on-pump or off-pump method. Patients were randomized into 2 groups: on-pump (n=137) or off-pump (n=142). There were 209 male patients (on-pump=110; off-pump=99) and 70 female patients (on-pump=40; off-pump=30). Composite major events were: death, unstable coronary syndrome, stroke, and minor events were analyzed according to sex and pump use.
Results: Male patients had significantly more Caucasian (81% vs. 64%, p=0.003), and females had more hypertension (84% vs 61%, p<0.01). There were more major combined events in female patients (27% vs 13%, p=001) with both techniques. However, we did not observe differences regarding mortality between male and female patients. Furthermore, no significant differences were found among number of events and mortality stratified according to sex and cardiopulmonary bypass (CPB) use.
Conclusion: In the present study, the number of combined events was significantly higher in women than in men. However, CPB did not significantly influence outcomes between genders.

9:30 a.m.

1050-147 **Should Use of Troponin Measurement for the Diagnosis of Myocardial Infarction After Coronary Artery Bypass Graft Surgery Be Reconsidered?**

Asim A. Mohammed, Arvind Agnihotri, Roland RJ van Kimmenade, Abelardo Martinez-Rumayor, Sandy Green, Rene Quiroz, James L. Januzzi, Jr., Massachusetts General Hospital, Boston, MA

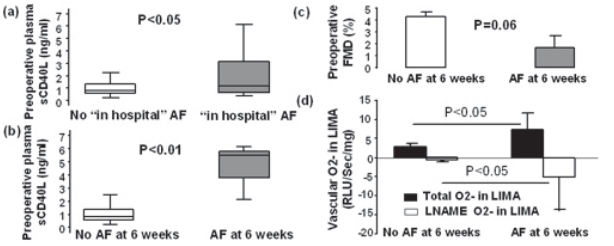
Background: Consensus guidelines define post coronary artery bypass grafting (CABG) myocardial infarction (MI) using a troponin cut-point 5 times the upper reference limit (e.g. a troponin T [cTnT] >.15 ng/mL), together with symptoms and electrocardiographic (ECG) changes. However, post-CABG, symptoms are frequently not reliable, and ECG changes are not specific. Significant reliance on biomarkers to diagnose post-CABG "MI" is inevitable; the ramifications of this are unknown.
Methods: Measurement of cTnT was performed at three time points during the first 24 hours following CABG surgery in 847 consecutive, unselected patients.
Results: The peak cTnT median (with inter-quartile range, IQR) was 1.08 ng/ml (IQR=0.60-1.73 ng/ml). 97% of all patients studied, as well as 77% of patients who had off-pump CABG, were over the cTnT >0.15 ng/ml consensus-recommended cutoff for post-CABG MI detection. Despite prevalent release of cTnT, a linear association was found between cTnT and the incidence of complications, with cTnT remain independently predictive of mortality in adjusted analyses (HR=3.20; *P* <.001). In contrast to the consensus endorsed cut-point, a cTnT level of 1.60 ng/mL had excellent negative predictive value (NPV) for excluding likelihood of death (NPV=99%), death/heart failure (NPV=98%), death/need for prolonged vasopressor support (NPV=94%), or the composite of death/heart failure/prolonged vasopressor support (NPV=93%).
Conclusions: Over-reliance on troponins following CABG will lead to a large number of inappropriate diagnoses of "MI", particularly if using cut-points endorsed by consensus guidelines. As the goal of cTnT testing is to stratify risk following CABG, we believe a higher cTnT cut-point of 1.60 ng/mL will provide an improved NPV for excluding impending complications.

9:30 a.m.

1050-148 **Preoperative Circulating sCD40L And Vascular Redox State in LIMA Grafts, Predict The Development Of Atrial Fibrillation Post-Coronary Artery Bypass Grafting**

Charalambos A. Antoniades, Tim Van-Assche, Jonathan Diesch, Alexios S. Antonopoulos, Dimitris Tousoulis, Christodoulos Stefanadis, Barbara Casadei, David Taggart, Keith M. Channon, Paul Leeson, University of Oxford, Oxford, United Kingdom, University of Athens, Athens, Greece

Background: Atrial fibrillation (AF) is accompanied by endothelial dysfunction, increased oxidative stress and platelet activation (increased circulating sCD40-ligand). Myocardial oxidative stress has been associated with increased risk of AF following coronary artery bypass grafting (CABG). We examined whether preoperative endothelial dysfunction and platelet activation predict the development of post-operative AF.
Methods: We studied 147 patients undergoing CABG. The day before CABG, endothelial function was assessed by flow mediated dilation (FMD) in the brachial artery. Plasma sCD40L was measured by ELISA. Vascular O2- generation in LIMA grafts was measured by using lucigenin chemiluminescence, in the presence and absence of NOS inhibitor LNAME and NADPH. Patients were followed up prospectively for 6 weeks.
Results: The "in hospital" newly developed AF was 31.2%. The relative risk for post-operative AF of patients in the highest vs lowest third of serum sCD40L was 3.83 [95%CI: 1.12 -12.94], p=0.03 (Fig a). 3.4% of patients were still in AF at 6 weeks. These patients had higher pre-operative sCD40L (Fig b), lower FMD (Fig c), higher total O2- and higher LNAME-inhibitable O2- (Fig d).
Conclusions: Elevated preoperative levels of serum sCD40L, a measure of platelet activation, predicts the development of AF post-CABG. Patients with persistent AF at 6 weeks have higher preoperative sCD40L, lower FMD and higher vascular O2- mainly due to uncoupled eNOS, at the time of surgery.



9:30 a.m.

1050-149 **Calcification at the Distal Anastomosis Is a Novel Predictor of Early Asymptomatic Vein Graft Failure in First-Time CABG Patients**

Rhondalyn C. McLean, Susanna M. Nazarian, Tyler J. Gluckman, Edward P. Shapiro, Steven P. Schulman, 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 multi-detector computed tomography (MDCT) coronary angiography.
Methods: Patency was assessed in 611 SVGs in 291 patients from the prospective, multi-centered 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 >1.5mm (OR 2.78, P = .001) and skip grafts (OR 2.49, P = .001, when compared to independent grafts) were 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 pre-operative evaluation of the coronary vessels by MDCT may be useful to guide the approach of cardiothoracic surgeons in the future.

9:30 a.m.

1050-150 **Comparison of Drug-Eluting Stents and Coronary Artery Bypass Surgery for the Treatment of Left Main Coronary Artery Disease: Two-Year Follow-up Results From a Single Institution**

Shengshou Hu, Yan Li, Zhe Zheng, Bo Xu, Wei Li, Runlin Gao, National Heart Center and Fuwai Hospital, Beijing, People's Republic of China

Background: Several studies have compared the treatment effects of coronary stenting with drug-eluting stents and coronary-artery bypass grafting (CABG). However, limited data exist on the long-term outcomes of these two interventions for patients with unprotected left main coronary artery disease.
Methods: We evaluated 220 patients with unprotected left main coronary artery disease who received drug-eluting stents and 768 patients who underwent isolated CABG between April 2003 and February 2006. We compared adverse outcomes (death; myocardial infarction; and target-vessel revascularization) after adjustment for differences in baseline risk factors among the patients.
Results: Patients who underwent CABG were older and had more comorbidities than patients who received drug-eluting stents. Patients receiving drug-eluting stents had considerably higher 24-month rates of target-vessel revascularization (8.18% vs 1.70%). There was no significant difference between the drug-eluting stents and CABG groups in the risk of death (hazard ratio [HR]for the drug-eluting stents, 1.16; 95% confidence interval [CI], 0.75 to 1.82). However, drug-eluting stents were associated with higher rates of myocardial infarction (adjusted HR 1.627, 95%CI 1.116 to 2.424). Among patients with left main plus multi-vessel disease, the comparison between drug-eluting stents (n=130) and CABG surgery (n=690) produced similar results.
Conclusions: In a cohort of patients with unprotected left main coronary artery disease, we found no significant difference in rates of death between patients receiving drug-eluting stents and those undergoing CABG. However, CABG was associated with lower rates of myocardial infarction, and target-vessel revascularization than does drug-eluting stents.

9:30 a.m.

1050-151 Results of Radial Artery Grafting in Diabetic Patients

Robert F. Tranbaugh, Darryl M. Hoffman, Charles M. Geller, Loren J. Harris, Paul Stelzer, Bertram Cohen, Beth Israel Medical Center, New York, NY

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%), heart failure (6.3 vs. 1.5%), 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 sepsis (2.0 vs. 0.5%, 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 (ns).
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.

9:30 a.m.

1050-152 Comparison of Bivalirudin and Unfractionated Heparin Plus Protamine in Patients With Coronary Artery Disease Undergoing Elective Percutaneous Coronary Intervention: Final Six-Month Result of the Antithrombotic Regimens aNd Outcome (ARNO) Trial

Guido Parodi, Angela Migliorini, Renato Valenti, Benedetta Bellandi, Umberto Signorini, Piergiovanni Buonamici, Nazario Carrabba, Guia Moschi, David Antoniucci, Department of Cardiology, Careggi Hospital, Florence, Italy

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 bleedings). 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 hours before PCI. GP IIb/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 coronary 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 comparred 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)

9:30 a.m.

1050-153 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, Hiroyuki Daida, 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 if the anatomy was suitable for both CABG and PCI, CABG only, or PCI only. We enrolled 493 patients, of whom 137 and 356 underwent SES and off-pump CABG, respectively, in our institute between 2003-2007. The incidence of the primary endpoint of major adverse cardiac and cerebrovascular events (MACCE) during follow-up (4.1+/-2.9 years) was similar between SES group and off-pump CABG group (24% vs. 16%, p=0.42). After adjusting for baseline variables, SES and off-pump CABG did not differ in terms of cardiac death (hazard ratio [HR] 0.88; 95% confidence interval [CI] 0.19- 3.60; p=0.89), myocardial infarction and death (HR 0.44; 95%CI 0.10-1.65; p=0.25) and MACCE (HR1.25; 95%CI 0.71-2.11; p=0.43). However, the risk for the incidence of revascularization was significantly higher in the SES group than in the off-pump CABG group (HR 2.47; 95%CI 1.65-3.28; P=0.01).Conclusion: Although SES was associated with a significantly higher risk of revascularization than off-pump CABG, long term adverse cardiac and cerebrovascular events did not significantly differ between the two procedures in diabetic patients with multivessel disease.

9:30 a.m.

1050-154 The Predictive Value of SPY Intraoperative Angiography on Longterm Graft Patency Post Revasculalization

Christine McCarty, Aaron Rastoka, Amy Helmuth, Lynn McLuckie, PinnacleHealth, Harrisburg, PA

Background: Intraoperative SPY angiography has been used to evaluate and revise coronary bypass grafts. The specificity and sensitivity of this operative study is high. However, longterm studies on graft patency have not been entertained. We examined the results of SPY patients to see if confirmed intraoperative graft patency yielded improved longterm results.
Methods: From 2006 to 2007, 200 patients undergoing coronary revascularization were evaluated retrospectively. 100 patients were studied with SPY while the other 100 patients served as a control group. The studied endpoint for graft complications posoperatively included a positive stress test, ECHO or readmission with MI or with PCI, with follow-up time of one year.
Results: There were no differences between the two groups with regard to gender or significant comorbidities such as HTN, DM, or cigarette smoking. Table 1 shows the type and distributions of the grafts placed in both groups. In the SPY group (98%) (98/100) were off pump while the nonSPY group had 33% (33/100) off pump. In the SPY group 3.9% (11/286) of grafts were revised while no revisions occurred in the nonSPY group. There were 3 graft failures in the SPY group vs 11 in the nonSPY group. The Pearson Chi square value is 4.154, P-value of 0.042.
Conclusions: Statistical significance was obtained defining improved longterm graft patency with SPY angiography. This becomes important in an era of more minimally invasive revascularization, OPCAB, prior PCI and more arterial conduits

Type (Arterial-A or SVG-V) and Distribution of Grafts

	SPY	NONSPY
LAD-A	123	94
LAD-V	1	27
PCA-A	34	3
RCA-A	22	70
CX-A	80	17
CX-V	26	87
Total	286	298

9:30 a.m.

1050-155 Association Between new Onset Postcoronary Artery Bypass Graft Atrial Fibrillation and Body Habitus Measures and Gender

Giovanni Filardo, Cody Hamilton, Baron Hamman, Robert F. Hebeler, Jr., Paul Grayburn, Institute for Health Care Research and Improvement, Baylor Research Institute, Dallas, TX, Department of Cardiothoracic Surgery, Baylor University Medical Center, Dallas, TX

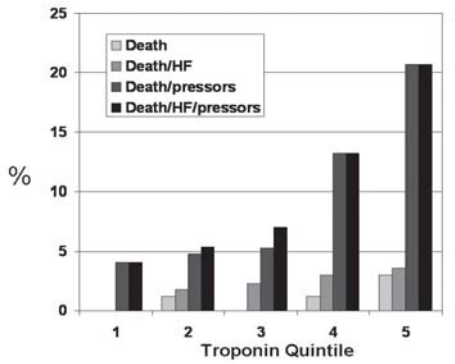
Background: Considering the increased prevalence of obesity and the growing number of patients undergoing cardiac surgery, addressing the uncertainty regarding the impact of body size/adiposity on risk for post-operative atrial fibrillation (AFIB) is critical. Results regarding the relationship between body mass index (BMI) (Kg/m^2) or body surface area (BSA) (m2) and AFIB following coronary artery bypass graft surgery (CABG) are inconsistent. Moreover, the effect of gender on this association is under-investigated.
Methods and Results: Post-operative AFIB was assessed in a cohort of 7,027 consecutive patients without preoperative AFIB undergoing isolated CABG at Baylor University Medical Center, Dallas, TX between 1/1/1997-12/31/2006. Two propensity-adjusted models controlling for risk factors identified by the Society of Thoracic Surgeons and other clinical/non-clinical details were used to determine how gender affected the relationship between post-CABG AFIB and BMI or BSA. After adjustment, BMI and BSA (both modeled using smoothing techniques to avoid categorization) were strongly associated (p<0.0001) with postoperative AFIB -higher BMI or BSA resulted in increased risk. Although evidence existed that gender was associated with AFIB (p<0.0001 and p=0.108 for BSA and BMI models, respectively), there was no indication that the effect of BMI or BSA on postoperative AFIB varied by gender.
Conclusions: Understanding BMI and BSA could assist decisions regarding referral and patient management pre-post CABG surgery. This study suggests that increased BMI and BSA are associated with higher risk of post-CABG AFIB and that risk for men is higher for the entire BSA spectrum and for extreme values of BMI.

9:30 a.m.

1050-156 **Causes and Importance of Troponin Elevation After Coronary Artery Bypass Graft Surgery: Prospective Analysis of 847 Patients**

Asim A. Mohammed, Arvind Agnihotri, Roland RJ van Kimmenade, Abelardo Martinez-Rumayor, Sandy Green, Rene Quiroz, James L. Januzzi, Jr., Massachusetts General Hospital, Boston, MA

Background: Troponin (cTnT) release after coronary artery bypass graft (CABG) is not understood, and the ramifications of cTnT elevation after such procedures remain controversial.
Methods:cTnT was measured at 3 time points during first 24 hours after CABG in 847 consecutive patients
Results: Median peak cTnT (interquartile range, IQR) was 1.08 ng/ml (IQR=0.60-1.73 ng/ml). Multivariable linear regression analysis showed post-op cTnT was predicted by myocardial infarction < 1 week of surgery (T=5.45; *P* <.001), pre-op IABP (T=5.42; *P*<.001), intra/post-op IABP (T=3.61; *P*<.001), number of distal anastomoses (T=2.84; *P*=.005), bypass time (T=8.85; *P*<.001), number of intra-op defibrillations (T=2.61; *P*=.009), GFR (T=-5.93; *P*<.001), off-pump CABG (T=-3.01; *P*=.003) warm cardioplegia (T=-2.40; *P*=.02). Quintiles of cTnT were associated with complications (figure 1). In a multivariable model including the Society for Thoracic Surgery (STS) Risk Model, cTnT remained independently prognostic for death at 30 days (OR=3.20; *P* =.003), the composite of death/HF (OR=2.04; *P*=.008), death/need for multiple vasopressors (OR=2.70; *P*<.001), and the triple composite of death/HF/pressors (OR=2.57; *P* <.001).
Conclusions:cTnT values following CABG are determined by complexity of presentation, as well as extent of grafting, procedure complexity, and cardioprotection strategies. cTnT values are additively prognostic to the STS risk score for adverse outcomes following CABG.



ACC.ORAL CONTRIBUTIONS

918

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.

0918-3 **A Randomized Comparison of Transradial Versus Transfemoral Approach for Coronary Angiography and Angioplasty**

Martin Brueck, Dirk Bandorski, 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 anticoagulation and antiplatelet treatment. The aim of the study was therefore 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: Between July 2006 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.

Table

	Transfemoral (n=512)	Transradial (n=512)	p-value
Catheterization success	511 (99.9%)	494 (96.5%)	<0.0001
Cross over	1 (0.001%)	18 (3.5%)	<0.0001
Angioplasty	192 (37.5%)	178 (34.8%)	NS
Procedural success	191 (99.5%)	172 (96.6%)	NS
Duration of procedure (min)	37.0 + 25.9	40.2 + 25.8	<0.05
Contrast dye (ml)	128.8 + 65.0	132.0 + 76.0	NS
Radiation exposure (Gycm2)	38.21 + 26.26	41.85 + 29.69	<0.05
Fluoroscopy time (min)	5.79 + 5.96	9.02 + 8.65	<0.01
Vascular complications	19 (3.7%)	3 (0.6%)	0.001

10:45 a.m.

0918-4 **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, G.B. John Mancini, Eric R. Bates, Bernard R. Chaitman, John Spertus, William J. Kostuk, Marcin R. Dada, Vipul Gupta, Steven P. Sedlis, Daniel S. Berman, Leslee J. Shaw, Robert A. O'Rourke, William S. Weintraub, Buffalo General Hospital, Buffalo, NY

Background: Both SWISSI-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:

Outcomes: SMI Pts	PCI + OMT N=135	OMT N=148	P value
D or MI	19 (14%)	27 (18%)	0.34
Death Alone	7 (5%)	16 (11%)	0.11
MI Alone	14 (10%)	12 (8%)	0.51
ACS Alone	10 (7%)	11 (7%)	0.99
D/MI/Stroke	20 (15%)	28 (19%)	0.36
D/MI/ACS	27 (20%)	35 (24%)	0.46
Subsequent Revasc	18 (13%)	28 (19%)	0.20

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 SWISSI-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.

11:00 a.m.

0918-5 **In Acute Coronary Syndrome Medical Therapy Is Superior to Early Coronary Revascularization for Patients With Low Risk Profile**

Raffaele Bugiardini, Markku Eskola, Heini Huhtala, Kari Niemelä, Pekka Karhunen, Rossella Miglio, Olivia Manfrini, Kjell Nikus, University of Bologna, Bologna, Italy, University of Tampere, Tampere, Finland

Background: The aim of the study was to evaluate the effect of early coronary revascularization on major acute cardiovascular events (MACEs) accordingly to patients risk profile.
Methods: We enrolled 1188 consecutive patients with acute coronary syndrome who were admitted in a single academic hospital in Finland. Of these patients, 279 underwent in-hospital coronary revascularization and 909 were managed only with medical treatment. The outcome measure was the composite endpoint of death, stroke, myocardial infarction, and unstable angina requiring re-hospitalization. We used propensity analysis to compensate for lack of random assignment to treatment groups and stratified patients into quintiles of risk accordingly to 10 clinical relevant variables
Results: At a median follow-up of 6 months, the rates of MACEs were similar in the two groups (34.5% versus 38.3%; p=0.25).. In the highest-risk group (1st quintile), those patients who received early revascularization did not have any major adverse event, whereas those who did not undergo early revascularization had a relevant number of MACEs (28.7%) and deaths (24.7%). Conversely, for the lowest-risk group (5th quintile), patients who underwent early coronary revascularization had a significantly higher risk for MACEs (HR= 4.74, CI: 1.36-16.49, p=0.014) compared with patients managed only with medical treatment. No significant difference was observed across the remaining three categories of propensity scores.
Conclusions: The analysis of this registry suggests that in acute coronary syndrome, early-revascularization is more effective than medical therapy only in high-risk patients. Conversely, medical therapy is superior to early coronary revascularization in patients with low-risk profile.

11:15 a.m.

0918-6 **Comparative Efficacy of Primary Percutaneous Coronary Intervention, Facilitated Percutaneous Coronary Intervention and Fibrinolysis in Chinese Patients With ST-Elevation Myocardial Infarction: A Multicenter Randomized Clinical Trial**

Yun Zhang, Shi Liang Jiang, Xiao Ping Ji, The Shandong Clinical Trail Group, The Key Laboratory of Cardiovascular Remodeling and Function Research, Jinan, People's Republic of China

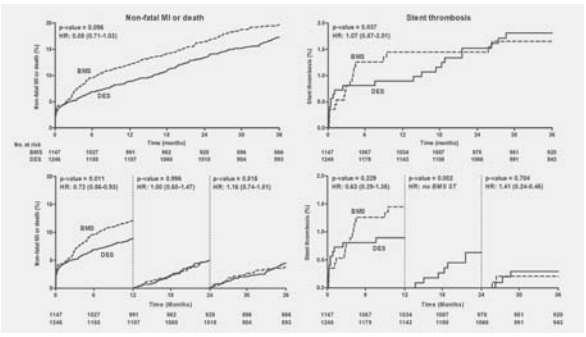
Background: Primary percutaneous coronary intervention (PPCI) is superior to facilitated percutaneous coronary intervention (FPCI) and fibrinolysis in patients with ST-elevation myocardial infarction (STEMI) if the door-to-balloon time is less than 90 minutes. The purpose of this study was to find out 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 119.5mins. Patients assigned to group B were first given an intravenous bolus of 8mg 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 FPCI is equal to that of PPCI if the door-to-balloon time is more than 90 mins.

11:30 a.m.

0918-7 **Three-Year Comparison of Drug-Eluting Versus Bare Metal Stents**

Robert J. Applegate, Matthew T. Sacrinty, Michael A. Kutcher, Renato M. Santos, Sanjay K. Gandhi, William C. Little, Wake Forest University School of Medicine, Winston-Salem, NC

Background. Long-term safety concerns after "off-label" drug-eluting stent (DES) use persist despite recent 2 year data showing comparable safety to bare metal stent (BMS) use.
Methods. We compared 3-year cumulative outcomes to landmark 2nd and 3rd year outcomes (non-fatal MI, all-cause mortality) in 1,147 consecutive patients who received BMS in the year prior to introduction of DES at Wake Forest University Baptist Medical Center and 1,246 consecutive patients that received DES after it became our routine choice with equivalent complete 3-year follow-up.
Results. Stents were used for "off-label" indications in 80% of patients. At 3 years, the hazard ratio for DES compared to BMS for cumulative target vessel revascularization was 0.65 (0.51-0.82), non-fatal MI or death was 0.85 (0.71-1.03), and all-cause mortality 0.80 (0.64-1.01). The DES clinical benefits occurred entirely within the first year, with similar rates of these clinical endpoints in the second and third year. The cumulative HR of stent thrombosis DES compared to BMS was 1.07 (0.57-2.01), with similar rates of stent thrombosis in the third year, p=0.70 (see Figure).



Conclusions. The routine clinical use of drug-eluting stents for "off-label" indications was associated with lower clinical endpoints at 3 years than in a comparable group of patients treated with BMS, with similar cumulative rates of stent thrombosis. There was no evidence of late "catch-up" of adverse DES events.

ACC.ORAL CONTRIBUTIONS

923

Assessment of Risk in NSTE ACS Populations

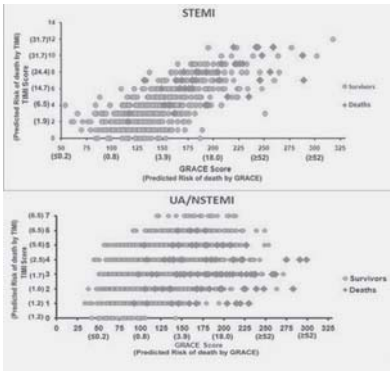
Tuesday, March 31, 2009, 2:00 p.m.-3:30 p.m.
Orange County Convention Center, Room W307A

2:00 p.m.

0923-3 **Different Risk Scores Predict Different Risk for the Same Patient With an Acute Coronary Syndrome: Implications for Contemporary Practice**

Umesh U. Tamhane, Ralph H. Stern, Krishna Aragam, James B. Froehlich, Eva Kline-Rogers, Kim A. Eagle, Hitinder S. Gurm, University of Michigan Medical Center, Ann Arbor, MI

Background: Current ACC/AHA guidelines advocate the Global Registry of Acute Coronary Events (GRACE) and Thrombolysis in Myocardial Infarction (TIMI) scores in risk stratification of patients with ACS. We assessed the correlation between the predicted mortality by GRACE and TIMI score in an unselected ACS patient population.
Methods: We studied 2753 UA/NSTEMI and 698 STEMI patients admitted to University of Michigan between 1999-2005. We calculated appropriate GRACE and TIMI risk scores for each patient. Discriminatory performance of each score to predict in-hospital mortality was measured by the c-statistic. Within the UA/NSTEMI and STEMI subpopulations, scatter plots of TIMI versus GRACE risk scores were generated.
Results: The c statistics for in-hospital mortality for GRACE and TIMI score were 0.85 versus 0.54 in UA/NSTEMI and 0.84 versus 0.83 in STEMI population. There were major clinically relevant differences in the predicted risk of death with the two scores (figure). In the UA/NSTEMI cohort, for a TIMI score of 5 (predicted mortality 5.6%), the predicted mortality with GRACE score ranged from ≤ 0.2% to ≥ 52%. In the STEMI cohort, for a TIMI score of 5 (predicted mortality 11.6%) the mortality risk with GRACE score ranged from 0.6% to 36%.
Conclusion: The two commonly used risk scores can provide markedly discrepant estimates of risk for the same patient even with similar discrimination in the overall population. These data call into question the value of routine use of these scores for risk prediction.



2:15 p.m.

0923-4 **Renal Dysfunction and Rapid Coronary Artery Disease Progression in Patients With Non-ST-Segment Elevation Acute Coronary Syndrome**

Tatsuya Nakachi, Masami Kosuge, Kiyoshi Hibi, Toshiaki Ebina, Kengo Tsukahara, Jun Okuda, Noriaki iwahashi, Yoshio Tahara, Satoshi Umemura, Kazuo Kimura, Yokohama City University Medical Center, Yokohama, Japan

Background Renal dysfunction is a powerful predictor of adverse outcomes in non-ST-segment elevation acute coronary syndrome (NSTE-ACS); however, its underlying mechanism has not been fully elucidated. Although renal dysfunction has been shown to be associated with the severity of coronary artery disease (CAD), the relation between renal dysfunction and CAD progression is unknown.
Methods We studied 231 patients with NSTE-ACS who underwent percutaneous coronary intervention for culprit lesion, followed by coronary angiography a mean of 8 months later. Rapid progression of non-culprit lesion was defined as an increase ≥15% in stenosis severity at follow-up angiography. Estimated glomerular filtration rate (eGFR), high-sensitivity C-reactive protein (hsCRP), cardiac-specific troponin T and lipid profiles were measured on initial admission. Patients were divided into the 2 groups according to the presence (n=73) or absence (n=158) of renal dysfunction defined as eGFR <60 mL/min/1.73 m^2.
Results There were no differences in diabetes mellitus, hyperlipidemia, smoking, lipid profiles, positive-troponin T and medications between patients with and without renal dysfunction. Renal dysfunction was associated with older age (70 ± 8 vs 64 ± 10 years, p<0.0001) and higher rates of male (90% vs 77%, p=0.022) and hypertension (80% vs 53%, p=0.0002), a higher level of hsCRP (0.195 vs 0.111 mg/dl, p=0.024). Patients with renal dysfunction were more likely to have multivessel disease (62% vs 45%, p=0.023

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.

2:30 p.m.

0923-5 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

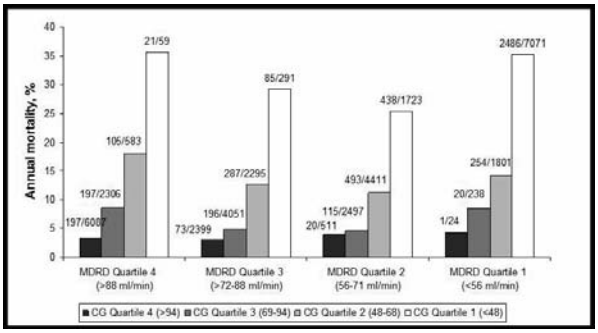
Karolina Szummer, Stefan H. Jacobson, Pia Lundman, Johan Lindback, Ulf Stenestrand, Lars Wallentin, Tomas Jernberg, Karolinska University Hospital Huddinge, Karolinska Institutet, Stockholm, Sweden

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 71.6 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**.**



2:45 p.m.

0923-6 Warfarin Is Independently Associated With Lower Risk of Six-Month Death or Myocardial Infarction in Patients With Atrial Fibrillation Following Acute Coronary Syndromes

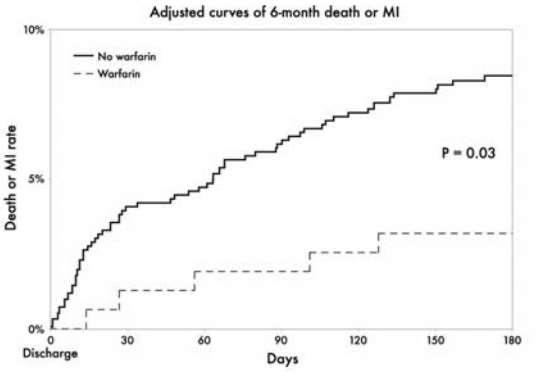
Renato D. Lopes, Aijing Starr, Sana M. Al-Khatib, L. Kristin Newby, Rajendra H. Mehta, Frans Van de Werf, Kenneth W. Mahaffey, Paul W. Armstrong, Robert A. Harrington, Harvey D. White, Lars Wallentin, Christopher B. Granger, Duke Clinical Research Institute, Durham, NC

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 alive. Cox proportional hazards models were performed to assess 6-month outcomes after discharge.

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.



3:00 p.m.

0923-7 Anemia for Risk Assessment of Patients With Acute Coronary Syndromes

Francois Schiele, Nicolas Meneveau, Marie-France Seronde, Vincent Descotes-Genon, Joanna Dutheil, Romain Chopard, Fiona Ecarnot, 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.