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, Zharma Ivanov, Bin Wang, Parkinson Lee-Gau Chong, Deborah L. Craibe, 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). Immunohistochmical staining with CD31, and DIO2, 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.

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

Hugo P. Sondemeijer, Finna See, Tetsunori Steki, 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 coatedly 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 3x106 neonatal rat cardiomyocytes (nCM), 3x106 neonatal rat cardiac fibroblasts (nCF) or 1x106 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), 1x106 hMSCs (low dose, n=13) or 3x106 hMSCs (high dose, n=6) were applied to the epicardial surface of nude rat hearts 48 hours after MI. Intramyocardial saline injected animals served as controls. 1 week later, cardiac function was determined by echocardiography.

Results: At 1 week, nCM viability inside scaffolds increased from 3.3±1.2% (0 mg/g cRGDK) to 12.3±0.1% (10 mg/g cRGDK) + gelatin (p<0.05). Clusters of beating myocytes could be detected. nCF viability increased from 48.8±21% (0 mg/g cRGDK) to 77.2±3.2% (10 mg/g cRGDK) (p=0.005). Human Msc viability increased from 15.3±0.7% (0 mg/g cRGDK) to 59.5±2.2% (20 mg/g cRGDK) (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% (3x106 hMSCs), whereas FS increased by 6.9±10.3% (1x106 hMSCs) (p>0.05).

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

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

Elisabetta Cerqua, Patrizia Danielli, Chiara Ciuflendra, Andrea Di Marco, Roberto Bassani, Marianna Roccio, Gianluca Viarengo, Peter J. Schwartz, Massimiliano Gnecchi, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, Universiti 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 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 of fetal origin may exert more powerful cytoprotective effects compared with adult MSC. Production of AAF was measured by RT-PCR. Rat neonatal cardiomyocytes (H9c2 cells) were used to test the anti-apoptotic effects on hypoxic cardiomyocytes. A-MSC may represent a novel and powerful approach to cardiovascular repair.

Results: Following IR injury, the serum troponin I level was significantly higher in UCP3-/-. In addition, myocardial nucleotide profile, as a marker of cellular energy status, was measured by HPLC. We hypothesize that UCP3 may prevent myocardial necrosis during IR by maintaining cardiomyocyte energetics through preserving mitochondrial function and structure.

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

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

Ceyher 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. 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.

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

Ceyher 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. 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.

1014-128

1014-125

1014-126

1014-129

Myocardial Ischemia/Infarction--Basic

Orange County Convention Center, West Hall D

Sunday, March 29, 2009, 9:30 a.m.-12:30 p.m.

9:30 a.m.

9:30 a.m.

9:30 a.m.

9:30 a.m.
A306  ABSTRACTS - Myocardial Ischemia and Infarction

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

Yuuki Jo, Toshikira Aruzai, Koji Ueno, Takashi Kohno, Kotaro Naito, Yuj Nagatomo, Yukhiro Maekawa, Toshikyi Takahashi, Tsutomu Yoshikawa, Satoshi Ogawa, Division of Cardiology, Department of Medicine, Keio University School of Medicine, Tokyo, Japan

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

**Methods:** Eleven-week-old rats were divided into 2 groups and given intravenous administration of erythromycin (25 mg/kg, EM) or saline as control group (CON/IR), 30-minute prior to myocardial ischemia. Rats underwent 30-minute occlusion of left coronary artery, followed by reperfusion. Myocardial contrast echocardiography was performed to assess myocardial microvascular return after normothermic ischemia and reperfusion injury. Release of matrix metalloproteinase (MMP) inhibitors and MMPs were determined via WST-1 assay. Histology revealed that neutrophil infiltration in EM/IR was significantly lower than that in CON/IR (P<0.05). Myocardial 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 for reperfusion for acute myocardial ischemia.

**T1014-131**

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

Satoshi Matsuhashi, Anthony J. White, James S. Forrester, Tanun Chakravarty, Edvard Marban, Raj Makkar, Cedars-Sinai Medical Center, Los Angeles, CA

**Background:** In the mammalian embryo, 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 injured myocardium by RT-PCR (baseline, 2, 7 and 14 d. following infarction (n=5 each)) and Western blotting. Immunohistochemistry was used to localize transcription factor(s) and c-Kit to identify stem cells. Periostin and collagen expression were measured by immunohistochemistry and Masson’s trichrome staining to identify collagen markers.

**Results:** Infarction was confirmed by upregulation of collagen (37.6±10.6 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±2.4 fold at 7d) [means±SE, ANOVA±P<0.01]. Isl1, the most upregulated gene at 14 d, was also accompanied by an 18.3±6.6 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 ventricle in the embryonic heart. Isl1 is a marker of the embryonic second heart field, and its expression disappears as the cells begin to express perinatal 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.

**T1014-132**

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

Vien Khach Lai, José Linares-Palomino, Manuel Gallinanes, 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 low PV 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 normal LVEF (EF>50%) patients.

**Results:** BMC 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 allogeneic BMCs. However, when non-diabetic myocardium was co-incubated with autologous BMCs or with allogeneic diabetic BMCs there was a significant reduction in CK release (from 927±176 IU/mg wet wt) and TUNEL (% of apoptotic cells) compared to ischaemia-reperfusion (IR). TUNEL release was higher in diabetic BMCs (28±5%) compared to normal BMCs (12±3%). Cell necrosis (from 9.5±4.0% to 3.2±0.1%) and 0.60±0.50% (p<0.05) and apoptosis (from 11.5±9.3% to 0.92±0.46% and 1.01±0.63%; p<0.05, n=6/group). Muscle samples from patients with poor LV function were not protected by autologous BMCs but, importantly, CK release and cell necrosis were significantly reduced by allogeneic 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 8.08±1.53% to 8.06±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.

**T1014-133**

**Adjunctive Infusion of AZD6100, 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 Khali, Dominik Wiktor, Yu Peng, Marc S. Penn, The Cleveland Clinic, Cleveland, OH

**Background:** We assessed the effect of AZD6100, the first reversible oral P2Y12 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 AZD6100 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. Reoxygenation rate, cyclic flow variation, and infarct size were significantly decreased with ACDZ6140 (P<0.05). ADP-induced (20 μmol/L) platelet aggregation was decreased by ACDZ6140 (1.9 mm ± 6.7%) 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 ACDZ6140 (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 ACDZ6140 group (73% recovery, P<0.001) compared to CLOP (50% recovery, P=0.05) and saline group (62% recovery, P=0.06). Conclusion. Administration of ACDZ6140 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 ACDZ6140 has a better antiplatelet effect than clopidogrel.

<table>
<thead>
<tr>
<th>RR (%)</th>
<th>TR (min)</th>
<th>HD (min)</th>
<th>CVF (%)</th>
<th>Reoxygenation (%)</th>
<th>Infarct size (cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>90</td>
<td>24.4±7</td>
<td>84.7±4.4</td>
<td>50</td>
<td>13.6±3.4</td>
</tr>
<tr>
<td>CLOP</td>
<td>100</td>
<td>27.2±6</td>
<td>66.9±3.8</td>
<td>50</td>
<td>14.3±4.2</td>
</tr>
<tr>
<td>AZD6410</td>
<td>100</td>
<td>22.9±8</td>
<td>120.0±0.0</td>
<td>50</td>
<td>6.3±1.2±8.6</td>
</tr>
</tbody>
</table>

P<0.05 vs CLOP and control groups. RR-reperfusion rate; TR-time to reperfusion; HD-reflow duration; CVF-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 Shum, Genevieve Tan, Yuci Gu, Shili Li, Ling Qian, Yingyong Csh, Yun Lim, Ting Hua Ooi, Eugene Sim, Terrance Chua, Seng Chye Chua, 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 Oil-labeled low dose MSCs (1x 10⁶, n=9) and high dose MSCs (5 x 10⁶, n=18) or CLCs (5 x 10⁶, 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 Micro-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 126.8 ± 27.7 mmHg [ESP]). In contrast, CLCs, but not MSCs, enhanced cardiac output (43672 ± 11854.6 mL/min, p<0.05) and stroke work (27 ± 13.1 ± 0.001 [W/min]), while improving contractile dynamics of dP/dt max (163.8 ± 53.6 mmHg, p<0.01) and dV/dt max (5842 ± 2547 uL/s, p<0.05) respectively when compared to medium-injected controls (14734 ± 2161 ± 5.16 ± 2.17 min, P<0.01). Compared to their own baseline, contrast echocardiography showed complete recovery of myocardial perfusion in the ACDZ6140 group (73% recovery, P<0.001) compared to CLOP (50% recovery, P=0.05) and saline group (62% recovery, P=0.06). Conclusion. Administration of ACDZ6140 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 ACDZ6140 has a better antiplatelet effect than clopidogrel.

9:30 a.m.

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


Methods: The role of the neutrophil in inflammatory events leading to coronary plaque rupture and occlusive thrombus is controversial. Neutrophils and monocytes contain myeloperoxidase (MPO) which is a potent oxidant. We hypothesized that increased neutrophil and monocyte MPO is a common feature of acute coronary syndromes (ACS) and chronic stable angina controls having elective PCI. Blood was sampled from the femoral artery in patients with ST elevation myocardial infarction (STEMI).

Results: Acute degranulation of neutrophils and monocytes was shown below. 64% of chronic stable angina controls having elective PCI. Blood was sampled from the femoral artery in patients with ST elevation myocardial infarction (STEMI).
**ABSTRACTS - Myocardial Ischemia and Infarction**

**A308**

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>WT (n)</th>
<th>eNOS-KO (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender/Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male: 8-12 weeks</td>
<td>% Infarct size</td>
<td>30-I/R</td>
</tr>
<tr>
<td>Male: 8-12 weeks</td>
<td>% Infarct size</td>
<td>30-I/P</td>
</tr>
<tr>
<td>Male: 8-12 weeks</td>
<td>% Infarct size</td>
<td>30-I/P</td>
</tr>
<tr>
<td>Male: 8-12 months</td>
<td>% Infarct size</td>
<td>30-I/R</td>
</tr>
<tr>
<td>Male: 8-12 months</td>
<td>% Infarct size</td>
<td>30-I/P</td>
</tr>
<tr>
<td>Female: 8-12 weeks</td>
<td>% Infarct size</td>
<td>30-I/R</td>
</tr>
<tr>
<td>Female: 8-12 weeks</td>
<td>% Infarct size</td>
<td>30-I/P</td>
</tr>
</tbody>
</table>

**Methods:**
- 17 pigs were divided into 3 groups. G-CSF (0.333 mg/kg/min, n=6, Group 1) and saline (n=4, Group 2) were administered for 30 minutes prior to a 45-minute left anterior descending artery occlusion and at the time of reperfusion. The pacing threshold (DPT), ERP, VFT, DFT, QTc and GRD duration were determined in each pig before and during I/R injury. In group 3 (n=7), G-CSF was infused without artery occlusion.
- **Results:** During ischemic period, G-CSF (group 1) significantly increased the DPT, ERP and VFT without altering the DFT (see table). The QT interval and GRD 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.

**A309**

### 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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>VFT</th>
<th>Reparfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTs</td>
<td>24±1</td>
<td>64±20</td>
</tr>
<tr>
<td>JTs</td>
<td>480±15</td>
<td>339±13</td>
</tr>
<tr>
<td>ERP</td>
<td>24±16</td>
<td>277±18</td>
</tr>
<tr>
<td>DPT</td>
<td>0.2±0.1</td>
<td>0.5±0.2</td>
</tr>
</tbody>
</table>

**Methods:**
- G-CSF was infused without artery occlusion.
- **Results:** During ischemic period, G-CSF (group 1) significantly increased the DPT, ERP and VFT 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.

**A310**

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>7-8 weeks</td>
<td>7-8 weeks</td>
<td>8-10 weeks</td>
<td>8-10 weeks</td>
</tr>
<tr>
<td>Protocol</td>
<td>IC</td>
<td>IC</td>
<td>IC</td>
<td>IC</td>
</tr>
<tr>
<td>VFT</td>
<td>24±1</td>
<td>64±20</td>
<td>30±16</td>
<td>30±16</td>
</tr>
<tr>
<td>JTs</td>
<td>480±15</td>
<td>339±13</td>
<td>30±13</td>
<td>30±13</td>
</tr>
<tr>
<td>ERP</td>
<td>24±16</td>
<td>277±18</td>
<td>243±36</td>
<td>243±36</td>
</tr>
<tr>
<td>DPT</td>
<td>0.2±0.1</td>
<td>0.5±0.2</td>
<td>3.7±0.2</td>
<td>3.7±0.2</td>
</tr>
</tbody>
</table>

**Methods:**
- **Conclusions:** This study demonstrates that neither cardiac function nor infarct size were significantly modified by the administration of ic or transcendocardial MSCs in our porcine model of MI.
Ischemia reperfusion impairs mitochondrial complex I, II and IV activity. IPC preserves both complex I and II activity in subsarcomeral 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.
Remote Ischemic Preconditioning Modifies Cardiac Increased Rho Kinase (ROCK) Activity in Hong Kong Pro-arrhythmic Risk of Embryonic Stem Cell-Myocardial Ischemia and Infarction

Method and Results: Sham procedure (n=5) 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 mRNA microarray containing 382 mRNA 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 mRNA’s were significantly down-regulated (n=17, fold change 0.83-0.67) or up-regulated (n=2, mRNA 206, fold change 2.23; p<0.05, and mRNA 346, fold change 10.31; p<0.01). Most of the mRNA’s modified by rIPC had hitherto unknown roles in myocardial function and proarrhythmia. Conclusions: rIPC has potent effects on myocardial mRNA expression. This novel observation suggests a role for mRNA in regulating myocyte responses to ischemia-reperfusion injury. Further studies of the role of individual mRNA’s will enhance our understanding of the mechanism of protection afforded by rIPC, and may establish new therapeutic targets.

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

Toshinari Tsukubawa, Chika Nakamichi, Kunimasa Yagi, Atsushi Nohara, Noboru Fujino, Hidetsuga Ino, Shotoku Tagawa, Masakazu 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 the 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 transiently overexpressed HO-1 in anti-oxidative and anti-apoptotic activities of MSC. Therefore, we examined the effect of transient overexpression of HO-1 in anti-oxidative and anti-apoptotic activities of MSC. 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.

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

Cheuk-man Yu, Ming Dong, Rui-je Li, Ming 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 hypercontractation 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 (4.7±1.64), NSTEMI (4.68±1.55), and UA subjects (3.7±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 (>10.1x10⁹/l) showed a higher ROCK activity than those with low level (<10.1x10⁹/l) (4.9±1.66 vs. 4.1±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.

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

William H. Boylston, Kalyamurthy Venkatachalam, Sumanth D. Prabhu, Anthony J. Valente, Byansi 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 (IR) causes oxidative stress and potentially induces proinflammatory cytokines, we hypothesized that IL-18 is induced following IR and contributes to inflammation and tissue injury. Neutralization of IL-18 should thus lessen IR-mediated tissue injury. We also asked whether simulated IR in vitro induces IL-18 expression in cultured cardiomyocytes, and identified the underlying molecular mechanisms.

Methods: IR studies were performed in a chronically instrumented, closed-chest mouse model. Male C57BL/6 mice underwent 30 min of 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 intramyocardial transplantation of 3x10⁶ 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 weeks post-MI. Electrocardiogram telemetry was performed to monitor for proarrhythmias.

Results: At 4 weeks, 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 1 and 3 weeks 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.
adult mouse cardiomyocytes underwent simultaneous I/R (30 min l4 h R); st/R. Downstream effectors were targeted by pharmacological inhibitors and adenosine transduction of dominant negative expression vectors.

Results: Our results demonstrate low levels of NF-κB activity and IL-18 expression in naive, sham-operated or ischemia alone animals. However, I/R significantly increased ROI generation, upregulated NF-κB activity and IL-18 expression in the ischemic LV tissue. Further, I/R upregulated IL-18Rp and IL-18R expression. In contrast, IL-18BP expression was induced in a delayed manner. Importantly, IL-18 neutralization significantly attenuated IR-induced tissue injury (31% reduction in infarct size vs. sham). Confirming these in vivo results, siRl enhanced ROI generation, IkK activity, NF-κB DNA binding activity, and IKK-NF-κB-dependent biologically active IL-18 expression in isolated adult mouse cardiomyocytes.

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

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

Fadi N. Salimun, 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 (H2S) plays an important role in cardioprotection against ischemia/reperfusion injury (I/R). Also, plasma levels of H2S in patients with coronary artery disease (CAD) are significantly lower than in angiographically normal control subjects. Since H2S-producing enzymes, cystathionine-γ-lyase (CSE) is expressed in the heart, we hypothesized that novel phosphodiesterase-5 (PDE-5) inhibitor, tadalafil (TAD) might utilize H2S signaling in cardioprotection.

Methods: After obtaining baseline left ventricular (LV) function using transhoracic echocardiography (TTE), adult ICR mice were injected i.p. with TAD (1 mg/kg), vehicle (10% DMSO), TAD+N-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).

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

Myocardial Protective Effect of Pioglitazone Against Ischemia-Reperfusion Injury: a PPAR-γ Dependent Effect

Yumei Wu, Jose R. Perez-Polo, Douglas L. Mann, Yochai Bimbaum, 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 IR injury (SIR) by PIO.

Methods: We used miRNA gene arrays to evaluate expression changes of miRNAs in the rat heart after 7-day PIO (5 mg/kg) administration, and then confirmed the result by Northern Blot. We studied the effect of GW9662, a PPAR-γ inhibitor, on the effect of PIO on miR-29 levels in H9C2 cardiomyocytes. We assessed the effects of miR-29 mimic and anti-sense inhibitor oligos, and their interactions with PIO on viability (MTT test), cell death (Trypan Blue) and apoptosis (Caspase-3 activity) of H9C2 cardiomyocytes exposed to 16h hypoxia and 2h reoxygenation (SIR). Finally, we assessed the effects of PI model mimic and anti-sense inhibitor oligos on Mol-1 (an anti-apoptotic Bcl-2 family member) cellular protein levels in H9C2 cells. Results: PIO significantly decreased miR-29a and miR-29c levels. Down-regulation of miR-29a and miR-29c by antisense inhibitors or by PIO treatment did not affect H9C2 cardiomyocytes exposed to SIR (increased MTT activity, decreased cell death and decreased Caspase-3 activity). In contrast, transfusion of cells with miR-29a and miR-29c mimic oligos promoted cell death. Co-transfection with miR-29a and miR-29c mimic oligos completely blocked the protective effect of PIO. The effect of PIO on miR-29a levels was blocked with GW9662. Overexpression of miR-29c in Mol-1 cellular protein levels and transfusion with inhibitor of miR-29 increased Mol-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 IR damage.

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

Ceverh Oxzan, 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 metabolic balance.

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 preconditioning (4 cycles of 4 min 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 nmol/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.

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

Marios R. Fernandes, Guilherme Silva, Cristiano Cardoso, Yi Zheng, Fred Baimbridge, Maria G. Cabreira, John Canales, Micheal Schuster, Siltiu 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 2x10^7 MPC or placebo were performed at 5 days [4 control (C) and 5 treated (T)] and at 10 days (6 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), and M1 macrophage (M1/M2) were assessed by immunofluorescence. Hematological parameters were measured. The content of high energy nucleotides was analyzed using HPLC.

Results: The incidence of VT was higher at 5 days post MI (4/4 vs 1 episode at 5 and 10 days, respectively, p<0.08). There was no peri procedural death or tamponade. Overall, 7 sheep had LEF improvement at 8 weeks (feg 1A). The maximum improvement was seen in T at 10 days post MI (fig1b). There was no inflammation or abnormal tissue growth. Increased arteriolar density (61.9±14 vs 40.3±12 vessels/mm², p<0.005) and a trend of higher cell proliferation (5.8±2.1 vs 3.9±1.7 positive nuclei/10^3 nuclei, p=0.06) were seen at the infarct border of the 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.
**ABSTRACTS - Myocardial Ischemia and Infarction**

**1014-155**

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

Xianghu Chen, Kai Cui, Jiancheng Xiu, Yi Lao, Hu Xue, Daogang Zha, Jianping Bing, Yili Liu, Nanfang Hospital, Guangzhou, People’s Republic of China

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

**Methods:** 24 male SD rats were randomly allocated to either normal saline containing 500 μg/ml of DRPs (n=12) or saline (n=12) at a constant rate of 3.5 ml/hr. The animals were subjected to coronary artery ligation. 24h after MI, non-invasive echocardiography was performed to assess the changes of impaired LV function. LV internal dimensions and the anterior wall thicknesses were measured, and wall motion score index and endocardial length of severe wall 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 (3.8±0.85 vs. 5.2±0.88mm, p< 0.01), better anterior diastolic and systolic wall thickness (1.63±0.2 vs 0.94±0.20mm, p< 0.01 and 1.91±0.35 vs 1.08±0.21mm, p< 0.01, respectively). Significant improvement in fractional shortening (34.8±4.10.35% 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±0.04 vs 0.64±0.06, p< 0.01). Compared with control group, both of contrast score index (1.73±0.42 vs 2.21±0.22, p< 0.05) and ratio of PD length to LV length were significantly reduced in DRP-group (0.27±0.19 vs 0.54±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 microvascular 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 Intracoronal Sera in Patients With ST Elevation Myocardial Infarction*

Gopal Ghimire, Ann McCormack, Jonathan Sprio, Rajesh Kharbanda, Marlene Rose, Miles Daby, Royal Brompton and Harefield NHS Trust, London, United Kingdom

**Background:** Integrity of endothelium is compromised in ST Elevation Myocardial Infarction (STEMI). We evaluated in-vitro the effect of sera derived from the atherothrombotic coronary artery aspirate (CA) and femoral arterial blood (FA) of patients with STEMI, on human umbilical vein endothelial cells (HUVECs). Since activated and apoptotic endothelial cells induce surface expression of vimentin and are an important source of autocytogens, 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, 9.48) of the HUVECs incubated with the CA and 10.21 % (7.35) with FA underwent apoptosis (AV-PI) p<0.05 [9.76]. 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 respectively 78.78 (36.8), p=1.71X10^-10 and 77.92 (23.7), p=0.0023.

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

**9:30 a.m.**

**1014-157**

*PI3k/Akt Activation and Nuclear Accumulation of β-Catenin Are Key Components in the Myocardial Protection Afforded by Remote Ischemic Preconditioning*

Jian 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 IPC (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-dimethylxanthine (DMP) (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 DMP (both p<0.05 compared with sham). Western blotting showed that rIPC significantly increased phosphoryso-Akt (1.66±0.11 fold vs. sham), inhibited GSK-3β by increasing phosphorylated GSK-3β (1.63 fold), and was associated with a 1.92-fold increase in nuclear β-catenin. All of these changes were completely abrogated by pretreatment with Wortmannin.

**Conclusions:** The myocardial protection afforded by rIPC is mediated via the PI-3K/Akt/GSK-3β 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 Synthese (NOS) Activity: Potent Cardioprotection With BH4 Treatment*

Jianshuang 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

Trihydrodibioterin (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/R 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.

**9:30 a.m.**
Background: We hypothesized that therapy with the angiotensin II type 1 receptor blocker candesartan (CN) or the vasopressinopeptide inhibitor omapatrilat (OMA), by reducing effects of angiotensin II, modulate healing-specific matricellular proteins such as secretory leucocyte protease inhibitor (SLPI), secreted protein acidic 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), 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 LV-systolic 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, Smad-2 and -3, and myeloperoxidase proteins in the ischemic zones. Both drugs normalized these changes and improved MMP-9/TIMP-3 balance.

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

9:30 a.m.

1014-159

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

Both I. Jugdutt, Arvazhagh Palaniyappan, Halliday Idiok, University of Alberta, Edmonton, AB, Canada

10:30 a.m.

1014-160

Leptin Modulates Metabolic Substrate Utilization in Ischemic Cardiac Tissue Through Inactivation of Andenosine Monophosphate Kinase

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

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

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

Methods/Results: Coronary artery ligation (CAL) (n=10) or sham (n=10) surgery was performed on 9-week old C57BL/6 male mice. After 3 days, equal numbers were treated with vehicle (0.3 ml/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<0.05). Leptin signaling, measured by phosphorylated total (p/t) cardiac STAT3 protein, was increased 3.7±0.7 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 respectively, after 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 sham).

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 R9939609 in the FTO Gene Is Associated With Early-Onset Myocardial Infarction

Diego Ardissino, Carlo Berzuini, Piera Angelica Merlini, Daniela Lina, Maria Francesca Notarangelo, Marco Taburo, Pier Mannuccio Mannucci, Luisa Foco, Luisa Bernardelli, David Althueler, 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 a large 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 geneticistic 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 1.09-1.38; 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, Lily H Droll, Daynene Vykoukal, Echard Alt, University of Texas, MD Anderson Cancer Center, Houston, TX

Background: Various stem cells have shown a 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 MI 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 66.1 ± 1.74% at baseline, respectively. EF in both groups declined by more than half (28.44 ± 9.32% 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 TGFβ1 and IGFI

Brian Hynes, Arun HS Kumar, Sharon Weiss, Jeffery Schmeckpeper, Graeme 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). Preclinical investigation demonstrated an important role of TGFβ1 and IGFI in the observed beneficial effects, which we have further explored.

Methods: Landrace pigs (25-28 kg) underwent renal occlusion 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-IGFI, or X-vivo 15 (control) was administered in three mice
Collagen Matrix as a Delivery Vehicle Prevents Injected Extracellular Matrix Scaffold Restores Ventricular Myocardial Ischemia and Infarction

Youth Kim, Max J. Smith, Carine M. Laporte, Jeffrey R. Muenzer, Alex J. Gambogi, Y. Orange County Convention Center, West Hall D

Sunday, March 29, 2009, 1:30 p.m.-4:30 p.m.

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

Warode Dai, Sharon L. Hale, Gregory L. Kay, Aarne J. Jyrää, Robert A. Klener, 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 isocitolic 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 no NP detected in the tissues that received saline or collagen alone. NP were detected in the heart and remote organs in SAL+MSC group. Labeled cells (expressed as cell number/tissue weight) were present in 3/13 lungs (mean value equivalent to 12,724±7,060 cells/g), 4/13 livers (12,300±4,924 cells/g), 11/13 spleens (57,229±11,483 cells/g), 9/13 kidneys, 13/13 MI (3,006,835±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 not detected in 2/13 lungs (4,631±3,176 cells/g, p<0.05), 0/13 livers (0 cells/g, p=0.05), 4/13 spleens (4,006±1,737 cells/g, p<0.05), 0/13 kidneys (p=NS), 5/13 non-infarcted myocardium (51,22±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.
Coronary Flow Velocity Reserve Gradually Decreases According to Glucometabolic State in Patients With Acute Myocardial Infarction

Brian B. Legstrup, Dan E. Heltsen, 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 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, pre-study = 0.05) 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 AMI is, continuously decreased according to glucometabolic state. This finding may reflect microvascular dysfunction in prediabetic and diabetic patients with AMI.

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

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-terminus</td>
<td>0.78</td>
<td>0.83</td>
</tr>
<tr>
<td>C-terminus</td>
<td>0.57</td>
<td>0.67</td>
</tr>
<tr>
<td>H-FABP</td>
<td>0.50</td>
<td>0.72</td>
</tr>
</tbody>
</table>

1023-130

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

Brian B. Legstrup, Dan E. Heltsen, 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 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, pre-study = 0.05) 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 AMI is, continuously decreased according to glucometabolic state. This finding may reflect microvascular dysfunction in prediabetic and diabetic patients with AMI.

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

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-terminus</td>
<td>0.78</td>
<td>0.83</td>
</tr>
<tr>
<td>C-terminus</td>
<td>0.57</td>
<td>0.67</td>
</tr>
<tr>
<td>H-FABP</td>
<td>0.50</td>
<td>0.72</td>
</tr>
</tbody>
</table>

1023-130

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

Brian B. Legstrup, Dan E. Heltsen, 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 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, pre-study = 0.05) 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 AMI is, continuously decreased according to glucometabolic state. This finding may reflect microvascular dysfunction in prediabetic and diabetic patients with AMI.

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

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-terminus</td>
<td>0.78</td>
<td>0.83</td>
</tr>
<tr>
<td>C-terminus</td>
<td>0.57</td>
<td>0.67</td>
</tr>
<tr>
<td>H-FABP</td>
<td>0.50</td>
<td>0.72</td>
</tr>
</tbody>
</table>
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 ys 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 year) 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 2-3) (OR 0.93, CI 0.02-0.57, 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.

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, Mehrdad 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.

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 recent use 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 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 0.91), beta blockers (OR 0.92), ACE-inhibitors (OR 0.88) and thienopyridines (OR 0.78) 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 according to light microscopy analysis.

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 cardioactive medications. Expanded use of preventive therapies appears to have favorably altered the pattern of presentation of ACS.

3:30 p.m.

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

Sanddeep Gautam, Jonathan Menachem, Sudeesh Srivastav, Patrice Delafontaine, Aanand 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 role of chronic stress in pathogenesis of AMI is poorly understood, and little is known about the role of chronic stress in the pathogenesis of AMI after a large natural disaster.

Methods: Using the Nationwide Inpatient Sample, hospitalizations for AMI among adults admitted to Tulane University Hospital and Tulane University Medical Center were identified. Patients were stratified by race and gender. Using the hospital discharge data, the number of hospitalizations for AMI in August 2005 (pre-Katrina) and August 2006 (post-Katrina) were compared. Differences in the racial distribution in the two groups.

Results: There was a 17% decrease in the number of hospitalizations for AMI in post-Katrina (p<0.0001), as compared to pre-Katrina. The post-Katrina group had 21,229 patients (0.71%) in the pre-Katrina group (p<0.0001). The post-Katrina group had significantly higher prevalence of unemployment (p<0.0001), 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 tourists (p=0.0001), and people living in temporary housing (p=0.0003). 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.

Impact of Gender on Treatment and Clinical Outcomes in Acute Coronary Syndrome Patients in the Middle East

Ayman A. El-Menyar, Mohamed Zubaid, Wael Almahmeed, Kadhim Souliman, Ahmed Al-Motareh, Haidam Amin, Nadil Asaad, Khalid Al-Habb, Jasmin 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 study of 8172 (1996 women and 6201 men) consecutive patients hospitalized with ACS from February to June 2007 in 6 middle eastern countries. Data were analyzed according to gender. RESULTS: When compared to men, middle-eastern women were 9 years older (62.1± versus 53.1± years; P<0.001) and more often had diabetes (54.6% versus 35.9%, p < 0.001), hypertension (>70/43%, 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=0.001 and 8.0%/versus 6.1%; p=0.012). Women were less likely to be appropriately treated with thrombolytic therapy (79.9%/versus 83.8%), primary PCI (4.9%/versus 8.4%)-blockers (57%/versus 64%), clopidogrel (54%/versus 60%), and glycoprotein IIb/IIIa inhibitor (2.2%/versus 9.5%; p<0.001) than men. Door to needle time was more prolonged in women (median, IQR; 40.40, 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%/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.

3:30 p.m.

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

Robert A. Knorr, 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 representative of local population participated in the Super Bowl. To the best of our knowledge, this is the first study to investigate total 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 1988 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 due to 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 (1.0566 versus control 1.1199; p = 0.0628), 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 as cardiovascular deaths; in contrast, the positive emotions surrounding a win may actually lower deaths.

3:30 p.m.

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 4,519 (9.4%) BMS and 84 of 1,883 (4.5%) DES) at WUFMC 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.

1023-143

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

David A. Appel, Jennifer A. McNear, Lena Avedissian, Laudio M. Castillo-Rojas, John E. Atwood, Lisa A. Pearse, Robert N. Potter, Allison P. Burke, Ladd Tremaine, Eric A. Siny, Phil J. Gentleski, Stephen S. Reich, Robert E. Eckert, 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 588 (77.5%) and idiopathic in 150 (19.7%). Coronary disease represented the leading coronary etiology (n=426, 56.1%). Of the death of disease of the coronary arteries, atherosclerosis was the leading abnormality; but less common in those <40 years (88.7%) compared to those >40 years (86.4%, 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 (25.3±5.3 kg/m2, p<0.002).

Conclusions: Coronary artery disease is the most common cause of cardiovascular death in the armed forces, especially in those over 40 years. Different types of coronary artery pathology have different clinical presentations 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 during 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 presenting during working hours (weekdays 7 AM to 6 PM) versus off hours (weekends, holidays, and 6 PM to 7 AM weekdays).

Results: Overall, 2628 STEMI patients (55.9%) presented during off hours. Compared with patients presenting during working hours, off-hours patients were less likely to arrive in 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 thrombolyse 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=0.638) 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

Keil C. Nikus, Markku Eskola, Heart Center, Cardioiology Department, Tampere University Hospital, Tampere, Finland

Background: The ECG pattern with widespread ST-depression, maximally in leads V4-V6 with inverted T waves and STElevation 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 (23%), pathological Q waves without ST-elevation (23%), typical LBBB (6%), LVH without ST-elevation, 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%).

Conclusions: Of patients with acute coronary syndrome presenting within 6 hours from symptom onset, LM-ECG (n=97) was present in 97 patients (8.2%). Of these, the following characteristics were more common in patients with LM-ECG: female gender (60% vs 52%, p=0.01), Killip class >2 (48% vs 38%, p=0.01), left bundle branch block (93% vs 80%, p<0.001), STElevation in lead aVR (93% vs 70%, p<0.001), and lower left ventricular ejection fraction (29% vs 36%, p=0.001). There were no differences in age, diabetes, hypertension, hypercholesterolemia, smoking, family history of premature coronary artery disease, body mass index, and prior cardiovascular disease. In-hospital mortality rate was 7% for patients with LM-ECG and 4% for patients without LM-ECG (p=0.13), and 3-month mortality rate was 11% for patients with LM-ECG and 6% for patients without LM-ECG (p=0.03).

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

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

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

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

3:30 p.m.

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


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

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

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

Conclusions: In an acute MI population, stage CKD 3-4 (eGFR 15-59 ml/min/1.73m²) and non-fatal MI or death [HR 3.43 (1.93-6.11)] at one year. There was a dose-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 difference in risk of ST as GFR declined (see figure). Dipstick proteinuria (≥1+) was associated with a trend increased risk for any outcome. Patients with both a lower eGFR and ≥1+ dipstick proteinuria had significantly higher rates of ST, all-cause mortality and non-fatal MI or death compared to patients with either condition alone.

3:30 p.m.

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

François Schiele, Nicolas Meneneau, Marie-France Seronde, Vincent Descolles-Geron, Joanna Duflot, Romain Chopard, Fiona Ecar, Jean-Pierre Bassand, University Hospital Jean Minjoz, Besançon, France

Background: Fondaparinux (fond) 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 wereolder, hadmore 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 fondaparinux 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.

1023-149 Troponin Positive, MB Negative Patients With Non-ST Elevation Myocardial Infarction: An Under-Treated but High-Risk Patient Group: Results From NCDR ACTION-GWTG Registry

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

Background: Despite the 2002 redefinition of myocardial infarction (MI), patients (pts) who are troponin (Tn) + but MB - may not be considered to have MI, particularly in the absence of known coronary disease (prior MI or revascularization; CAD), in which case Tn elevation may be described as 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.

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 variables for predicting in-hospital mortality in pts with and without known CAD.

Conclusions: Tn+MB+ pts were less likely to receive early GP 2b/3a antagonists (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.
Differential treatments in Patients With Systemic Lupus Chronic Kidney Disease May Raise the Risk for Myocardial Ischemia and Infarction in a coronary artery.

The traced lumen was transferred and rendered to form a three-dimensional surface (Mercury Computer Systems). Coronary lumen was traced in all frame images of IVUS.

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 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 2.9 (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.

Novel Stereoscopic Image-Processing System for Plaque in a Coronary Artery: Angioscopic Study

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.

Differential treatments in Patients With Systemic Lupus Erythematosus or Rheumatoid Arthritis Hospitalized With Myocardial Infarction: A NRMI Data Analysis

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). Multivariate logistic regression analysis revealed CrCl 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: During hospitalization for MI, patients with RA and SLE face a therapeutic disadvantage with lower use of all the modalities of reperfusion strategy.
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 Corti, Erika Pagannone, Maria Beatrice Musumeci, Andrea Mannu, Marco De Giusti, Filippo Maria Caufl, Eleonora Dito, Sebastiano Scarretta, Camillo Autore, Massimo Volpe, II Faculty of Medicine, University of Rome, Rome, Italy, IRCCS Neuromed, Pozzilli (IS), Italy

Background: Large unstained cells (LUC), also referred 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 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 70±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 proximity, as well as haemoglobin (Hb), WBC, and LUC at time 1 (admission, LUC1), 2 (3rd day of admission), and 3 (discharge), CXMB and troponin I peaks and AUCs, were recorded. As normally distributed, continuous variables were compared with Student t-test, and the relation between LUC1,2, and 3 and measures of infarct area and EF corrected for age, gender, time from symptom onset, recanalization performed/not performed, TIMI flow and vessel proximity, was tested with multivariate analysis.

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

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

**Table 1. Patient Characteristics and Non-MI Subsets Based Upon the New Universal MI Definition**

Usman Javed, Waqas Aftab, John A. Ambrose, Deepak Thatai, Ralph Wessel, Mouatou Neuromed, Pozzilli (IS), Italy

**Introduction:** Myocardial Infarction (MI) has recently been redefined and classified according to elevated Troponin I (Tnl) 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 Tnl have not been previously reported.

**Methodology:** Over a 3 month period, all patients admitted to the hospital with Tnl >0.04 ng/ml, with either associated clinical, EKG and/or myocardial ischemia were performed. MI was defined as Tnl >0.04 ng/ml, with either associated clinical, EKG and/or myocardial ischemia. In-hospital mortality of Type 1 (spontaneous plaque rupture/erosion), type 2 (altered supply demand) MI and non MI with increased Tnl have not been previously reported.

**Results (Table 1: Mean ± SEM):** Of 701 patients with elevated Tnl, 216 (30.8%) had MI, 396 (56.5%) had non MI and 79 (11.2%) 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 Tnl 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 iliac drug use. Non MI patients with increased Tnl commonly have non significant coronary disease in spite of a high in-hospital mortality.

**Background:** Mitogen-Activated Protein Kinases are Upregulated Patient Characteristics in Myocardial Infarction (MI)

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 Corti, Erika Pagannone, Maria Beatrice Musumeci, Andrea Mannu, Marco De Giusti, Filippo Maria Caufl, Eleonora Dito, Sebastiano Scarretta, Camillo Autore, Massimo Volpe, II Faculty of Medicine, University of Rome, Rome, Italy, IRCCS Neuromed, Pozzilli (IS), Italy

**Background:** Large unstained cells (LUC), also referred 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 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 70±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 proximity, as well as haemoglobin (Hb), WBC, and LUC at time 1 (admission, LUC1), 2 (3rd day of admission), and 3 (discharge), CXMB and troponin I peaks and AUCs, were recorded. As normally distributed, continuous variables were compared with Student t-test, and the relation between LUC1,2, and 3 and measures of infarct area and EF corrected for age, gender, time from symptom onset, recanalization performed/not performed, TIMI flow and vessel proximity, was tested with multivariate analysis.

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

**Conclusions:** Our data show that higher admission LUC are independently associated with a better ventricular function (EF), thus suggesting that bone marrow-mediated LUC output exert a favourable role on EF in AMI, regardless of type and efficacy of therapeutic strategy employed. Further investigation on topic is warranted.
Conclusions: Patients with PP have higher inflammatory condition and positive remodeling with large plaque burden, and more post-stenting cardiac enzyme elevation compared with patients without PP. NC component is a major component of post-stenting myonecrosis.

1023-158 Thin Cap Fibroatheroma Is an Important Predictor for Rapid Plaque Progression: An Intravascular Ultrasound-virtual Histology Study
Jang-Ho Baeg, Taek-Geun Kwon, Ki-Young Kim, Chan-anjit 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±8.1 years old, 68 males) with intermediate coronary artery lesion (stenosis 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 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±1.2mm², number of lesion with minimal luminal area (MLA)<4.0mm² 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±2.8months 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<4.0mm² showed also higher risk (35.3% vs. 6.5%, p=0.010) than lesion MLA<4.0mm². The risk of rapid lesion progression requiring PCI was highest (66.7%) in those presenting with MLA<4.0mm² and TCFA, followed by MLA<4.0mm² 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<4.0mm² by gray scale IVUS.

1023-159 Prognostic Implications of the New Universal Definition of Myocardial Infarction
Rita Calé, Pedro Carmo, Nuno Santos, Jorge Ferreira, João Figueira, Carlos Aguiar, João Figueira, J. Aniceto Silva, Cardiology Department, Hospital Santa Cruz, CHLO, Lisbon, Portugal

Background: In high-risk STEMI pts: those with prior CABG were less likely to undergo primary PCI. Their mortality (19.0% vs. 5.7%, p=0.05).

Methods: Fixed time point follow-up (1,05-2,51) 0.029

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

Table. Selected patient characteristics and 90-day outcomes.

<table>
<thead>
<tr>
<th>Criteria of MI</th>
<th>No Prior CABG</th>
<th>Prior CABG</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>9917</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>Age, yrs (median, IQR)</td>
<td>81(52.71)</td>
<td>89(58.3-76)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female, %</td>
<td>23.3</td>
<td>14.1</td>
<td>0.014</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>49.0</td>
<td>70.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior MI, %</td>
<td>10.9</td>
<td>64.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior PCI, %</td>
<td>9.2</td>
<td>36.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior HF, %</td>
<td>3.3</td>
<td>16.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>15.7</td>
<td>25.0</td>
<td>0.004</td>
</tr>
<tr>
<td>Multivessel disease, %</td>
<td>40.2</td>
<td>81.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>90-day death, %</td>
<td>4.6</td>
<td>11.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Adj HR: 1.9, 95%CI(1.1-3.3) p=0.025</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>90-day death, HF, shock, %</td>
<td>10.1</td>
<td>16.4</td>
<td>0.019</td>
</tr>
<tr>
<td>Adj HR: 1.1, 95%CI(0.7-1.7) p=0.816</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A322 ABSTRACTS - Myocardial Ischemia and Infarction JACC March 10, 2009
Background: Acute myocardial infarction (AMI) is the leading cause of death for both men and women in the western world, and studies in human subjects with coronary artery disease have shown that Endothelial Progenitor Cell (EPC) levels directly correlate with mortality after AMI. Currently, use of EPC for treatment of patients with ischemic heart disease involves delivery of ex vivo-processed EPC to patients during percutaneous coronary intervention or by direct injection of EPC to ischemic myocardium. A major limitation of EPC therapy in this patient population is lack of drugs to mobilize EPC in vivo.

Methods: In a preclinical study to evaluate the efficacy of mobilized EPC, saline or recombinant human interleukin-11 (HIL-11) was administered intravenously at a dose of 200 microgram/kg/d to 8-week old C57BL/6 mice (n=6 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-infarction 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 HIL-11 has a novel role in reduction of infarct size and has a favorable effect on post-infarct remodeling suggesting a novel role of HIL-11 as an adjunctive therapy for patients with AMI.
Trends in the Medical Management and Thirty-Day Mortality Among Patients With Renal Dysfunction Admitted With Acute Myocardial Infarction

Paul A. Santolicicuto, 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±14.7 years) 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 30-59), 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.

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. 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.
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.

1032-T12 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 yrs (OR 0.93 CI 0.57-1.54) and >85 yrs (OR 0.86, CI 0.44-1.69).

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

1032-T13 An Increased TIMI Risk Score Is Associated With a Decrease in TIMI Patency in Patients Treated With Thrombolitics for ST-Elevation Myocardial Infarction
Hans-Peter Hobbach, Uwe Zeymer, Peter Schuster, St. Marien-Krankenhaus Siegen, Siegen, Germany, Klinikum der Stadt Ludwigshafen, Ludwigshafen, Germany
Background: While primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy in ST-elevation myocardial infarction (STEMI) the majority of patients (pts) is admitted to hospitals without PCI facilities. For the most part these pts will be treated with thrombolysis. Therefore clinical models to predict the success of thrombolysis are still needed.

Methods: 314 pts (age 62±12 years) with STEMI (<6 h) 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 there was no significant benefit of thrombolysis.

Conclusions: TRS for STEMI is a convenient clinical risk score for predicting mortality among pts with STEMI and may also be 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.

1032-130 Percutaneous Intramyocardial Stem Cell Injection and Electromechanical Mapping in Patients With Acute Myocardial Infarction: First-in-Man Study
Kerth T. Krause, Kai Jaquet, Carsten Schneider, Stefanie Haupt, Karl-Heinz Kuck, Asklepios Clinic St. georg, Hamburg, Germany

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

Methods: On day 10.5±5 after AMI and PCI with stent implantation (culprit lesion: 18 LCA, 2 RCA) 20 patients (mean 60.4±11.4 years) received 28 mL mononuclear cells (BMPC) in the vital low voltage area of the infarction area using left ventricular electromagnetic tracking (EMM-guided) PICi. We injected 2.0±0.3±10³ cells including 1.0±0.3±10³ (CD45+/CD144+) stem cells in each patient. EMM (NCGA), 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 procedural complications or major adverse events during the 12-month follow-up. EMM showed an improvement from baseline 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.

Impact of Time to Therapy on the Efficacy of FX06
Karl Heinz Kuck, Kurt Heintz, Peter Buser, Dan Atar, Fibrex Medical Research & Development GmbH, Jonas Hallen, Bernard Petzelbauer, Peter Schuster, Asklepios Clinic St georg, Hamburg, Germany

Background: Known FX06 (fibrin peptide) reduces infarct size (IS) by mitigating reperfusion injury after 5 days in a fibrinogen-depleted rat model. First-in-man studies have shown benefit in IMPACT-AMI with FX06 1.8 mg/10 kg (0.33 mg/kg) (FX06) vs placebo (PL). Whether efficacy is related to the timing of reperfusion, here we report outcomes in early and late presenters (EP, LP). Time to therapy was available for 98% of patients (pts). The relationship between IS at 5-7 days (LGE) and pain-to-balloon-time of 0-3 hrs versus 3-6 hrs. The 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 results are summarised below.

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 28 mL mononuclear cells (BMPC) in the vital low voltage area of the infarction area using left ventricular electromagnetic tracking (EMM-guided) PICi. We injected 2.0±0.3±10³ cells including 1.0±0.3±10³ (CD45+/CD144+) stem cells in each patient. EMM (NCGA), 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 procedural complications or major adverse events during the 12-month follow-up. EMM showed an improvement from baseline 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.
Effect of pretreatment with clopidogrel on early reperfusion and adverse event rates.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Multivariate Adjusted Treatment Effect</th>
<th>Propensity Score Adjusted Treatment Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio</td>
<td>P</td>
</tr>
<tr>
<td>TIMI grade 2/3 flow</td>
<td>0.51</td>
<td>0.31-1.74</td>
</tr>
<tr>
<td></td>
<td>0.51</td>
<td>0.31-1.74</td>
</tr>
<tr>
<td></td>
<td>1.53</td>
<td>1.39-1.68</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.57</td>
<td>0.38-0.85</td>
</tr>
<tr>
<td></td>
<td>0.57</td>
<td>0.40-0.81</td>
</tr>
<tr>
<td></td>
<td>0.52</td>
<td>0.41-0.67</td>
</tr>
<tr>
<td>Duxtye reinfarction</td>
<td>0.54</td>
<td>0.38-0.75</td>
</tr>
<tr>
<td></td>
<td>0.54</td>
<td>0.39-0.73</td>
</tr>
<tr>
<td></td>
<td>0.50</td>
<td>0.40-0.62</td>
</tr>
</tbody>
</table>

*Adjusted for age, gender, history of diabetes mellitus, history of hypertension, hapanin dose (high vs low dose), symptom duration, smoking, and year of publication.

## 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. Skibning, Vladimir Dzavik, Venu Menon, Lea Liu, Aldo P. Maggioni, Antonio C. Carvalho, Luis Gruberg, Rudney Eduardo Uchoa Arezedo, Ewmin 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 or older pts (HR 1.28, p=0.003), but rates were reduced with PCI vs. MED for both age groups (HR 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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Death</th>
<th>Fatal and Non-Fatal MI</th>
<th>Class IV Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger MED (%)</td>
<td>12.8</td>
<td>8.6</td>
<td>4.5</td>
</tr>
<tr>
<td>Younger PCI (%)</td>
<td>18.1</td>
<td>10.3</td>
<td>8.0</td>
</tr>
<tr>
<td>Older MED (%)</td>
<td>23.4</td>
<td>19.5</td>
<td>6.5</td>
</tr>
<tr>
<td>Older PCI (%)</td>
<td>20.9</td>
<td>14.9</td>
<td>6.4</td>
</tr>
<tr>
<td>Younger PCI vs MED H.R. (99% CI)</td>
<td>1.4 (1.0-2.0)</td>
<td>p=0.02</td>
<td>1.7 (0.7-2.0)</td>
</tr>
<tr>
<td>Older PCI vs MED H.R. (99% CI)</td>
<td>0.8 (0.5-1.4)</td>
<td>p=0.37</td>
<td>0.9 (0.5-1.7)</td>
</tr>
</tbody>
</table>

*The pre-specified significance was defined as p<0.01.*

## 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 Sviiaas, Kevin Dammam, Bart J. de Smet, Jan G. Tijssen, Hans L. Hilleg, 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.** Jacknife estimation was used to establish the robustness of the multivariate model. A propensity score was calculated based on matching of all 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.

### 5:30 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. Umanis, Paul Knaapen, Jan H. Cornel, Friso van der Zand, MCA, Alkmaar, The Netherlands**

**Background:** Primary percutaneous coronary intervention (PCI) performed in large community hospitals without cardiac surgery back-up facilities (off-site) reduces door-to-balloon time compared with tertiary intervention centers (on-site). The present study was performed to explore whether off-site PCI for acute myocardial infarction reduces in 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, 99-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 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 Tagliari, Francesco Saia, Cinzia Marrozzi, Vincenzo Guiducci, Guido Rocchi, Elena Biagni, Giancarlo Piovaccari, Antonio Manari, Angelo Branzi, Antonio Marzocchi, Istituto di Cardiologia, Università di Bologna, Policlinico S. Orsola-Malpighi, Bologna, Italy, Unità Operativa di Cardiologia Interventistica, Ospedale S. Maria Nuova, Reggio Emilia, Italy**

**Background:** Abciximab during primary percutaneous coronary intervention (PCI) has shown to ameliorate left ventricular function recovery (LVFR). High-Dose Bolus (HDB) 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 PCI. Further we sought to define the predictors of favorable (≥50%) left ventricular ejection fraction (LVEF) and LVFR.

**Methods:** This study comprised 314 patients (abciximab, n=154; tirofiban, n=160) undergoing PCI in the randomized Facilitated Angioplasty with Tirofiban or Abciximab trial. LVEF and wall-motion-score-index (WMSI) were assessed within 48-72h post-PCI and at 30-day. Among patients with left ventricular systolic dysfunction at baseline, LVFR was defined by one of the following: 1) increase of LVEF ≥10% 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...
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 Scardalia, Francesca Calabrese, Gennaro Sardella, Emanuela Ageri, Francesco Fedele, Roberto Passariello, Luciano Agati, University ‘La Sapienza’, Rome, Italy

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

Methods: Seventy patients with first STEMI, successfully treated with primary PCI within 12 hours from symptom onset, underwent CMR 5±2 days after hospital admission. Patients were subcategorized into 4 quartiles on the basis of pain-to-balloon time: <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 and microvascular 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%, 6.0%, p=0.038, 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). Late 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.
**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.**

**Authors:** Maria Krzeminska - Pakula, Maciej Piek, Jose P. Henriques, Academic Medical Center, Amsterdam, The Netherlands

**Background:** We sought to determine 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 left ventricular 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.

**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**

**Authors:** Niels J. Verouden, Karel T. Koch, José P. Henriques, Jan Baan, René J. van der Schaaf, Marije M. Vis, Jan G. Tijsen, 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 STE-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 IRA being the RCA.

<table>
<thead>
<tr>
<th>IRA (RCA)</th>
<th>ECG algorithm</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive value (%)</th>
<th>Negative predictive value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRA (RCA)</td>
<td>IRA (RCA)</td>
<td>70</td>
<td>72</td>
<td>62</td>
<td>89</td>
</tr>
</tbody>
</table>

9:30 a.m. 1032-144 Enoxaparin in Patients Not Undergoing Reperfusion for ST-Elevation Myocardial Infarction

**Authors:** Gabriel Tatu-Chitoiu, Dragos Vinereanu, Mirea Cinteza, Maria Odeanu, Olavia Mantrini, Crina Sinecu, 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 unfractionated heparin in the Romanian registry of STElevation acute myocardial infarction (RO-STEMI), which enrolled 9288 consecutive patients from January 2000 to December 2007.

**Results:** There were 3812 (41.0%) patients who did not receive mechanical or pharmacological reperfusion, but admission therapy with enoxaparin (no=1462) or unfractionated heparin (no=2350). Logistic regression was used to adjust the outcome of inhospital death for baseline characteristics. Patients who were given enoxaparin were more likely to have history of hypertension (60.1% vs. 51.7%, P<0.001), lipid disorders (42.3% vs. 29.5%, P<0.001), and prior myocardial infarction (13.4% vs. 9.0%, P<0.001), and to present heart failure (48.6% vs. 34.3%, P<0.001). They were more likely to receive concomitant medication with aspirin and/or clopidogrel (93.7% vs. 83.5%, P<0.001). The rate of death was reduced by enoxaparin compared with unfractionated heparin (14.5% versus 16.9%; OR, reference unfractionated heparin: 0.83; 95% CI 0.69-0.99, P<0.05). After adjustment for age, any clinical confounder and antplatelet 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 Mitral Regurgitation Is an Independent Predictor of One-Year Mortality in ST-Elevation Myocardial Infarction Patients Presenting in Cardiogenic Shock on Admission

**Authors:** Annemarie E. Engstrom, Krishan D. Sjauw, Marije M. Vis, Rene J. van der Schaaf, Jan Baan, Bert J. Bouma, Karel T. Koch, Robbert J. de Winter, Jan G. Tijsen, Jan J. Piek, Jos 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.

---

**1032-149** The Effect of Failure Mode and Effect Analysis On 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

**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 412 patients with AMIEST (n=412). From them, 76 patients were submitted to conventional PCI with stent (CPCI) and 76 patients treated with thrombectomy aspiration catheter (TAC). Primary endpoints were evaluated as the >70% ST reduction and ≤2 myocardial blush grade. The secondary outcomes were occurrence of major adverse cardiac events (MACE), in-hospital, at 1 month and after 9 months (death, new AMI, thrombosis and target lesion revascularization).

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

**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

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

**Methods:** hASCs were transduced with the lentiviral vector carrying luciferase gene. Half 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 XGene 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 v3.0. 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±0.93)x106 (mean±SD) to (9.09±3.7)x105 in units of photons per second per centimeter squared per steradian. After that time, the BLSs gradually increased and arrived at (1.40±1.2) x106 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.
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

Joon D. Haenk, Niels J. Verouden, Wichert J. Kuijt, René J. Van der Schaaf, José P. Henriques, Marjolein M. Vis, Jan Baan, Jr., Jan J. Piek, Gunter 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 outcome. Resolution of ST-segment deviation (STR) during transportation before primary PCI had a significant impact on the resolution of ST-segment deviation during transportation (24.6% vs. 70.3%, P<0.001) and more often were treated with HDT (55.9% vs. 48.0%, P=0.03). Complete STR before primary PCI was defined as ≥70% STR at time of last PCI and CMR was used to determine left ventricular function and late enhancement to measure infarct size.

Conclusions: Patients with complete STR during transportation had a significantly larger enzymatic infarct size (650±851 IU/L vs. 2139±1816 IU/L, P=0.03) and LVEF <45% (OR 3.25 [1.11-9.50], P=0.031, OR 5.18 [1.86-14.5, P=0.002, 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) and LVEF <45% (OR 3.25 [1.11-9.50], P=0.031, OR 5.18 [1.86-14.5, P=0.002, 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) and LVEF <45% (OR 3.25 [1.11-9.50], P=0.031, OR 5.18 [1.86-14.5, P=0.002, respectively)
Background: Previous studies have shown that acute myocardial infarction due to the occlusion of the left main coronary artery (LMCA) 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 LMCA-MI 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 LMCA-MI (75.3% male, age 67.6±11.8 y.o.). We sought to observationally assess treatments and prognosis of LMCA-MI using the database of the OACIS. Results: Among them, 132 patients (age 67.5±12.0 y.o.) received primary PCI for LMCA-MI: resuscitation 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 LMCA-MI was significantly higher than that of non-LMCA-MI (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 LMCA-MI was higher than in non-LMCA-MI (14.0%, 8.3%, 7.1%, 4.6% for LMCA-MI, 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 LMCA-MI 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 LMCA-MI is still poor even in the contemporary reperfusion era. In-hospital mortality of LMCA-MI 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 LMCA-MI may be needed.
Correlation between HRV parameters and platelet reactivity variables

<table>
<thead>
<tr>
<th></th>
<th>SDNN</th>
<th>HF</th>
</tr>
</thead>
<tbody>
<tr>
<td>AT (PPA-100)</td>
<td>R=0.6, P=0.025 &lt;br&gt; R=0.4, P=0.19</td>
<td></td>
</tr>
<tr>
<td>MPA Baseline</td>
<td>R=0.7, P=0.008 &lt;br&gt; R=0.6, P=0.015</td>
<td></td>
</tr>
<tr>
<td>MPA ADP</td>
<td>R=0.6, P=0.012 &lt;br&gt; R=0.6, P=0.017</td>
<td></td>
</tr>
</tbody>
</table>

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 Chrysochoou, Panagiotis Aggelopoulos, Ioanna Kehagia, George Metalloinos, Christos Pitsavos, Christodoulos Stefanadis, Athens Medical School, Athens, Greece

Background: We evaluated whether adherence to this traditional diet is associated with the development of left ventricular systolic dysfunction (LVSD) in patients who had an acute coronary syndrome (ACS). Methods: During 2006-2007, 351 post ACS patients (68±13 years) who developed LVSD (ejection fraction<50%) 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 anthropometric characteristics, were retrieved from all patients. A semi-quantitative food frequency questionnaire was applied to assess the consumption of a variety of food groups, while the assessment of adoption of Mediterranean Diet conducted through the MedDietscore (range 0-55) that incorporates the inherent characteristics of this traditional dietary pattern. Results: Patients with LVSD reported less adherence to the Mediterranean diet, compared to those with preserved left ventricular systolic function (p=0.01). The MedDietscore showed good accuracy in predicting LVSD (AUC: 0.55±0.02, p=0.05). Moreover, one unit increase in the diet score (i.e., greater adherence) was associated with 3.5% lower risk of developing LVSD (95%CI 0.93-1.00), after adjusting for age, gender, BMI, clinical status and presence of the common cardiovascular disease risk factors. A value of 31/55 in the MedDietscore constitutes the optimal threshold for better diagnosing LVSD (sensitivity = 81%). Furthermore, the MedDietscore seems to be more accurate among people >65 years old (AUC:0.59±0.036, p=0.05), men (AUC:0.55±0.03, p=0.09) and diabetic patients (AUC:0.59±0.04, p=0.05). Conclusion: Greater adherence to the traditional Mediterranean diet seems to independently protect against development of LVSD after an ACS. The suggested MedDietscore is an accurate diet tool for screening ACS patients who are prone to develop LVSD. Our findings expand the beneficial effects of this traditional diet on human health, and should be further promoted.

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. Fouskas, Merihel M. Zairis, Stamatis Makrygiannis, Dimitrios Mylas, Georgios Z. Tzouvekas, Nikolaos Patsoyeras, Joseph Papadopoulos, Andreas Melidonis, Anastasios Koutsosilis, 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. Results: Patients with LVSD reported less adherence to the Mediterranean diet, compared to those with preserved left ventricular systolic function (p=0.01). The MedDietscore showed good accuracy in predicting LVSD (AUC: 0.55±0.02, p=0.05). Moreover, one unit increase in the diet score (i.e., greater adherence) was associated with 3.5% lower risk of developing LVSD (95%CI 0.93-1.00), after adjusting for age, gender, BMI, clinical status and presence of the common cardiovascular disease risk factors. A value of 31/55 in the MedDietscore constitutes the optimal threshold for better diagnosing LVSD (sensitivity = 81%). Furthermore, the MedDietscore seems to be more accurate among people >65 years old (AUC:0.59±0.036, p=0.05), men (AUC:0.55±0.03, p=0.09) and diabetic patients (AUC:0.59±0.04, p=0.05). Conclusion: Greater adherence to the traditional Mediterranean diet seems to independently protect against development of LVSD after an ACS. The suggested MedDietscore is an accurate diet tool for screening ACS patients who are prone to develop LVSD. Our findings expand the beneficial effects of this traditional diet on human health, and should be further promoted.

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 Ozzor, Jonathan Murrow, Saurabh Dhabhan, 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. 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 ischemia/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/infarction. Conclusions: Peri-procedural ischemia as assessed by Troponin I after BMS placement independently predicts a higher risk of developing late ISR requiring re-intervention at 5 years.

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

Shaibu Huruma, Brenda Brownell, P Diane Gabraith, Jean F. Legare, William A. Ghali, Merrill 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.
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<0.0001) (c statistic 0.69). After controlling for multiple cardiovascular mortality risk factors, adjusted HR remained significant: Group 5 (HR 4.2, p<0.0001), and Group 3 (HR 2.0, p=0.002) (c statistic 0.69). 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.

Therapeutic Consideration In the Patient Undergoing CABG

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

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

Methods: This was a retrospective, observational, cohort study of prospectively collected data on 10,023 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.
Aspirin-Insensitive Platelet Hyper-reactivity and Thrombogenesis: Are Independent Risk Factors for Early Vein Graft Occlusion After Coronary Artery Bypass Surgery

Jeffrey J. Rate, Tyler J. Gluckman, Rhondayl 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. Klicker, 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 multilayered 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 (<88 sec) and UTXB2 level >321 pg/mg creatinine were associated with odds ratios for VG occlusion of 3.1 (p = 0.002) and 1.9 (p = 0.047), respectively. VGs in 74 (28.8%) patients at highest risk, defined by low PFA-100 C/ADP CT and high UTXB2 level, had 6.5 times the odds of occlusion (p = 0.003) compared to VGs in 67 (26.1%) patients at lowest risk, defined by a high PFA-100 C/ADP CT and low UTXB2 level.

Conclusion: Despite suppression of platelet COX-1 activity by ASA, global platelet hyper-reactivity (defined by low PFA-100 C/ADP CT) and persistent thrombogenesis (defined by an elevated UTXB2 level) are common 6 months after CABG surgery and are independent risk factors for early VG occlusion.

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

Giovanni Filardo, Cody Hamilton, Robert F. Hebeier, Jr., Baron Hamman, Paul Grayburn, John F. Gersh, Brian L. Karch, Alexander J. Reina, Thomas Thiemann, Giovanni Galderisi, David J. Williams, Andrea S. Fuchs, Giovanni Filardo, Thomas H. Goetz, Robert F. Hebeier, Jr., Duke University, Durham, NC

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 (AFL) resulting in potentially higher risk of adverse outcomes. In the early postoperative course, new-onset post-CABG AFL 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 AFL on long-term survival, and this relationship is unclear.

Methods and Results: Survival was assessed in a cohort of 6,899 consecutive patients 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.

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

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

Shantil V. Parad, James A. de Lemos, Michael Jessen, Emmanuel Brikats, 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 - GWGT (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.

Conclusions: While delayed CABG was associated with lower risk of adverse outcomes after STEMI, no difference was seen for early vs. delayed CABG in NSTEMI patients (death: OR 1.36, 95% CI 0.88 - 2.19; composite: OR 1.10, 95% CI 0.76 - 1.59). 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

<table>
<thead>
<tr>
<th></th>
<th>NSTEMI (n=2784)</th>
<th>STEMI (n=974)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early (n=670)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delayed (n=2114)</td>
<td>66.8%</td>
<td>72.5%</td>
</tr>
<tr>
<td>STEMI (n=974)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early (n=61)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delayed (n=463)</td>
<td>52.5%</td>
<td>47.5%</td>
</tr>
</tbody>
</table>

- Age: (yrs)*
  - NSTEMI: 62.0 (55.0,72.0)
  - STEMI: 65.0 (57.0,75.0)
- Diabetes: (%) 30.8 vs 39.1 <0.0001
- Prior MI: (%) 17.1 vs 21.8 0.01
- Prior Revascularization: (%) 17.6 vs 21.2 0.01
- Prior CHF: (%) 3.9 vs 9.8 <0.0001
- Prior Stroke: (%) 5.6 vs 8.7 0.04
- Arrival to catheterization (hrs)* 8.4 (2.9,17.5) vs 26.5 (15.5,49.0) <0.0001
- Clopidogrel within 24 hours of arrival (%) 27.9 vs 38.1 0.002

* Median (25th, 75th percentiles)

ACC.Poster Contributions

Unstable ischemic syndrome/long-term outcome; Stable ischemic syndrome

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

1041-125
Oral proton pump inhibitors and their impact on the effectiveness of dual anti-platelet therapy during the first year after elective coronary stenting

Georgios Z. Tsiaousis, Michael N. Zaira, Nikolaos Patsourakis, Stamatios Makrygiannis, Konstantinos Vogiatzis, Evridiki Gougourela, Stelisias 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 prevent gastrointestinal bleeding. Due to the fact that clopidogrel is converted to its active metabolite by P450 isoenzymes, which are also involved in the metabolism of PPIs, there is a concern about whether the action of clopidogrel would be reduced in pts also taking PPIs. The 3C (Combined Clopidogrel and aspirin resistance in Coronary stenting) study afforded us the opportunity to examine the effect of the treatment with PPIs on the long-term prognosis in pts also treated with clopidogrel and aspirin following coronary stenting.

Methods: The 3C (Combined Clopidogrel and aspirin resistance in Coronary stenting) study was a prospective study which evaluated the impact of the resistance to the combined therapy with clopidogrel and aspirin on the 1 year incidence death and myocardial infarction in a total of 612 consecutive pts who underwent elective coronary stenting related data among the 2 groups. There was any difference in the impact of anti-platelet drug therapy during the first year following coronary stenting.

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

Conclusions: The 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.

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

Victor Serbroun, 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)

1041-127
Influence of Gender on Long-term Mortality in Patients Presenting with non-st elevation acute coronary syndromes

Dharam J. Kumbhari, Mehdi H. Shishehbor, Anthony A. Bavry, Stephen G. Ellis, Evin 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. Multivariable 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 multivariable model, but the interaction term between age & gender was significant (p=0.09). On age-stratified analysis, mortality was higher in women >60 years than men (p=0.04) (Figure). On subgroup analysis, the differential impact of age was true for troponin (TN negative (p=0.005), but TN+ (p=0.02) 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.

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

byunghoon Lee, Seung-Hwan Lee, Jun-Won Lee, Young-Jin Youn, Seong-Yoon Kim, Jang-Young Kim, Byung-Su Youn, Junghun 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 definite and 1 probable) and 10 pts of low group (4.2%, 7 definite, 2 probable and 1 possible)(p=0.028). The associations between cardiac death and clopidogrel low-responsiveness were evaluated with 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.

Impact of Microvascular Dysfunction on Long-Term Cardiovascular Outcomes After Primary Coronary Intervention for Acute Myocardial Infarction

Koichi Tamaki, Atsushi Yamamura, Shuichiro Kaji, Minako Katayama, Takeshi Kitai, Takafumi Yamane, Makoto Kinoshita, Natsuhiko Ebara, Yukata 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.
A Clinical Risk Stratification Model Provides Accurate Long-Term Risk Stratification For ACS Patients: The Olmsted County Acute Chest Pain Study

Louie Razouk, Vergheese Mathew, Guy S. Reedor, Peter A. Smans, Sameer Bansal, Ryan J. Lemmon, 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 Olmstead 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 = <0.05) 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.

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 Chul Chae, Jong Hyun Kim, Seung Ho Hur, Jeong Gwan Chao, Korea Acute Myocardial Infarction Registry (KAMIR) Study Group of Korean Circulation Society, Gwangju, South Korea

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

Methods: Between May 2005 and Aug 2007, 5,409 patients with NSTE-ACS (64.6± 12.4 yrs, 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).

Conclusions: 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.

Relation Between Red Blood Cell Distribution Width and Mortality in Patients With Acute Myocardial Infarction

Salim Dabbah, Haim Hammerman, Michael Kapelowitch, Rafael Beyer, 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 RDW and in-hospital and six-month mortality.

Conclusion: RDW is a useful and easily obtained parameter which independently predicts mortality in ACS patients.

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.

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

Eleftheria Tsagaliou, Charris Matsouka, Evangelos Repasos, Eleni Tseliou, Panagiota 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 recurrent 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 antplatelet effects.

Methods: Consecutive patients with recent (<1 month) 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 7±10 for Group A and B respectively, p=0.038). 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 7 (44%) patients on the 70% 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 resistance. A 150-mg maintenance dose of clopidogrel was not associated with enhanced antiplatelet effects compared with 75 mg in this high risk patient population.

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

Yuko Onaki, Shinya C. Kan, Hiroaki Naruse, Masanori Okumura, Kiousuke Hattori, Makoto Hikawa, Tomoko Kawai, Hiroto Harigaya, Shigero Matsui, Sadakazu Motoyama, Masayoshi Sarai, Junichiro Ishi, Hitoshi Hishida, Masanori Matsuzaki, JAPAN-ACS Study Group, Fujita Health University Hospital, Toyoyama, 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 to 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 260 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.

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

Robert Drags, Michael Kapelovich, Haim Hammerman, Rambam Health Care Campus, Haifa, Israel

Background: To assess the prevalence and long term prognostic significance of changes in serum albumin 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 hypoalbuninemia (<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) vs. 0.31 g/dl lower than 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=0.001). 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 hypoalbuninemia is frequent during hospitalization of patients with AMI and is strongly related to long term mortality.

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, Genjiro 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 (NMD), 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 (p<0.05) than that of KDM patients. The development of hypoalbuninemia is frequent during hospitalization of patients with AMI and is strongly related to long term mortality.
Interrelationships of Impaired Erectile Function, Enhanced Monocyte Expression of Adiponectin, Persistent Elevated Levels of Plasma Myeloperoxidase

Different Contributors to Thrombus Formation Between Chronic Coronary Artery Disease and Peripheral Arterial Disease

Background: Adiponectin is reduced in patients with CAD. Adiponectin receptors (ADRs) are expressed on monocytes and their activation may contribute 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 (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 decreased significantly compared with the acute phase. hs-CRP levels at the 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 acute phase (low-MPO group: <16.0 and high-MPO group: >16.0 ng/ml). Kaplan-Meier survival curves showed that the high-MPO group had significantly (P=0.016 by log-rank test) worse outcomes than the low-MPO group. Multivariate analysis showed that elevated plasma MPO levels at the chronic phase were an independent factor associated with the cardiovascular events (OR = 1.78, 95% CI: 1.03-3.09, P = 0.031). 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.

Conclusions: These findings indicate the importance of the mechanism of thrombus formation of SES and PES has not been clarified. Late stent thrombosis after sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) has been a major concern. Previous angiographic and pathological studies have revealed prevalence of yellow plaques and incomplete neointimal coverage related to drug-eluting stents greatly increase thrombotic risk. However, the mechanism of thrombus formation of SES and PES has not been clarified.

Methods: We examined 63 SES-implanted and 12 PES-implanted lesions. Angiographic and angiographic examinations of stent-implanted lesions were serially performed immediately (baseline) and 10.7 ± 3.8 months (follow-up) after implantation. Maximum yellow color grade (Max color grade: 0, white; 1, light yellow; 2, yellow; 3, intense yellow), neointimal coverage (Max color grade: 0, white; 1, light yellow; 2, yellow; 3, intense yellow), neointimal coverage of stent and prevalence of thrombus were angiographically 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 neointima 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 Group 3 (p<0.001 and p<0.01, respectively). These findings suggest that persistence of an increased arterial stiffness and severity of ED may help to identify underlying cardiovascular disease in men with ED.

Conclusions: ED severity is associated with increased arterial stiffness and the latter is a predictor of CAD presence. Determination of arterial stiffness and severity of ED may help to identify underlying cardiovascular disease in men with ED.

Different Contributors to Thrombus Formation Between Sirolimus-Eluting Stents and Paclitaxel-Eluting Stents: Serial Angiographic Observations

Tomoki Higo, Shizumi Hirono, Nobuyuki Ogasawara, Kazunori Kashiwase, Yasunori Ueda, Osaka Police Hospital, Osaka, Japan

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

Methods: We examined 63 SES-implanted and 12 PES-implanted lesions. Angiographic and angiographic examinations of stent-implanted lesions were serially performed immediately (baseline) and 10.7 ± 3.8 months (follow-up) after implantation. Maximum yellow color grade (Max color grade: 0, white; 1, light yellow; 2, yellow; 3, intense yellow), neointimal coverage of stent and prevalence of thrombus were angiographically 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 neointima 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 stents 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 stentlesed stents with incomplete neointimal coverage was higher in PES than in SES. Our data suggest that contributors to thrombus formation are
Prevalence of Extra Coronary Arterial Disease in Patients With Coronary Artery Disease Undergoing Coronary Intervention

Yoshimitsu Sogo, Hiroaki Kobayashi, Tatsuki Dojiri, Tomoko Unakawa, Kenji Ando, Hiroshiyo Yokoi, Masashi Isahayihide, Yukiyo Nosaka, Masakyo Nobuyoshi, kooka 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 coexistence 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 36 (4.4%), respectively. On multivariate analysis, age, history of coronary artery bypass surgery (CABG), hemodialysis, 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

<table>
<thead>
<tr>
<th>variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodialysis</td>
<td>3.12</td>
<td>1.59–6.15</td>
<td>0.0010</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>2.27</td>
<td>1.18–4.38</td>
<td>0.0142</td>
</tr>
<tr>
<td>Age &gt; 70</td>
<td>2.10</td>
<td>1.50–2.93</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HDL &lt; 40mg/dl</td>
<td>1.72</td>
<td>1.15–2.58</td>
<td>0.0086</td>
</tr>
<tr>
<td>Prior Stroke</td>
<td>2.00</td>
<td>1.25–3.20</td>
<td>0.0038</td>
</tr>
</tbody>
</table>
The Prognostic Utility of Lipoprotein-Associated Phospholipase A2 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 A2 (LpPLA2) is believed to contribute to atherosclerosis. The relative prognostic utility of LpPLA2 measured as enzyme activity versus mass remains undefined.

Methods: LpPLA2 activity and mass (DiaDexus) were measured at baseline in 3743 subjects in PEACE, a randomized trial oftrandolapril vs placebo in stable CAD. The primary endpoint (EP) was CV death, MI or coronary revascularization (median 4.8 year follow up). Multivariable Cox regression was used to adjust for demographics, risk factors, and medications.

Results: Modeled separately, the adjusted risk for the primary endpoint per 1-SD increase was 1.23 (95% CI 1.16-1.31, P<0.001) for LpPLA2 activity versus 1.12 (95% CI 1.04-1.19, P=0.002) for LpPLA2 mass. Analyses by quartile are shown in Figure (left). In ROC analyses, LpPLA2 activity (P=0.035), but not mass (P=0.16), significantly improved the C-statistic over traditional predictors. LpPLA2 activity and mass were moderately strongly correlated (r=0.59, P<0.001). In a model that included both markers, activity (P<0.001) but not mass (P=0.70) remained significantly associated with outcomes. In quartile analyses, elevated LpPLA2 activity was predictive of risk regardless of mass (Fig, right).

Conclusion: LpPLA2 activity and mass each independently predict outcomes in patients with stable CAD. The two markers are moderately correlated, and LpPLA2 activity appears to be the stronger independent predictor of outcomes.
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 QT (cQTD) following percutaneous coronary interventions (PCI) and long-term survival.

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

Results: PCI reduced cQTD in 343 patients (56%). QTc 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 cQTD - 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 cQTD 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 cQTD and 0.645 for peak CK-MB. The 82 patients (13%) who were in the first tertile of cQTD and experienced a post-procedural increase of CK-MB above normal limit had a 4-year cardiac mortality rate of 14.6%, significantly higher than the remaining population (2.9%, P=0.001).

Conclusions: 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.

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

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

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

Methods: We prospectively assessed 181 CSA patients (symptoms stable for > 3 months) (age 69±9 years; 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 and not CRP and LVEF (n=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.

"Intravenous Administration of Subpressor Dose of Short-Acting Beta-Blocker Lanzololid 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, itakatsuki, 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
**JACC March 10, 2009**

**ABSTRACTS - Myocardial Ischemia and Infarction**

**A343**

**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 Tritt, Gaetano A. Lanza, Fausto Rigo, Stefano Favale, Oberdan Parodi, M. Lorenzo Muzi, 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 identifying patients at higher risk of cardiovascular events. This condition is rare, so 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 [81±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 29.9%, smoking 22.4%, diabetes 10%. At a median follow up of 40 months (Interquartile range 30.0-108.3), cardiovascular events were rare: 1 patient suffered acute coronary syndrome (0.4%) and 2 developed heart failure (0.8%). However, 83% of women and 46% of men (<p=0.05) still complained of angina among them, 60% have >1 annual episode/week, in 20% 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 4.25; 95% C.I. 2.36-7.65; p<0.0005), and family history of coronary heart disease (adjusted Odds Ratio of 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 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.**

**1041-161**

**Diabetes Mellitus and Adiponectin Synthesis at Long-Term Prognosis of Patients With Cardiac Syndrome X**

Constantinos Bakogiannis, Chalarambos Antoniades, Dimitris Tousoulis, Alexandros S. Antonopoulou, Antigoni Millos, Costas Triantafyllou, Constantinos Robin Choudhury, Janis Dagiy, Ilia Kyliantzas, George Ekonomonos, Christodoulou 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 adiponectin synthesis and its human in 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 respectively: (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 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=0.826, p=0.02) but not with femoral (r=0.25, p=NS) AT. Importantly, patients with DM had significantly lower serum adiponectin (9.6±2.1 vs 31.2±4.9µg/ml, p<0.001) as well as lower adiponectin synthesis in subcutaneous (126.6±18.6 vs 194.5±17.7pg/mg) and pericardial AT (152.7±25.5pg/mg vs 231.1±25.7pg/mg, p=0.05). In DM, adiponectin synthesis was negatively associated with advancing atherosclerosis.

**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.

---

**1044-176**

**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. Pesaró, Carlos V. Serrano, Jr., Herlon Saraiva Martins, James De Lemos, Paulo R. Parra, Juliano L. Fernandes, Renata T. Ladeira, Roberto Rocha C.V. Giraldez, Joso A. Nicoli, Heart Institute (InCor), University of Sao Paulo, Medical School, Brazil, Sao Paolo, 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) (patients with stable CAD).

**Methods:** Patients (n=47, 63±9±0.03 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 6.1%, respectively; p=0.20).

**Conclusions:** S 80 and E10/S20, are effective to reduce cholesterol and platelet aggregation in patients with stable CAD. However, only S 80 was able to reduce CRP effectively. Higher simvastatin doses may be necessary to provide a larger pleiotropic effect.
New Frontiers in Risk Assessment: From Genes to Proteins

Monday, March 30, 2009, 4:30 p.m.-6:00 p.m.
Orange County Convention Center, Room W307A

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. Wykryzkowska, Hector Garcia-Garcia, Andrew Zalewski, Patrick W. Serruys, Thoraxcenter Erasmus MC, Rotterdam, The Netherlands, GiaxoSmithKline, Philadelphia, PA

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

Methods and Results: CRP and IL6 as well as Lip/PLA2 levels were observed to decrease in patients with acute coronary syndromes over time. With the exception of CRP and IL6, the expression of classical biomarkers did not correlate with the presence of echogenic plaque on IVUS gray scale imaging or paclitaxel. 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 the two randomization arms. 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 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, CXCL9/L10/MIG, platelet factor 4/ CXCL4/L, CTACK, C6 Kine, follistatin, GDF-7). The second subset increased over time (PAI-1, anti-apolipoprotein protein and 1-309 - chemokine induced on the human endothelium by Lpa(i)l). Only two analytes MPI-1d, TGF-6 RII showed change in expression at steady-state from 3 to 6 months.

Conclusions: Biomarkers identified by this exploratory analysis all appear to denote further large vulnerable plaque natural history studies are needed to better define patients at risk.

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

Kai M. Eggen, Kai C. Wollert, Bo-Lagerqvist, Bertil Lindahl, Lars Wallenin, 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 patients included in the FRISC II (Framinghat and Fast Revascularisation 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 to decrease in patients with acute coronary syndromes over time. With the exception of CRP and IL6, the expression of classical biomarkers did not correlate with the presence of echogenic plaque on IVUS gray scale imaging or paclitaxel. 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 the two randomization arms. 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 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, CXCL9/L10/MIG, platelet factor 4/ CXCL4/L, CTACK, C6 Kine, follistatin, GDF-7). The second subset increased over time (PAI-1, anti-apolipoprotein protein and 1-309 - chemokine induced on the human endothelium by Lpa(i)l). Only two analytes MPI-1d, TGF-6 RII showed change in expression at steady-state from 3 to 6 months.

Conclusions: Biomarkers identified by this exploratory analysis all appear to denote further large vulnerable plaque natural history studies are needed to better define patients at risk.
Promotion of Coronary Collateral Growth by External Counterpulsation in Patients With Coronary Artery Disease

Stefan Gloecker, Stefano F. de Marchi, Tobias Rutz, 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 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) and shaming control (n=6). 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.

Results: Compared to the reference group, WISE participants had higher aortic systolic pressure and wasted LV energy which increase left ventricular (LV) afterload and myocardial O₂ consumptions.

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 arteriogenic effect.

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

8912-7

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 Quizaiu, Thomas Meinert, 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 cardiac events. However, only few data from intravascular ultrasound (IVUS) studies on plaque size and correlation with SNPs are available.

Methods: In 173 out of 734 patients with established coronary artery disease from the ENCORE trials coronary plaque volume was assessed by IVUS and vessel size by quantitative coronary angiography. All 173 patients were genotyped for polymorphisms of CRP C1444T, MMP3 promoter 5A/6A, using the single-nucleotide polymorphism polymerase chain reaction (SNP-PCR) approach.

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

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

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

1050-125

Albuminuria, the Glomerular Filtration Rate, and Angiographically Determined Coronary Atherosclerosis

Philipp Rein, Christoph H. Saely, Lorenz Risch, Stefan Beer, Alexander Vonbank, Christian Boehnig, Ulric Kopp, Heinzi Drexel, Vorarberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria, Private University in the Principality of Liechtenstein, Trienz, 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 <90 ml/min/1.73 m² and 204 had albuminuria (ACR >30 mg/g). When compared to subjects with both normal eGFR and normal urinary albumin excretion (n=487), 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 1.30 [95% CI 1.06 - 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.

1050-126

Promotion of Coronary Collateral Growth by External Counterpulsation in Patients With Coronary Artery Disease

Stefan Gloecker, Stefano F. de Marchi, Tobias Rutz, Pascal Meier, Kerstin Wustmann, Stefan 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 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) and sham-control (n=6). 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.

Results: Compared to the reference group, WISE participants had higher aortic systolic pressure and wasted LV energy which increase left ventricular (LV) afterload and myocardial O₂ consumptions.

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 arteriogenic effect.

1050-127

Significant Association of Left Mammary Arterial Wall Thickness With Arteriogenic Stiffness in Hypertensive Patients With Coronary Artery Disease

Maria Markotou, Anastasios Koutsopoulos, Theoxenios Xenakiakis, 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 forces of venous 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 mm tissue sections were cut and stained with hematoxylin and eosin for the evaluation of arterial 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/externum ratio, the media thickness and the media/lumen ratio. 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 thickness and media stiffness 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.
Incident Diabetes Mellitus in Patients With Stable Coronary Artery Disease

Apurva Badheka, Neha Gang, Mohammad A. Kizilbash, Samrat Bhat, Ankith Rathod, Sony Jacob, Luis Alonso, Wayne State University, Detroit, MI

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

Methods: The NHLBI Limited access dataset of the multicenter Prevention of Events With Angiotensin Converting Enzyme Inhibition (PREDICT)-II 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=451) included patients with non obstructive (<50%) vessel stenosis (NOCAD) without prior MI or revascularization.

Results: Incident NOD occurred in 733 patients over mean follow-up of 4.6 yrs. Statistically significant covariates (HR, 95% CI) associated with NOD were use of beta blockers (0.66, 0.55-0.80), trandolapril (0.74, 0.62-0.87) and BMI (1.11, 1.10-1.12). 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.

Mycardial Ischemia and Infarction

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


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-II 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 referred for coronary catheterization (CATH).

Results - The mean age was 58 ±12 yrs, 412 (47%) were women and 210 (24%) had diabetes. Stable or symptomatic symptoms were present in 78% and 22% of pts and 67% (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.

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


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 placed over the left chest (4msec, 27.12MHz, 50mG at Y ork, NY)

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 have been linked with significant CAD in genome-wide association studies. Whereas the association of variant rs1333049 with CAD was analysed in several subsequent studies, replication studies of SNPs rs6922269 and rs2436344 have been lacking and March 10, 2009
Significant Impact of Genetic Variants on Chromosomal Postload Reduced Insulin Level Is Associated With High Granulocyte-Colony Stimulating Factor (G-CSF) Promotes Coronary Collateral and Myocardial Microvascular Function in Patients With Coronary Artery Disease: A Randomized, Double-Blind, Placebo-Controlled Study

Steffen Gloeckler, 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 monocytocyte-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 aneurysm leakage. Intention-to-treat analysis

Results: CFI changed from 0.16 ± 0.08 to 1.06 ± 0.08 in the G-CSF group (p = 0.000012), and from 0.15 ± 0.08 to 1.32 ± 0.07 (p = 0.02) in the placebo group (figure). FFR changed from 0.85 ± 0.11 to 0.85 ± 0.10 in the verum group (p = 0.04), and from 0.86 ± 0.11 to 0.84 ± 0.12 (p = 0.05) in the placebo group. In the intracoronary and extracoronary EC50, 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). An angioplasty during coronary occlusion was also reduced in G-CSF patients after therapy (p = 0.059).

Conclusions: This study shows for the first time that G-CSF is both efficient and safe for promotion of coronary collateral growth in patients with CAD.

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

Leah A. Swanson, Kaile M. Edelman, William M. Parham, Christopher E. Kapsner, Barbara T. Unger, Mary E. Kelb, 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 (OHCA) with ST elevation myocardial infarction (STEMI) leads to poor neurologic outcome. Therapeutic hypothermia (TH) has been shown to improve survival and neurologic outcome following OHCA 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. OHCA pts with STEMI are transferred to 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 (84% vs. 41%, p = 0.052) and neurologic outcome (100% vs. 82%, p = 0.048).

Conclusions: OHCA 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 OHCA patients with acute MI. Given these positive outcomes, TH should be included as a part of acute MI programs that function as tertiary centers.
**1050-137**  
Incidences of Infection in Patients With Sudden Cardiac Death Treated With Therapeutic Hypothermia Versus Conventional Care  
Brian E. Gubris, Andrea C. Hall, James Constable, Punit S. Parasher, Christopher Y. Kim, RagHAVENDRI Moturi, Tazbayeh Mohyudin, Saurab Sanon, Santiago Segovia, Ramal Weragoda, H. V. Anderson, Stefano SiriGingola, Richard W. Smalling, Ali E. Enskas, 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 hygroscopy 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  
Laudizio M. Castillo-Rojas, David A. Appel, Jennifer A. McNear, Lena Avedissian, John Shry, Philip J. Gentlesk, Stephen S. Reich, Robert E. Eckart, Department of Defense Cardiovascular Death Registry Group, Brooke Army Medical Center, San Antonio, TX, Armed Forces Institute of Pathology, Washington, DC  
Background: Some types of genetic disease have a predilection towards a temporal association of sudden death with exertion. We sought to identify the activities associated with sudden death in a young cohort.  
Methods: Records from the Office of the Armed Forces Medical Examiner from 1998 to 2008 were reviewed for sudden death in those less than 40 years of age known with 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%). Exertional deaths due to malignant ventricular tachyarrhythmia had ST elevation (6.3%, 10/158) and were associated with marked QT prolongation (10 of 158, 64.1%). 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). 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: In anterior myocardial infarction, ST-segment elevation in the right precordial lead, anterior AMI.

**3:45 p.m.**

**1050-139**  
Etiology of Sudden Death Among Younger Adults in the Community: Results of Anatomical Metabolic and Genetic Evaluation  
A. Seluck Adabag, Gary Peterson, Fred S. Apple, Jack Titus, Richard King, Russell V. Luepker, University of Minnesota, Minneapolis, MN  
Background: Identifying the community-dwelling persons at risk for sudden cardiac death (SCD) is challenging. Few studies have investigated the victim with contemporary laboratory techniques and few have focused on a community-based population. We hypothesized that a comprehensive examination of out-of-hospital SCD victims in the community will reveal clues about the risk factors for SCD.  
Methods: It is mandatory to report all out-of-hospital SCD to the Medical Examiner’s (ME) office in Hennepin County (population 1.2 million), Minnesota. We studied all SCD victims between the ages 25-60 years without an initially apparent cause of death and evaluated by the ME. We reviewed clinic records, conducted next-of-kin interviews and performed autopsies of laboratory studies and genetic analysis for mutations in genes associated with the long QT syndrome. From August, 2001 to July, 2004, 114 cases were eligible. The next-of-kin consented to the study in 71.  
Results: Mean age was 49.5±7 years, 86% were male and only 2 subjects had history of coronary heart disease (CHD). Coronary risk factors were highly prevalent for age (e.g. smoking 61%; hypertension 25%; diabetes 25%). On autopsy, 80% of the victims had high-grade coronary stenoses (≥75% obstruction). Acute coronary lesions and previous silent myocardial infarction were found in 27% and 34% of the victims, respectively. Further, 60% had recently ingested analgesics. Possible deleterious mutations of the ion channel genes were detected in 5 (7%) of the victims. Of these, 4 were in the sodium channel gene 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. Anagistic 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  
Alan Barshefshek, Hanoch Hod, Dan Oener, Athanasios Michelakis, Ilan Goldenberg, Michael Glikson, Michael Eldar, Shlomi Mateczyk, Heart Institute, Sheba Medical Center, Tel Hashomer, Israel  
Background: The clinical implications of ST-segment elevation in the right precordial leads in the circumstances of acute anterior myocardial infarction (AMI) are unknown. We aimed to assess 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=0.019, for HF 15/39 (38%) vs. 14/81(17%), p=0.021). Patients in group A compared with group B had a trend towards less spontaneous reperfusion (14% vs. 32%, p=0.063) and had higher incidence of multivesSEL coronary artery disease [median (interquartile range) of 2 (1-3) vs. 1 (1-2), p=0.07] 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, Brahmadee K. Nallamothu, Karl B. Kern, Paul S. Chan, University of Michigan, Ann Arbor, MI, Saint Luke’s Mid-America Heart Institute, Kansas City, MO  
Background: Survival after in-hospital cardiac arrest may be influenced by patients’ Body Mass Index (BMI), which may affect the quality and effectiveness of resuscitation measures.  
Methods: From 2006 to 2007, there were a total of 34,588 cases of cardiac arrest at 328 hospitals within the NRPDC. 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 kg/m2), overweight (25.0-29.9 kg/m2), and very obese (>35.0 kg/m2) and survival to discharge using multivariable logistic regression, after stratifying by cardiac arrest rhythm type and adjusting for differences in patient and hospital characteristics.  
Results: Of 4,499 patients with a pulseless arrest due to ventricular fibrillation or tachycardia, 1,825 (40.6%) patients survived to discharge. Compared with overweight patients, patients at other BMI levels had lower rates of survival (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.
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 ventricle viewed by ICE was 8.7 ± 3.4 cm². 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 morbidity and mortality following cardiac arrest needs more evaluation.
Influence in Female Patients With Stable Multivessel Coronary Disease Submitted to Off-Pump and On-Pump Coronary Surgery

Felipe Paulstitz, Neusa Lopes, Fernando Costa, Cibele Garzillo, Alexandre Pereira, Noedir Stoff, Luiz Cesar, Whady Hueb, Heart Institute 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, presented to left ventricular function, and the possibility of surgery by either the on-pump or off-pump method. Patients were randomized into two 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). Complete 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=0.001) 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 pump use.

Conclusion: In the present study, the number of combined events was significantly higher in women than in men. However, Off-pump did not significantly influence outcomes between genders.

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

Asim A. Mohammed, Avnind Agnihotri, Roland R. van Kimmenade, Ab elelo Martinez-Rumayor, Sandy Green, Rene Quirce, 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 related, 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: It 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=0.001). In contrast to the endorsed consensus 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.

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

Cheralambous A. Antoniades, Tim Van-Assche, Jonathan Desch, Alexios S. Antonopoulous, Christoudoulos Stefadienas, 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 sCD40L-igand). 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 and methemoglobin (MethHb) as markers of circulating O2 were measured in LIMA and non-coronary artery bypass grafting (CABG). We examined whether preoperative endothelial dysfunction and platelet activation and oxygenation predict the development of post-operative AF.

Results: 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 and methemoglobin (MethHb) as markers of circulating O2 were measured in LIMA and non-coronary artery bypass grafting (CABG). We examined whether preoperative endothelial dysfunction and platelet activation and oxygenation predict the development of post-operative AF.

Conclusions: Elevated preoperative levels of serum sCD40L, a marker of platelet activation, predicts the development of AF post-CABG. Patients with persistent AF at 6 weeks had higher preoperative sCD40L, lower FMD and higher vascular O2- mainly due to uncoupled eNOS, at the time of surgery.
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, 1996 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 more women (26.8 vs. 12.4%), previous strokes (7.8 vs. 2.7%), PVD (11.2 vs. 3.5%), 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), renal failure (1.0 vs. 0.6%), and death (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 reoperative 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.

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 trended towards a higher rate of postoperative morbidity. The RA appears to be an excellent choice as an additional arterial conduit in DM patients.
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


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 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 893 pts (12%) with SMI at BL. Other than diabetes (OMT+34.3%; PCI+24.3%), 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:

<table>
<thead>
<tr>
<th>Outcomes: SMI Pts</th>
<th>PCI + OMT</th>
<th>OMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-d MI</td>
<td>19 (14%)</td>
<td>27 (18%)</td>
</tr>
<tr>
<td>Death Alone</td>
<td>7 (5%)</td>
<td>16 (11%)</td>
</tr>
<tr>
<td>MI Alone</td>
<td>14 (10%)</td>
<td>22 (16%)</td>
</tr>
<tr>
<td>ACS Alone</td>
<td>10 (7%)</td>
<td>11 (7%)</td>
</tr>
<tr>
<td>D/MI/Stroke</td>
<td>30 (11%)</td>
<td>38 (11%)</td>
</tr>
<tr>
<td>D/MI/ACS</td>
<td>27 (20%)</td>
<td>36 (24%)</td>
</tr>
<tr>
<td>Subsequent Hevasc</td>
<td>18 (13%)</td>
<td>26 (19%)</td>
</tr>
</tbody>
</table>

Conclusions: In COURAGE, the addition of PCI to OMT did not reduce long-term cardiac events in SMI pts with stable CAD. While SMI pts in SWISSII-II differ from both ACIP and COURAGE, the ~2-fold trend toward lower mortality with PCI suggests the need for a more definitive trial of PCI vs OMT in SMI pts.
**Comparative Efficacy of Primary Percutaneous Coronary Intervention, Facilitated Percutaneous Coronary Intervention and Fibrinolysis in Chinese Patients With ST-Elevation Myocardial Infarction: A Multicenter Randomized Controlled Trial**

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

**Background:** Primary percutaneous coronary intervention (PCI) 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 PCI 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 583 patients with STEMI were enrolled and randomized to one of the three reperfusion strategies: (A) PCI, (B) FPCI and (C) fibrinolysis. Patients assigned to group A received immediate PCI at a median door-to-balloon time of 119.5 mins. Patients assigned to group B were first given an intravenous bolus of 80mg rt-PA followed by an infusion of 42mg rt-PA over a period of 60 mins and then PCI. Patients in group C received a dose of 100mg t-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 differences in the secondary endpoint were 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 PCI and FPCI is superior to fibrinolysis in the treatment of Chinese patients with STEMI. The efficacy of PCI is equal to that of FPCI if the door-to-balloon time is more than 90 mins.

---

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

Robert J. Applewhite, Matthew T. Sacrinity, Michael A. Katcher, Renato M. Santos, Sanjai K. Gandhi, William C. Little, Wake Forest University School of Medicine, Winston-Salem, NC

**Background:** Long-term safety concerns about “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 in 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.

---

**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

**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 Kling-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.

---

**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 Iwashashi, 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 syndromes (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 m².

**Results** There were no differences in diabetes mellitus, hyperlipidemia, smoking, lipid profiles, high-sensitivity C-reactive protein (hsCRP), cardiac-specific 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).
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

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 (55.6-97.9), 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.

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

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.

Anemia for Risk Assessment of Patients With Acute Coronary Syndromes

Background: In patients 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.