Myocardial Ischemia and Infarction

1003
Myocardial Ischemia–Basic

Sunday, March 30, 2008, 9:00 a.m.-12:30 p.m.
McCormick Place, South Hall

11:00 a.m.

**1003-41** Oral Glyburide, but not Glimepiride, Blocks the Infarct-Size Limiting Effects of Pioglitazone

Yumei Ye, Yu Lin, Sarawathy Manickavasagam, Regino J. Perez-Polo, Yochai Birnbaum, University Of Texas Medical Branch, Galveston

**Background:** Many patients with diabetes mellitus type 2 (DM2) receive several oral hypoglycemic agents, including sulfonylurea-urea drugs. Intravenous glyburide (GLYB), a sulfonylurea agent, blocks the protective effects of preconditioning in various animal models without affecting myocardial infarct size (IS). However, there are conflicting results when other sulfonylurea drugs are used. Pioglitazone (PIO) reduces IS in the rat. We asked whether oral GLYB and glimepiride (GLIM) affect the IS-limiting effects of PIO.

**Methods:** Sprague-Dawley rats received 3-day oral treatment with: PIO (5mg/kg/d); PIO-GLYB (10mg/kg/d); PIO-GLIM (4mg/kg/d) or water alone. Drugs were administered by oral gavage. Sugar 5% was added to water to prevent hypoglycemia. Rats underwent 30min coronary artery occlusion and 4hr reperfusion (n=6 in each group). Area at risk (AR) was assessed by blue dye and IS by triphenyl-tetrazolium-chloride. Results: Body weight and the AR size were comparable among groups. IS (% of the AR) was significantly smaller in the PIO (p<0.001) and PIO+GLIM (p=0.001) groups than in the control group. GLYB completely blocked the effect of PIO (p<0.001). GLIM did not affect the protective effect of PIO (p=0.993). **Conclusions:** Oral GLYB, but not GLIM, blocks the IS limiting effects of PIO. It is plausible that GLYB affects other pleiotropic effects of PIO and thus may attenuate favorable effects on cardiovascular outcomes. In contrast, GLIM does not attenuate the protective effect of PIO.

11:00 a.m.

**1003-42** Resolvin E1 Protects the Rat Heart Against Reperfusion Injury

Yochai Birnbaum, Yumei Ye, Yu Lin, Sarawathy Manickavasagam, Regino J. Perez-Polo, Per Gjorstrup, University Of Texas Medical Branch, Galveston, TX, Resolvix Pharmaceuticals, Inc., Bedford, MA

**Background:** Resolvin E1 (RvE1) is an endogenously formed oxidation product of the omega-3 polyunsaturated fatty-acid eicosapentaenoic acid (EPA), originally isolated from exudates during the resolution phase of an acute inflammation. Its further investigation has established its anti-inflammatory and anti-angiogenic properties. In this study, we investigated the effect of RvE1 against reperfusion injury.

**Methods:** Male Sprague-Dawley rats received 3-day oral treatment with: PIO (5mg/kg/d); PIO+RvE1 (0.03 mg/kg, 0.1 mg/kg or 0.3 mg/kg) or vehicle alone (control). Just before reperfusion rats received i.v. RvE1 (0.03 mg/kg, 0.1 mg/kg or 0.3 mg/kg). Heart function (% FS: 32.1% (MSCHO-1 group) V.S. 20.4% (control group), infracted size: 0.3 mg/kg) or vehicle alone (control). Area at risk (AR) was assessed by blue dye and IS by triphenyl-tetrazolium-chloride. Results: Body weight and the AR size were comparable among groups. IS (% of the AR) was significantly smaller in the PIO (p<0.001) and PIO+RvE1 (p=0.001) groups than in the control group. GLYB completely blocked the effect of PIO (p<0.001). GLIM did not affect the protective effect of PIO (p=0.993). **Conclusions:** Oral GLYB, but not GLIM, blocks the IS limiting effects of PIO. Resolvin E1 protects against reperfusion injury and limits myocardial infarct size.

11:00 a.m.

**1003-43** Phosphodiesterase-5 Inhibitors Reduce Myocardial Infarction, Apoptosis and Improve Post-Ischemic Ventricular Function in Female Mice

Fadi N. Salim, Antonio Abbate, William R. Brown, Ramzi A. Ockaili, Nicholas N. Hoke, Rakesh C. Kukreja, Virginia Commonwealth University Medical Center, Richmond, VA

**Background:** Phosphodiesterase-5 (PDE-5) inhibitors sildenafil (SIL) and vardenafil (VAR) induce powerful cardioprotection against ischemia/reperfusion injury (IR) in male animal models. Since the impact of PDE-5 inhibitors on the female cardiovascular system following ischemia remains unknown, we interrogated the effect of SIL and VAR on IR in female mice.

**Methods:** Adult female mice were pretreated (i.p. bid) with SIL (0.71 mg/kg), VAR (0.14 mg/kg) or saline one hr before left coronary artery ligation for 30 min and reperfusion for 24 hr. At the end of reperfusion, infarct size (IS) was measured using TTC staining and apoptosis was measured using TUNEL assay. Left ventricular (LV) function was evaluated using echocardiography. Results: Myocardial IS (mean ± SE) was reduced with SIL (9.1 ± 1.0%) and VAR (8.8±1.1%) as compared to saline (9.9±4.5%), P<0.05. The apoptotic index was 9.0 ± 3.3% for saline, 1.9 ± 0.9% and 2.4 ± 0.9% for SIL and VAR, respectively. LV end-diastolic and end-systolic diameters increased 7 days post MI with saline. In contrast, no dilatation was detected in SIL and VAR groups. Moreover, fractional shortening (FS) decreased 7 days post MI with saline, but was well preserved with SIL and VAR (Table). Furthermore, survival rate was higher with saline (57%) as compared to SIL (95%) and VAR (100%). **Conclusions:** PDE-5 inhibitors induce powerful cardioprotection in female mice. We propose that PDE-5 inhibition may be a novel therapeutic strategy against IR in women with coronary artery disease.

11:00 a.m.

**1003-44** Transient Overexpression of Human Heme Oxygenase-1 in Transplanted Mesenchymal Stem Cells Results in Enhanced Repair of Myocardial Infarction

Toshinari Tsukobawa, Kunimasa Yagi, Atsushi Nohara, Chiaki Nakanshi, Hatsue Ueda, Noboru Fujino, Masaaki Kawashiri, Hidekazu Iino, Noritoshi Nagaya, Masakazu Yamagishi, Division of Cardiovascular Medicine, Kanazawa University Graduate School of Medicine, kanazawa, Japan, Departments of Regenerative Medicine and Tissue Engineering, National Cardiovascular Center, Osaka, Japan

**Background:** Bone marrow-derived mesenchymal stem cells (MSC) could be of great therapeutic potential after ischemic myocardial injury. However, intolerance and poor cell viability associated with oxidative stress after transplantation has limited the reparative capacity. Under these conditions, Heme Oxygenase-1 (HO-1) plays a pivotal role as antioxidant stress molecule.

**Methods:** Transfer of human HO-1 gene in cultured MSC was performed by lipofection method and expression of HO-1 mRNA was analyzed by RT-PCR. To evaluate the effect of HO-1 overexpression, MSC or MSC/HO-1 were exposed to culture conditions with serum deprivation and hypoxia (SD/hypoxia) over different periods of time and characteristics of cell damage were analyzed by flow cytometry. In vitro, cell viability was determined by MTS assay after exposing MSC or MSC/HO-1 to H2O2 as an oxidative stress, VEGF level in the supernatant of each cells culture after the load of H2O2 were measured by using ELISA. In rat infarction model, MSC (5x106 ±0.4 x106 cells/rat) or MSC/HO-1was injected into the infracted border zone, and cardiac examination was performed on 28th day after cell transplantation. Results: The efficiency of HO-1 gene transfer was about 80%. HO-1 overexpression was observed in MSC and which prevented MSC from SD/hypoxia-induced apoptosis. In addition, MSC/HO-1 as resistant to cell death under condition of oxidative stress (400-500μM H2O2) and secreted a large amount, 2.5-fold more VEGF compared with MSC.Transplantation of MSC/HO-1 attenuated left ventricular remodeling and improved function (% FS: 32.1% (MSC/HO-1 group) V.S. 20.4% (control group), infracted size:
21.1% (MSCHO-1 group) V.S. 36.9% (control group), p < 0.05. Capillary density was markedly increased in the MSCHO-1 group.

Conclusion: The results demonstrate transplantation of MSC with transient overexpression of HO-1 can enhance the reduction of myocardial injury after acute ischemia, probably through suppression of the allogeneic reaction and graft loss in early stages. We suggest the advantage of combined transplantation of cardiac stem cell and MSC in salvaging ischemic myocardial injury.

11:00 a.m.

1003-45 Endogenous Thymosin Increases During Acute Myocardial Ischemia
Atman P. Shat, Niral Beohar, Scott Youngquist, Gary Josephson, John P. Rosborough, James T. Niemann, Harbor-UCLA Medical Center, Torrance, CA

Background: Efforts to promote tissue repair following myocardial infarction through the use of stem cells usually requires isolation and introduction of progenitor cells. Thymosin A1 (TA1) and thymosin B4 (TB4) have been shown to promote cell migration and cell survival after ischemia. The purpose of this study was to determine the time course of TA1 and TB4 appearance during acute myocardial ischemia.

Methods: 15 anesthetized and instrumented domestic swine underwent balloon occlusion of the proximal LAD. LAD occlusion was confirmed angiographically in all animals. During occlusion, venous blood samples were collected from the right atrium at 5 min intervals for 30 min. Plasma levels of TA1, TB4, and MMP-9 (matrix metalloproteinase-9, selected as a marker for remodeling and repair) were measured by ELISA. Changes in concentrations over time were assessed with one way RMANOVA on ranks with Dunnett's test.

Results: Changes in TA1, TB4, and MMP-9 are shown in the figure (median, 25%-75% IQR) from baseline to 30 minutes of occlusion. TA1 and MMP-9 were statistically increased over control at 20 minutes and TB4 was increased over control at 15 minutes (p<0.05).

Conclusion: Endogenous thymosins increase shortly after the onset of myocardial ischemia and increase in parallel to proteases involved in remodeling. The thymosins may represent an endogenous mechanism to recruit undifferentiated stem cells in response to myocardial ischemia.

11:00 a.m.

1003-46 Inhibiting Protease-Activated Receptor 4 Activation Limits Myocardial Ischemia/Reperfusion Injury in Rat Hearts by Unmasking Adenosine Signaling
Jennifer L. Strand, Jidong Su, Xiangping Fu, Anna Hsu, Garrett J. Gross, John E. Baker, Medical College of Wisconsin, Milwaukee, WI

Background: Harnessing endogenous cardioprotectors is a novel therapeutic strategy to combat ischemia/reperfusion (IR) injury. Thrombin causes whereas exogenous adenosine prevents IR injury. We hypothesized that blocking thrombin activation with a Protease-Activated Receptor 4 (PAR4) antagonist would unmask the cardioprotective effects of endogenous adenosine.

Methods/Results: PAR4 mRNA and protein were detected in the rat heart by RT-PCR and immunoblot analysis. We then assessed the potential protective role of two structurally unrelated PAR4 antagonists, tc-Y-NH2 and P4-pal10 in an in vivo and in vitro rat model of myocardial IR injury. P4-pal10 (0.1-100 µg/kg) treatment before ischemia decreased infarct size (IS) by 31% in the in vivo model at an optimal dose of 10 µg/kg. P4-pal10 also significantly decreased IS by 21% and 19% respectively when given after the onset of ischemia or at reperfusion. TC-Y-NH2 (10 µM) treatment immediately before ischemia decreased IS by 51% in the in vitro model and increased recovery in ventricular function by 26% following IR at a optimal concentration of 5 µM. To assess if the cardioprotective effects of PAR4 blockade were due to endogenous adenosine acting on adenosine receptors, isolated hearts were treated with a non-selective adenosine receptor blocker (8-SPT) with tc-Y-NH2 before ischemia. 8-SPT abolished the protective effects of tc-Y-NH2 but did not affect IS when given alone. Survival pathways known to be up-regulated by adenosine were then explored. The cardioprotective effects of tc-Y-NH2 were abolished by inhibition of Akt (wortmannin), ERK1/2 (PD98059), NOS (L-NMA) and KATP channels (glibenclamide). PD98059, L-NMA and glibenclamide alone had no effect on cardioprotection in vitro. Furthermore, inhibition of mitochondrial KATP channels (5H4D) and sarcolemmal KATP channels (HMR 1098) abolished P4-pal10-induced cardioprotection in vivo.

Conclusion: Thrombin receptor blockade by PAR4 inhibition provides protection against injury from myocardial IR by unmasking adenosine receptor signaling and supports the hypothesis of a coupling between thrombin receptors and adenosine receptors which may play a major role in cardioprotection.
1003-51 Injection of an Acellular Matrix Emulsion Enhances Angiogenesis and Improves Cardiac Function by Mobilizing Bone Marrow C-kit Cells after Ischemia and Reperfusion

Zhi-Qing Zhao, John D. Puskas, Di Xu, Ning-Ping Wang, Robert A. Guyton, Jakob Vinten-Johansen, Robert Matheny, Emory University, Atlanta, GA

Background: Recruitment of bone marrow-derived c-kit cells has been associated with tissue angiogenesis and repair after myocardial infarction. The purpose of this study was to test the hypothesis that injection of an acellular extracellular matrix emulsion in ischemic myocardium enhances angiogenesis and preserves cardiac function by mobilizing bone marrow c-kit cells. Methods: Thirty six rats were subjected to 45 minutes coronary occlusion followed by 3, 7 and 21 days of reperfusion with and without emulsion injection, respectively. Histological examination was performed by immunohistochemical staining and cardiac function was analyzed using echocardiography. Results: Emulsion (50 µl) was injected into the area at risk myocardium after reperfusion and localization of emulsion was confirmed with Masson’s trichrome staining. At 21 days after reperfusion, the population of c-kit positive cells in the bordering emulsion area and within emulsion area increased to a significant extent relative to the Control (32±0.6* vs. 15±3/1000 nuclei). Along with this change, strong immunoreactivity of VEGF with emulsion injection was detected in emulsion area. Angiogenesis in emulsion area was significantly enhanced relative to the Control, evidenced by increased density value of α-SMA-positive vessels (70±10* vs. 20±4/HPF) and WVF-positive vessels (95±14* vs. 34±8/HPF), respectively. Echocardiography showed improvements with emulsion in end-systolic volume (0.3±0.1* vs. 0.6±0.3 ml), fractional shortening (33±5* vs. 24±6%) and ejection fraction (67±6* vs. 53±10%). The wall thickness of the infarcted middle anterior septum with emulsion was also significantly greater than that in the Control (0.19±0.02* vs. 0.15±0.02cm).

Conclusion: Intramyocardial injection of acellular matrix emulsion into the ischemic/ reperfused myocardium enhances tissue angiogenesis and preserves cardiac function by recruiting bone marrow c-kit positive cells. *p<0.05 Emulsion vs. Control.

11:00 a.m.

1003-52 Pregnancy-associated plasma protein-A in cardiac and non-cardiac patients

Kasper Iversen, Ane Teisner, Borge Teisner, Peer Grande, Peter Clemmensen, Rigshospitalet, Copenhagen, Denmark, The London Bridge Fertility, Gynaecology and Genetics Centre, London, United Kingdom

Background: Pregnancy-associated plasma protein-A (PAPP-A) is a new biomarker in acute coronary syndromes that detect vulnerable plaques and potentially points out high-risk patients. Large studies of serial measurements of PAPP-A in patients with acute coronary syndromes are needed, so we assessed the levels of PAPP-A in a large patient cohort with acute coronary syndromes and compared it to healthy individuals and patients admitted with non-cardiac disease.

Methods: Serial measurements (1-5 samples) of PAPP-A were performed in 354 patients with ST-elevation myocardial infarction, 123 patients with non ST-elevation myocardial infarction and 415 patients with low-risk acute coronary syndromes. Single measurement of PAPP-A was performed in 1448 patients with non-cardiac disease and in 100 healthy volunteers. PAPP-A was analysed with a novel ELISA technique with a detection limit of 4.0 muL.

Results: Considering the PAPP-A value from each patient, 91% of patients with acute coronary syndromes were found to have significantly elevated PAPP-A levels relative to the Control, evidenced by increased density value of α-SMA-positive vessels (70±10* vs. 20±4/HPF) and WVF-positive vessels (95±14* vs. 34±8/HPF), respectively. Echocardiography showed improvements with emulsion in end-systolic volume (0.3±0.1* vs. 0.6±0.3 ml), fractional shortening (33±5* vs. 24±6%) and ejection fraction (67±6* vs. 53±10%). The wall thickness of the infarcted middle anterior septum with emulsion was also significantly greater than that in the Control (0.19±0.02* vs. 0.15±0.02cm).

Conclusion: In patients with low-risk acute coronary syndrome, 19% of patients with non-cardiac disease and 1% of healthy volunteers had detectable PAPP-A, 74% of patients with low-risk acute coronary syndrome, 123 patients with non ST-elevation myocardial infarction, 123 patients with non ST-elevation myocardial infarction and 415 patients with low-risk acute coronary syndromes. Single measurement of PAPP-A was performed in 1448 patients with non-cardiac disease and in 100 healthy volunteers. PAPP-A was analysed with a novel ELISA technique with a detection limit of 4.0 muL.

Results: Considering the PAPP-A value from each patient, 91% of patients with acute coronary syndromes were found to have significantly elevated PAPP-A levels relative to the Control, evidenced by increased density value of α-SMA-positive vessels (70±10* vs. 20±4/HPF) and WVF-positive vessels (95±14* vs. 34±8/HPF), respectively. Echocardiography showed improvements with emulsion in end-systolic volume (0.3±0.1* vs. 0.6±0.3 ml), fractional shortening (33±5* vs. 24±6%) and ejection fraction (67±6* vs. 53±10%). The wall thickness of the infarcted middle anterior septum with emulsion was also significantly greater than that in the Control (0.19±0.02* vs. 0.15±0.02cm).

Conclusion: PAPP-A is elevated across the entire spectrum of acute coronary syndromes and considerably higher than in patients with non-cardiac disease. PAPP-A is promising as a marker of the unstable plaque in coronary disease.
Postconditioning Markedly Reduces Reperfusion-Induced Ventricular Arrhythmias - Even in the Senescent Heart

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

Background: Studies suggest that in elderly populations, the cardioprotective effects of ischemic preconditioning are lost. Previously we observed that ischemic postconditioning markedly reduced reperfusion-induced ventricular arrhythmias in young adult rats. Whether postconditioning's benefit is lost in senescent hearts is unknown. Therefore, the purpose of this study was to determine if postconditioning's beneficial effect on ventricular arrhythmias is maintained in elderly hearts. Methods: Young adult rats (3 to 4 months old) or old rats (24 to 25 months old) were randomized to four groups: Young adult control, young adult postconditioning, old control, and old postconditioning. Young control (n = 11) and old control (n = 8) groups received 5 minutes of left coronary artery occlusion followed by 5 minutes of reperfusion while young postconditioning (n = 11) and old postconditioning (n = 10) were subjected to 5 minutes of occlusion; but then postconditioning regimen of 4 cycles of 20 seconds of reperfusion/20 seconds of reoxygenation prior to sustained 5 minutes of reperfusion. Results: Postconditioning reduced the number of young rats that developed reperfusion-induced ventricular tachycardia (VT); (4 in young postconditioning compared to >5 in young control). The number of episodes of VT (4.8 ± 3.1 vs. 11.6 ± 1.3; p = 0.01); the number of rats with sustained VT ≥ 10 sec (2 vs. 11; p = 0.0002); and the % of time during reperfusion spent in VT (2.7 ± 1.8% vs. 18.9 ± 4.0%; p = 0.002). In old rats postconditioning also reduced the number of rats that developed VT (4 in old postconditioning vs. 8 in old control; p = 0.01); the number of episodes of VT (1.3 ± 0.7 vs. 7.0 ± 2.3; p = 0.01); the number of rats with sustained VT (0 vs. 4; p = 0.02); and the % time during reperfusion spent in VT (0.33% ± 0.15% vs. 3.8 ± 1.3%; p = 0.03). Conclusions: Thus although overall amount of VT was less in old vs. young adults, postconditioning significantly improved LV function as associated with suppression of myocardial and plasma TNF-α, IL-6, and IL-1 β-induced ischemic left ventricular (LV) dysfunction by placing ameroid constrictors around the proximal left anterior descending coronary artery for 4 weeks. Our results suggest that myocytes or cells in the extracellular matrix may play an important role in perpetuating the inflammatory state of IC.

11:00 a.m.

Effect of Beta-blockade on Regional Function and Myocardial Cytokine Levels in Chronic Ischemic Cardiomyopathy: An Experimental Evaluation

Dae Tae Lee, Marco Pascotto, Ibrahim Sari, Thanjavur Bragadeesh, Antonio Micari, Henny Singo, Sanjiv Kaul, OHSU, Portland, OR

Background: The mechanisms of the beneficial effects of β-blockers in ischemic cardiomyopathy (IC) have not been fully elucidated. We hypothesized that the beneficial effects of β-blockers in IC are related to their anti-inflammatory properties. Methods: We induced ischemic left ventricular (LV) dysfunction by placing ameroid constrictors around the proximal left anterior descending coronary arteries in 11 rats (n = 11) and 22 dogs (n = 22). Microarrays were placed in the LV myocardium for interstitial fluid collection for myocardial cytokine measurement. After LV dysfunction developed, the dogs were randomized to 3 groups: placebo (n = 8); metoprolol (n = 11); and carvedilol (n = 10). Percent wall thickening (%WT) and myocardial and plasma TNF-α, IL-1 β, and IL-6 levels were measured at baseline and 1, 2, and 3 months after initiation of drug therapy.

WT (%) Baseline 1 month 2 months 3 months
Placebo 22.5 ± 8.0 21.9 ± 6.0 23.3 ± 5.2 22.1 ± 5.4
Metoprolol 27.3 ± 6.3* 25.7 ± 4.4* 27.7 ± 4.9* 28.4 ± 5.9*
Carvedilol 24.4 ± 6.4 25.6 ± 5.2 31.0 ± 5.8* 32.0 ± 5.9*

TNF-α (pg/mL)
Placebo 38.6 ± 39.5 50.6 ± 44.5 70.1 ± 38.9 62.0 ± 28.4
Metoprolol 53.3 ± 21.9 75.7 ± 35.5 70.0 ± 20.5 53.1 ± 24.3
Carvedilol 60.3 ± 35.2 47.6 ± 23.4* 66.1 ± 33.1 50.4 ± 8.8

IL-6 (pg/mL)
Placebo 3.48 ± 0.30 0.67 ± 0.25 3.59 ± 0.25 3.59 ± 0.27
Metoprolol 3.33 ± 0.16 0.39 ± 0.17 3.7 ± 0.18* 0.28 ± 0.19
Carvedilol 3.34 ± 0.12 0.39 ± 0.15 2.42 ± 0.15 0.42 ± 0.24

IL-1 β (pg/mL)
Placebo 60.0 ± 12.0 81.3 ± 15.8 81.6 ± 15.7 60.9 ± 6.0
Metoprolol 50.1 ± 15.0 44.1 ± 11.4 51.0 ± 16.7 50.4 ± 8.8
Carvedilol 52.7 ± 12.7 57.1 ± 9.6 50.1 ± 13.6 47.5 ± 3.5* p < 0.05 vs. Placebo; tp < 0.01 vs. Placebo; t p < 0.05 vs Metoprolol

Results: There was no difference in %WT and myocardial cytokine levels prior to drug therapy. At 1, 2, and 3 months after treatment, %WT improved in dogs receiving β-blockers compared with placebo, which was associated with a decrease in myocardial TNF-α, IL-6, and IL-1 β cytokine levels. Metoprolol improved LV function and reduced myocardial and plasma TNF-α, IL-6, and IL-1 β-induced ischemic left ventricular dysfunction by placing ameroid constrictors around the proximal left anterior descending coronary artery for 4 weeks. Our results suggest that myocytes or cells in the extracellular matrix may play an important role in perpetuating the inflammatory state of IC.

11:00 a.m.

Link Gene Deficiency Contributes to Cardiac Repair Post Myocardial Infarction by Equivalently Enhancing Regenerative Capacity of BM-derived Progenitor Cells and Resident Cardiac Stem/Progenitor Cells

Hiroto Iwasaki, Miki Horii, Sang Mo Kwon, Atsuhiko Kawamoto, Akira Oyamada, Ayumi Yokoyama, Hirogi Nishimura, Masaaki Ii, Takayuki Asahara, Kobe Institute of Biomedical Research and Innovation / RIKEN Center for Developmental Biology, Kobe, Japan

Background: Lnk is a negative regulator of self-renewal capacity of hematopoietic stem cells (HSCs). We have previously reported that gene deficiency of Lnk augments cardiac myangiogenesis post myocardial infarction (MI) via enhancing proliferation of both bone marrow (BM)-derived progenitor cells (BMPCs) and resident cardiac stem/progenitor cells (CSPCs). However, proportional contribution of each cell population to cardiac repair remains unknown.

Methods and Results: The c-kit+/ lineage- BMPCs isolated from Lnk -/- mice (KO) or wild type mice underwent transplantation into irradiated Lnk -/- mice or WT mice. Four weeks after BM transplantation, the echocardiograph and histologic analysis revealed significant preservation of LV function in Lnk -/- mice undergoing BM transplantation into Lnk -/- mice (KO) than all other groups, while in Lnk -/- mice receiving WT BM (WT->KO) and WT mice receiving Lnk -/- BM (KO->WT) than WT mice receiving WT BM (WT->WT) (1) Fractional shortening: WT->WT, 20.8±1.7; WT->KO, 31.8±0.5; KO->WT, 35.3±1.1; KO, 35.9±1.7%; p<0.05, (2) Regional wall motion score: WT->WT, 26.0±0.4; WT->KO, 20.3±0.7; WT, 20.3±0.6; KO, 18.4±0.4, p<0.05, (3) %P/D: WT->WT, 6508±604; WT->KO, 8783±444; WT, 10015±414; KO, 11278±358 mmHg/sec, p<0.05. Necropsy examination disclosed significant augmentation of myocardial density in KO mice than WT mice or KO->KO mice, while in KO->WT or WT mice than WT mice (WT->WT, 6516±176; WT->KO, 9411±176; KO, 10363±73; KO, 11231±177 mm2, P<0.05) and inhibition of LV fibrosis area in KO->KO mice than all other groups, while in WT->KO or KO->WT mice than WT mice (WT->WT, 20.1±2.2; WT->KO, 9.5±5.0; KO->WT, 9.1±3.7; KO, 5±4.2%, P<0.05). All parameters in WT->KO mice were similar as those in KO->KO mice. Conclusions: In Lnk deficient mice, BM-derived BMPCs and resident CSPCs equivalently contributed to cardiac repair in MI. Both BM and heart would be considered as the target organ/tissue of the novel therapeutic modality for cardiac regeneration.
Human Amniotic Membrane-derived Mesenchymal Stem Cell Acquired Immune Tolerance by HLA-G Expression and Differentiated into Cardiomyocyte in vivo

Hiroko Tsuji, Yukinori Ikegami, Shinichiro Miyoshi, Naoko Hida, Nobuhito Nishiya, Ikuko Togashi, Hikaru Nakamizo, Hiroshi Asada, Taro Uyama, Mamoru Tanaka, Kazu Segawa, Junko Inoue, Kazuhiro Minegishi, Hitoshi Ishimoto, Satoshi Ogawa, Yasunori Yoshimura, Akhiro Umezawa, Keio University school of Medicine, Tokyo, Japan, National Research Institute for Child Health and Development, Tokyo, Japan

Background: We have previously reported that human amniotic membrane-derived mesenchymal stem cell (HMAC) had a potential of “working” cardiogenic transdifferentiation in vitro (68%). In the present study, we aim to show the induction of immune tolerance by transplanted HMAC and survival of transdifferentiated cardiomyocyte from HMAC in vivo.

Methods & Results: Flowcytometric surface marker analysis revealed that HMAC was negative for HLA-DR and weakly positive for HLA-A, B, and C. Marked expression of HLA-G in vitro was shown by Western blot analysis. EGFP-labeled HMACs (approximately 200,000) were transplanted into the border zone of infarcted heart of wistar rat (xenograft), and immunohistochimical analysis was performed to determine the survival of EGFP-positive transdifferentiated cardiomyocytes. Six weeks after the transplantation, many rod-like and EGFP-positive transdifferentiated cardiomyocytes with clear striation of sarcomeric α-actinin (Fig) and cardiac troponin I (>2,000) were survived. Enzyme-linked immunoassay of sera revealed that 4 of 24 rats transplanted with HMACs were positive for soluble HLA-G.

Conclusions: Since HLA-G has been known to suppress natural killer cell-mediated graft rejection, the transplanted HMACs which transdifferentiated into cardiomyocytes in vivo might acquire immune tolerance by HLA-G expression. In allotransplantation, HMAC can be a promising cell source for cardiac stem cell therapy because of the absence of immune response to HMAC.

Decreased Parasympathetic Tone Worsens Left Ventricular Remodeling Following Myocardial Infarction

Xiaorong Zhou, Mazen Khalil, Kwangdeok Lee, Kai Wang, Marc S. Penn, Cleveland Clinic, Cleveland, OH

It has been demonstrated that the effluent nerve inhibits pro-inflammatory cytokine release and protects against systemic inflammation. The inflammatory response following MI impacts left ventricular remodeling and ultimately cardiac function. In this study we tested the effects of parasympathetic tone on left ventricular remodeling. We hypothesized that unilateral vagotomy would worsen left ventricular remodeling after MI. Methods and results: C57BL/6J wild type mice at age 8 weeks underwent sham surgery or left unilateral cervical vagotomy. After one month the animals from both groups underwent left coronary artery ligation. Animals were sacrificed at 3, 21 days after MI. The echocardiography was performed before vagotomy, after vagotomy (the day before AMI), and at day 3, 21 days after AMI. H&E and Mason's trichrome staining were performed to evaluate cellular infiltrate and collagen deposition. One month after unilateral vagotomy there were no differences in cardiac function or dimensions compared to sham operated animals (EF: 75.0±8.89 vs 76.1±0.03, P=NS). Similarly, unilateral vagotomy had no effect on ejection fraction (EF) 3 days after AMI (50.0±22.00 vs 56.0±21.21, P<0.05). There was a significant increase in myocardial inflammatory response following MI in vagotomized animals compared to sham operated animals (41.00±14.99 vs 56.00±21.21, P<0.05). There was a significant increase in collagen deposition and decreased cardiac function. These data suggest that parasympathetic tone at baseline significantly impacts ventricular remodeling and suggests a potential mechanism for the poorer outcomes observed in patients with a history of MI and evidence of decreased parasympathetic tone.

Ranolazine’s Mechanism of Action for Reducing Myocardial Infarct Size is Independent of Changes in Coronary Collateral Blood Flow

Sharon L. Hale, Robert A. Kloner, Heart Institute, Good Samaritan Hospital, Los Angeles, CA, Keck School of Medicine, University of Southern California, Los Angeles, CA

Background: The antianginal drug ranolazine is a selective inhibitor of the late sodium current relative to peak sodium channel current, and via this mechanism may decrease sodium-dependent intracellular calcium overload during ischemia and reperfusion. It has been suggested that one mechanism by which ranolazine protects the ischemic/ reperfused heart is by reducing intracardiac diastolic pressure during ischemia, which decreases capillary compression and thereby improves perfusion. The goal of this study was to test whether ranolazine causes changes in regional myocardial blood flow (RMBF) during ischemia and/or reperfusion in a myocardial occlusion model. Methods: Ten minutes before coronary artery occlusion (CAO), anesthetized rabbits were assigned to vehicle (n=13) or ranolazine (2 mg/kg I.V. bolus plus 60 µg/kg/min I.V. infusion, n=14). Hearts received 60 minutes of CAO and 3 hours reperfusion. RMBF was measured with radioactive microspheres, risk zone with blue dye and necrosis by tetrazolium staining. Results: Ischemic risk zone was comparable in the two groups (28±2% of the left ventricle in ranolazine group and 26±2% in the vehicle group, p=NS). Ranolazine reduced infarct size (46±4% vs risk zone versus 60±5% vehicle, P<0.03). However, RMBF was similar in both groups in the risk zone during ischemia (0.1±0.08 ml/min/g ranolazine and 0.1±0.06 ml/min/g vehicle, p=NS) and at 3 hours reperfusion (0.2±0.06 ml/min/g ranolazine and 0.3±0.03 ml/min/g vehicle). Body temperatures and rate-pressure products were similar in both groups. Conclusions: Ranolazine was effective in reducing myocardial infarct size by 23%. The mechanism by which it did this was independent of improving regional blood flow during ischemia or reperfusion, and unrelated to changes in the rate-pressure product. Therefore, it is likely that ranolazine’s protective effect involves a direct cellular mechanism.

Predictors of Sudden Cardiac Death Change With Time After Myocardial Infarction: Results From the VALIANT Trial

Jonathan P. Piccini, Karen S. Pape, Scott D. Solomon, Sana Al-Khatib, Frans Van de Werf, Marc A. Pfeffer, John J.V. McMurray, Robert B. Califf, Eric J. Velazquez, Duke Clinical Research Institute, Duke University Medical Center, Durham, NC

Background. The risk of sudden cardiac death (SCD) changes with time following myocardial infarction (MI). Little is known about whether predictors of SCD also vary with time after MI.

Methods. The VALIANT in Acute myocardial Infarction trial (VALIANT) enrolled 14,703 patients with acute MI, complicated by heart failure (HF), left ventricular (LV) dysfunction, or both. Landmark analysis and Cox proportional hazards modeling were used to predict SCD (CVD; and resuscitated SCD) during the initial hospitalization, from discharge to 30 days, 30 days to 6 months, and 6 months to 3 years.

Results. The cumulative incidence of SCD was 7.3% (n=1046). Reduced creatinine clearance (CrCl), hypotension, and tachycardia were strong predictors of SCD prior to discharge and in the first 30 days after MI (Table). While tachycardia and reduced CrCl remained predictors of SCD up to 3 years after MI, recurrent HF, diabetes, and a history of MI prior to enrollment were strong predictors of later events. Interestingly, quantitative evidence of LV dysfunction was not a significant predictor until after 30 days of follow-up and, even then, was less predictive than several other clinical variables. Conclusion. Both the incidence and predictors of SCD change with time after MI. Initially, indices of hemodynamic instability are strong predictors of SCD, however, with continued follow-up, prior MI, and clinical HF are more robust risk stratifiers.
Outcomes After Pimecrolimus-Elution From a Durable Polymer on a Stainless Steel Stent. First-in-Human Study Discordance With Preclinical Studies

John A. Ormiston, Mark W. Webster, Patrick Gladding, James T. Stewart, Peter N. Ruygrok, Robert Hattrick, Patrick Kay, Auckland City Hospital, Auckland, New Zealand

Background: Pimecrolimus has multiple anti-inflammatory effects, but does not bind to mTOR, and therefore does not directly affect cell cycle regulation. It may limit restenosis by reducing TGF-β, and therefore does not directly affect cell cycle regulation. It may limit restenosis by reducing TGF-β, and therefore does not directly affect cell cycle regulation.

Conclusions: Diabetic myocardium retains the ability to resist the effects of repetitive ischemia and reperfusion, 2) augmented glucose metabolism and glycogen deposition to 6th CS (-28±9% and -17±4%, respectively). Both groups showed no further decrease to treatment with culture-expanded non-modified MSC to improve cardiac contractility, regional systolic function, myocardial viability and vascularity after healed MI.

Conclusions: If this were the case, mTor could recapitulate the phenotype of MH, i.e., reduced but stable regional dysfunction and regional systolic function, myocardial viability and vascularity after healed MI.

To assess cardiac function, remodelling and viability before therapy (Baseline), and 9 and 16 weeks after cell injections. The echocardiographic wall motion score (WMS) index was used to assess the regional systolic function.

Results: Plasma glucose was elevated in STZ group, compared to CON group (489±87 vs. 100±3 mg/dl, p=0.01). MGE was increased 2-fold in CON group during 1st CS (and remained at 2nd CS), whereas MGE was not affected by stunning protocol in STZ group; glycogen deposition was prominent in CON group but negligible in STZ group. Nevertheless, the decreases in WT in CON and STZ groups during 1st CS were similar (-46±10 vs. -50±5, respectively), as were those just prior to 6th CS (-54±4 vs. -37±3, respectively). Both groups showed no further decrease in WT during 6th CS. Expression of cell survival proteins [X-linked inhibitor of apoptosis protein (XIAP) and heat-shock protein 70 (Hsp70)] was 2-fold increased in hibernating myocardium from both groups.

Conclusions: Diabetes mellitus retains the ability to resist the effects of repetitive ischemia and reperfusion, 2) augmented glucose metabolism and glycogen deposition are not essential for myocardial hibernation; and 3) upregulation of survival proteins may play a critical role in the development of this state.

Myocardial Ischemia and Infarction

Myocardial Hibernation in the Absence of Augmented Glucose Metabolism in Diabetic Hearts

Joanne B. Gonzalez, Shamal Kou, Alice Chen, Zbigniew Malecki, George J. Crystal, Song-Jun Kim, Advocate Illinois Masonic Medical Center, Chicago, IL

Background: Myocardial hibernation (MH) is a state of persistent regional ventricular dysfunction in patients with coronary artery disease which is reversible with revascularization. In our previous study, a porcine model of persistent stunning was used to recapitulate the phenotype of MH, i.e., reduced but stable regional functional parameters and glycogen deposition. It has been proposed that a shift to glucose metabolism is integral to achieve protection against ischemia in hibernating myocardium. If this were the case, diabetic hearts would be expected to have an impaired ability to hibernate.

Methods: Ten swine were divided into control (CON; n=5) and streptozotocin (STZ)-treated (100 mg/kg, n=5) groups. The animals were chronically instrumented to measure coronary blood flow (CBF) and regional wall thickening (WT); catheters were implanted in the aorta and coronary sinus to calculate myocardial glucose extraction (MGE). Persistent myocardial stunning leading to hibernation was induced by six repetitive episodes of 90-min coronary stenosis (CS) (30% reduction in baseline CBF) followed by full reperfusion every 12 hrs.

Results: Plasma glucose was elevated in STZ group, compared to CON group (489±87 vs. 100±3 mg/dl, p=0.01). MGE was increased 2-fold in CON group during 1st CS (and remained at 2nd CS), whereas MGE was not affected by stunning protocol in STZ group; glycogen deposition was prominent in CON group but negligible in STZ group. Nevertheless, the decreases in WT in CON and STZ groups during 1st CS were similar (-46±10 vs. -50±5, respectively), as were those just prior to 6th CS (-54±4 vs. -37±3, respectively). Both groups showed no further decrease in WT during 6th CS. Expression of cell survival proteins [X-linked inhibitor of apoptosis protein (XIAP) and heat-shock protein 70 (Hsp70)] was 2-fold increased in hibernating myocardium from both groups.

Conclusions: Diabetes mellitus retains the ability to resist the effects of repetitive ischemia and reperfusion, 2) augmented glucose metabolism and glycogen deposition are not essential for myocardial hibernation; and 3) upregulation of survival proteins may play a critical role in the development of this state.

Myelosuppressives Improve Cardiac Dysfunction After Myocardial Infarction by Activating Cell Survival Signaling, Mobilizing CD34 Positive Cells and attenuating Fibrosis and Apoptosis

Hiroshi Uchikoshi, Yu Misao, Takamasa Ohno, Yiseon Li, Ngin Cin Khai, Genzou Takemura, Takaharu Fujisawa, Hisayoshi Fujisawa, Shinya Minatoguchi, Gifu University Graduate School of Medicine, Gifu, Japan, Kyoto Women’s University, Kyoto, Japan

Background: Leukocytosis is a well-known effect of myocardial infarction (MI). Recently we reported that myelosuppressives improve left ventricular (LV) function following reperfusion-induced MI. However, the role of myelosuppressives in permanently occluded large MI remains unknown. Here we aimed to elucidate the beneficial effects of 5-fluorouracil (5FU) and cyclophosphamide (Cy) using a murine model. Methods: In 11:00 a.m.

Myocardial Ischemia and Infarction

Functional Improvement After Bone Marrow-Derived Mononuclear Versus Nonmodified Mesenchymal Stem Cell Therapy in Chronic Myocardial Infarction


Background: Stem cell therapy may facilitate cardiac repair after myocardial infarction (MI) but the optimal cell type remains discussed. The present study was designed as a randomized, investigator-blinded, placebo controlled head-to-head comparison of autologous bone-marrow mononuclear cells (BMNC) and nonmodified mesenchymal stem cells (MSC) in a large animal model of chronic MI. Methods: Twenty-four dogs underwent the ligation of the left coronary artery. Eleven weeks later, they received intramyocardial injections of either placebo (n = 8), BMNC (227±10 x 32±10 cells, n = 8) or culture expanded nonmodified-MSC (232±10 x 40±10 cells, n = 8). Echocardiography, magnetic resonance imaging (MRI), conductance catheter and histopathology were used to assess cardiac function, remodelling and viability before therapy (Baseline), and 9 and 16 weeks after cell injections. The echocardiographic wall motion score (WMS) index was used to assess the regional systolic function.

Results: While left ventricular ejection fraction remained unchanged, the WMS index showed a sustained improvement in the BMNC group (from 1.8±0.1 at baseline to 1.6±0.07 at 16 weeks, both p<0.001). In the MSC group, the WMS index improved moderately at late follow-up (from 1.9±0.8 at baseline to 1.7±0.1 at 16 weeks p<0.05). End systolic elastance increased only in the BMNC transfer (from 2.23±0.25 mmHg/ml to 4.42±0.55 mmHg/ml at 9 weeks, p<0.001). This was associated with a reduction in the MRS infarct size (from 13.6±6.7% at baseline to 10.0±1.17% at 16 weeks p<0.05) and an increased semi-quantitative arterial density in the infarct zone as compared to MSC group (p<0.01). No changes in contractility and infarct size were noted in the control group. Conclusions: In the canine model of chronic MI, stem cell therapy with BMNC appears to be superior to treatment with culture-expanded non-modified MSC to improve cardiac contractility, regional systolic function, myocardial viability and vascularisation after healed MI.

Myelosuppressives Improve Cardiac Dysfunction After Myocardial Infarction by Activating Cell Survival Signaling, Mobilizing CD34 Positive Cells and attenuating Fibrosis and Apoptosis

Hiroshi Uchikoshi, Yu Misao, Takamasa Ohno, Yiseon Li, Ngin Cin Khai, Genzou Takemura, Takaharu Fujisawa, Hisayoshi Fujisawa, Shinya Minatoguchi, Gifu University Graduate School of Medicine, Gifu, Japan, Kyoto Women’s University, Kyoto, Japan

Background: Leukocytosis is a well-known effect of myocardial infarction (MI). Recently we reported that myelosuppressives improve left ventricular (LV) function following reperfusion-induced MI. However, the role of myelosuppressives in permanently occluded large MI remains unknown. Here we aimed to elucidate the beneficial effects of 5-fluorouracil (5FU) and cyclophosphamide (Cy) using a murine model. Methods: 11:00 a.m.
Myocardial Ischemia and Infarction

A184
ABSTRACTS - Myocardial Ischemia and Infarction
March 11, 2008

vitrin. Primary cultured ventricular cardiomyocytes and cardiac fibroblasts were incubated in the presence or absence of 5FU and Cy, and cell growth was evaluated. (2) In vitro. An in vitro model was created by permanent coronary ligation. On the next day after MI, 5FU (100 mpg/kg), Cy (50mg/kg) or saline (control, C), were injected intraperitoneally. Cardiac function, histological changes, cell signaling and apoptosis were evaluated. To detect circulating CD34+ cells, FACS analysis was performed. Results: (1) 5FU and Cy induced cardiac fibroblast proliferation in a dose-dependent manner in vitro. (2) 5FU and Cy increased amplified peripheral CD34+ cells (5FU: 30.5 ± 5.5 µl, Cy: 21.8 ± 6.4 µl vs. C: 11.2 ± 6.1 µl, p < 0.05). Myelosuppressors also reduced the area of MI (5FU: 27.9 ± 4.3 %, Cy: 30.4 ± 5.3 % vs. C: 39.6 ± 8.6 %, p < 0.05) at one week after MI and improved cardiac function (LV EF: 42.9 ± 6.4 %, Cy: 38.9 ± 6.9 % vs. C: 28.2 ± 6.2 %, p < 0.05). Heart weight (p < 0.01) also decreased four weeks after MI. Histological findings showed an enhancement of angiogenesis at the border zone (by capillary density, p < 0.01), a decreased fibrosis area (p < 0.05) in 5FU treated hearts, and decreased Ki-67/TUNEL positive cells in both groups (5FU: 1.8 ± 1.0 %, Cy: 0.8 % vs. C: 4.4 ± 1.1 %, p < 0.01). Finally, immunoblotting revealed upregulated SDF1-1/CXCR4 axis, ANP, Bcl2 and activated Akt, indicating enhanced survival signaling in the treated hearts. Conclusions: Uptake of cell survival signaling, mobilization of CD34+ cells and attenuation of fibrosis and apoptosis may play important roles in the beneficial effects caused by myelosuppressives in acute-MI. These findings suggest that myelosuppressives are good candidates for protective therapy of the post-MI heart.

A184-66
Impaired Glucose Tolerance Is Associated With Endothelial Damage Following Acute Myocardial Infarction
Shahroos S. Jessani, Veerle J. Karthikeyan, Teri Millane, Gregory YH Lip, University department of medicine, City hospital, Birmingham, United Kingdom, Department of medicine, Basilion, United Kingdom

Background: Impaired glucose tolerance (IGT) post acute myocardial infarction (AMI) is largely ignored despite evidence of poorer clinical outcome. We hypothesized that endothelial damage following AMI, measured by a rise in von Willebrand factor (VWF), would be more pronounced in patients with IGT compared to those with normal glucose tolerance (NGT).

Method: Consecutive non-diabetic patients with AMI underwent oral glucose tolerance test (OGTT). VWF levels were measured by enzyme linked immunosorbent assay (ELISA).

Results: 125 patients [mean (SD) age 59 (12.5) yrs; 107 (86%) male] were studied. Baseline mean vWF levels were higher in IGT patients versus those with NGT (p < 0.001) (Table 1). The response of vWF levels in response to oral glucose tolerance test correlated with the change in plasma glucose levels (Spearman’s, r = 0.302, p < 0.001).

Conclusion: IGT post AMI is associated with significant endothelial damage when compared with NGT. Further endothelial damage appears to occur in response to a rise in plasma glucose levels. Interestingly, the degree of endothelial damage in subjects with IGT appears comparable to that observed in frank diabetes. IGT is not currently actively sought in this population, let alone treated - a change in clinical practice is warranted.

Parameters at baseline and 2 hours following OGTT

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline (PI)</th>
<th>2 hours following OGTT (n = 52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VWF (IU/mL)</td>
<td>169 ± 9 (5)</td>
<td>239 ± 17 (5)enas</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>89 ± 8 (5)</td>
<td>128 ± 9 (5)</td>
</tr>
<tr>
<td>Insulin (mU/l)</td>
<td>4.7 ± 1.7 (5)</td>
<td>7.8 ± 1.7 (5)</td>
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<tr>
<td>HDL (mg/dl)</td>
<td>43 ± 10 (5)</td>
<td>41 ± 10 (5)</td>
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<tr>
<td>LDL (mg/dl)</td>
<td>136 ± 23 (5)</td>
<td>134 ± 23 (5)</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>150 ± 41 (5)</td>
<td>150 ± 41 (5)</td>
</tr>
</tbody>
</table>

* Significantly higher (p < 0.001) compared to NGT.

A184-67
Fibroblast Growth Factor Promotes the Proliferation of Bone-Marrow Mesenchymal Stem Cells Through the Activation of the PI3K/Akt and ERK1/2 Signaling Pathways
Seung-Cheol Choi, Su-Jin Kim, Ji-Hyun Choi, Chi-Yeon Park, Wan-Joo Shim, Do-Sun Kim, Shahirose S. Jessani, Vellore J. Karthikeyan, Teri Millane, Gregory YH Lip, University department of medicine, City hospital, Birmingham, United Kingdom, Department of medicine, Basilion, United Kingdom

The purpose of this study is to identify the factors and signaling pathways involved in the self-renewal, differentiation into a variety of cell types including cardiac and endothelial cells of Sca-1+ BMMSCs. We sought in this population, let alone treated - a change in clinical practice is warranted. In the presence or absence of 5FU and Cy, and cell growth was evaluated. (2) In vitro. An in vitro model was created by permanent coronary ligation. On the next day after MI, 5FU (100 mpg/kg), Cy (50mg/kg) or saline (control, C), were injected intraperitoneally. Cardiac function, histological changes, cell signaling and apoptosis were evaluated. To detect circulating CD34+ cells, FACS analysis was performed. Cardiac function, histological changes, cell signaling and apoptosis were evaluated. To detect circulating CD34+ cells, FACS analysis was performed. Results: (1) 5FU and Cy induced cardiac fibroblast proliferation in a dose-dependent manner in vitro. (2) 5FU and Cy increased amplified peripheral CD34+ cells (5FU: 30.5 ± 5.5 µl, Cy: 21.8 ± 6.4 µl vs. C: 11.2 ± 6.1 µl, p < 0.05). Myelosuppressors also reduced the area of MI (5FU: 27.9 ± 4.3 %, Cy: 30.4 ± 5.3 % vs. C: 39.6 ± 8.6 %, p < 0.05) at one week after MI and improved cardiac function (LV EF: 42.9 ± 6.4 %, Cy: 38.9 ± 6.9 % vs. C: 28.2 ± 6.2 %, p < 0.05). Heart weight (p < 0.01) also decreased four weeks after MI. Histological findings showed an enhancement of angiogenesis at the border zone (by capillary density, p < 0.01), a decreased fibrosis area (p < 0.05) in 5FU treated hearts, and decreased Ki-67/TUNEL positive cells in both groups (5FU: 1.8 ± 1.0 %, Cy: 0.8 % vs. C: 4.4 ± 1.1 %, p < 0.01). Finally, immunoblotting revealed upregulated SDF1-1/CXCR4 axis, ANP, Bcl2 and activated Akt, indicating enhanced survival signaling in the treated hearts. Conclusions: Uptake of cell survival signaling, mobilization of CD34+ cells and attenuation of fibrosis and apoptosis may play important roles in the beneficial effects caused by myelosuppressives in acute-MI. These findings suggest that myelosuppressives are good candidates for protective therapy of the post-MI heart.
of EDL (0.1 ± 0.2 mm) and ESL (0.3 ± 0.3 mm), the reduction in FS (Figure A), and
(c) myocardial akinesia (0/7) and systolic bulging (0/7). RMFB for ischemic region was
significantly improved by Ran at 8 μM (Figure B).

Conclusion: Ran prevents ischemia induced myocardial electrical and mechanical
dysfunction, and improves blood supply to the ischemia region.

**ABSTRACTS - Myocardial Ischemia and Infarction**

**1003-72**

**Induction of HO-1 Reduces the Metabolic and Nitro/ Oxidative Effects of Ischemia-Reperfusion in Diabetic Rat Hearts**

Daniele Neglia, Cecilia Vecoli, Daniela Gianessi, Mariastella Mallinti, Virginia Ottaviano,
Simona Baldi, Michela Novelli, Pellegrino Masiello, Aldo Paolicchi, Renata Barsacchi,
Nader G. Abrahao, Antonio Llibre, CNR Institute of Clinical Physiology, Pisa, Italy

Background: Ischemia/reperfusion damage could be exacerbated in diabetic hearts by
metabolic rewakening of inducible nitric oxide synthase (iNOS) and the resulting
interaction of NO with superoxide (O₂⁻) and production of peroxynitrite (ONOO⁻). In this
study we hypothesized that cobalt protoporphyrin (CoPp), inducer of heme
gaseone-1 (HO-1), may ameliorate ischemia-reperfusion myocardial damage by reducing
iNOS expression and the production of ONOO⁻ and NOx.

Methods: Isolated perfused hearts (Langendorff model) from 22 rats with STZ-Nicotinamide
induced diabetes were subjected to an ischemia/reperfusion protocol: 20 min at control
perfusion pressure (80 mmHg) followed by 30 min at low perfusion pressure (20 mmHg) and
30 min of reperfusion at control pressure. Rats were pretreated (3 weeks) with CoPp (n=11) or
vehicle (n=11). Lactate and NOx were measured in the coronary perfusate during
all the experiments. O₂⁻ and malondialdehyde (MDA) myocardial levels as well as HO-1 and
iNOS protein expression were measured in the cardiac tissue at the end the experiments.

Results: Lactate release in the coronary effluent was documented during low perfusion
pressure followed by release of NOx at reperfusion. CoPp pretreatment reduced the
extent of metabolic ischemia and the production of ONOO⁻ as expressed by the integral
under the lactate and the NOx concentration curves, respectively (p<0.001 CoPp vs
no-CoPp). In CoPp-treated animals oxidative stress as measured by myocardial O₂⁻ and
MDA levels was reduced (p<0.001 CoPp vs no-CoPp). In CoPp-treated rats cardiac HO-1
was increased (p<0.001) but iNOS was decreased (p<0.05).

Conclusion: Induction of HO-1 in the diabetic rat prevents the increase in metabolic and
nitro/oxidative stress and may present a strategy to lessen myocardial damage following
ischemia-reperfusion injury.

**1009-78**

**Regional Myocardial Temperature During Coronary Occlusion in the Wtine: Comparison With Electrocardiographic Changes**


Background: EKG findings of ischemia can be confounded by conduction blocks,
electrolytes, medications, and effusions, hence making it vital to find complementary
diagnostic tools. We hypothesized that coronary artery occlusion (CO) would initially
increase temperature (T) of the myocardium, followed by a decreased T due to
cessation of oxidative metabolism.

Methods: We placed 2 T sensors ~2mm sub-endocardial (SE) and 4mm mid-myocardial
(MM) in the LAD territory of 7 pigs. EKG and T data were acquired using a data acquisition
system. Serial, timed balloon occlusions of the LAD were done for 3 and 5 minutes, with
3 minutes of reflow.
Conclusions: The myocardium exhibited a detectable temperature response to ischemia in the SE and the MI, prior to surface EKG changes. There was transtural heterogeneity during the ascending phase of this response, with a higher peak in the MI. Temperature monitoring may become a complement to EKG analysis for improved detection of ischemia; either intra-operatively or via pacemaker leads.

1003-74
Increased Vulnerability to Ischemia-Reperfusion Injury in UCP3 Null Mouse Hearts

Chevre Ocean, Monica Palmeni, Raymond R. Russell, III, Yale University School of Medicine, New Haven, CT

Background: Uncoupling of mitochondrial oxidative phosphorylation by endogenous uncoupling proteins (UCP) has emerged as a cardioprotective mechanism by preventing cardiac cell death under metabolic or oxidative stress. However, it is not clear whether lack of myocyte UCP3 is associated with increased vulnerability to oxidative stress and contributes to the development of detrimental ischemia-reperfusion injury.

Methods: This was tested in a model of left coronary artery (LCA) ligation induced ischemia-reperfusion injury by using multi parametric measurements including infarct size, area at risk, ST changes, heart rate and rhythm in 8-10 week-old male UCP3 null (UCP3-/-) mice compared with age- and gender-matched wild type mice. Hearts were subjected to 20-min ischemia by complete occlusion of the LCA followed by 2 hours of reperfusion. The infarct size and area at risk were measured with triphenyltetrazolium chloride staining.

Results: The infarct area in UCP3-/- mice was significantly larger than in wild type mice following ischemia-reperfusion injury (30.8±6.6% vs. 12.4±1.2%, p<0.009). Accordingly, there were significant differences in the infarct size at risk ratio (0.52±0.07 versus 0.27±0.03, p=0.004). However the area at risk was similar in both groups (61.9±3.2 versus 48.7±9.5%, p=0.08). Reperfusion arrhythmias, including bradycardia, atrioventricular block and ventricular arrhythmias, were more pronounced in UCP3-/- mice while the overall heart rate response to ischemia reperfusion injury was similar. LCA ligation was associated with a greater ST segment elevation in UCP3-/- mice than in wild type mice in addition to persistent ST segment depression during reperfusion suggesting a component of no-reflow in the UCP3-/- mice.

Conclusions: Thus there is increased myocardial vulnerability to ischemia-reperfusion injury in mouse hearts lacking UCP3. We conclude that UCP3 deficiency may provide insight into inflammatory responses after AMI, as well as potential therapeutic targets for effective myocardial protection in oxidative stress.

11:00 a.m.

1003-75
Real-Time Magnetic Resonance Imaging (MRI) of the Time Course of Myocardial Injury and Cell Death in a Canine Model of Regional Ischemia and Reperfusion

Patrick M. Burns, Patrick N. Kearns, Yoshinori Nishijima, Pedro Vargas-Pinto, Yu Ding, Mihaela Jekic, Jianrui Lian, Hung-Yu Lin, Kun Huang, Orlando P. Simonetti, Jay L. Zweier, The Ohio State University, Columbus, OH

Background: Questions remain regarding when cell death occurs in the ischemic and reperfused heart. Therefore, we developed a technique for real-time MRI of myocardial function and infarction in hearts subjected to regional ischemia and reperfusion.

Methods: Left anterior descending artery was occluded in 7 dogs via an intracoronary balloon and a coronary sinus catheter was placed. Myocardial signal enhancement was measured every 10 min with a constant infusion of gadolinium during 90 min of ischemia followed by 120 min of reperfusion, and again at 24 and 48 hours post-reperfusion. Wall motion was measured by cine MRI.

Results: At occlusion the at-risk region became akinetic whilst the remote myocardium showed increased isovasy. During ischemia, myocardial signal intensity showed no change. Upon reperfusion, infarct region end-diastolic thickness increased by >80% (13.5±2.1 vs. 7.4±0.9 mm), immediately followed by an increase in infarct signal intensity to 244% of remote (124.6±18.7 vs. 51.1±11.9) and infarct area reached a peak after 60 min reperfusion. CPK measured across the coronary circulation showed no change during ischemia, but increased upon reperfusion returning to baseline by 48 hr.

Conclusions: We observed myocardial injury and cell death occur primarily upon reperfusion with continued necrosis and enzyme leak for up to 120 min after the onset of reflow. These results demonstrate that reperfusion injury occurs with a critical window of cell death during the first two hours of reflow.

11:00 a.m.

1003-76
Identification of Characteristic Expression Profiling of Acute Coronary Syndromes Associated with STEMI: Large-Scale Diagnostic Markers for STEMI

Pum-Joon Kim, Ki-Bae Seung, Ki-Yuk Jang, Sang Hong Baek, Hae Ok Jung, Woo Seung Shin, Hun Jun Park, Ju Yeal Baek, Seong Gyu Yoon, Man Won Park, Yoon Seok Koh, Suk Woo Nam, Kyu Bo Choi, The Catholic University of Korea, Kangnam St Mary’s Hospital, Seoul, South Korea

Background: The purpose of this study is to identify characteristic transcriptomic profile of AMI and recapitulate genetic elements whose expression is markedly elevated in AMI, as well as to suggest large-scale genetic markers which allow diagnosing AMI in early times.

Methods: To define testing group for early AMI detection, peripheral blood samples were obtained from 40 patients with confirmed AMI (20 STEMI and 20 NSTEMI). These data provide insight into inflammatory responses after AMI, and should be helpful in understanding pathogenesis and development of new treatment for AMI.

Results: Unsupervised hierarchical clustering analysis of gene expression profiling resulted in distinct molecular signature between AMI and healthy, follow-up groups. Large-scale genetic elements included S100 calcium binding protein P, MMP9, TNF-α, induced protein 6, IL-2 receptor β, and BCL6, and many of them were previously reported as genetic marker for ischemic stroke.

Conclusions: We present characteristic molecular signature of AMI by using whole genomic expression analysis and suggest large-scale genetic elements as early diagnostic marker or surrogate makers for guiding AMI from the peripheral blood of patients. These data provide insight into inflammatory responses after AMI, and should be helpful in understanding pathogenesis and development of new treatment for AMI.

11:00 a.m.

1003-77
Heart-Kidney Connection: Renal Fibrosis and Activation of Renal Molecular Remodeling After Myocardial Infarction in the Absence of Heart Failure

Fernando L. Martin, Brenda K. Huntley, Gerald E. Harders, Horng H. Chen, Alessandro Catalotti, John C. Burnett, Jr., Mayo Clinic, Rochester, MN

Background: Studies in human myocardial infarction (MI) suggest that even in the absence of heart failure (HF) alterations in renal function may occur and contribute to poor outcomes. After MI a decline in renal function may be seen acutely by mechanisms which are unclear. The long term consequences of MI upon renal function and structure remain poorly defined. We hypothesized that even without preexisting renal disease, renal functional and structural changes would be present following MI.

Methods: Cardiorenal function and structure were assessed in Wistar rats, Sham (S; n=10) and MI groups (n=9) 3 weeks after MI. GFR was determined by inulin clearance. Blood was obtained for PRA and aldosterone. Hearts and kidneys were harvested for histological analysis. Cardiac function was assessed by echo.

Results: PRA and aldosterone activity were absent. Blood pressure (BP) was not different between groups. There was no HF as sodium and water excretion was maintained. GFR tended to decrease (S:2.9±0.3, MI:2.4±0.2 ml/min, NS). Picrosirius Red staining for collagen in the KC and KM after MI showed greater fibrosis especially in the KM (KC S:1.1±0.2, MI:3.5±0.6 %, p<0.001 and KM S:1.0±0.2, MI:18.8±6 %, p<0.005). Microarray analysis revealed that 303 genes significantly changed in KM and 407 genes in RM (KC S:1.1±0.2, MI:3.5±0.6 %, p<0.001 and KM S:1.0±0.2, MI:18.8±6 %, p<0.005).

Conclusion: We conclude that experimental MI results in renal structural remodeling characterized by renal cortical and medullary fibrosis with a mild reduction in GFR and extensive modulation of molecular pathways related to renal growth and metabolism. This investigation provides evidence for a heart-kidney connection after MI by mechanisms which remain to be defined. We also conclude that therapies for MI targeting the heart also should be evaluated for properties of renoprotection.

11:00 a.m.
**11:00 a.m.**

**Paracrine Cytotoxic Effects of Inner Chorion-Derived Human Mesenchymal Stem Cells**

Kazukiyo Henke, Noritoshi Nagaya, Shunsuke Ohnishi, Shin Ishikane, Michihiko Fujimura, Tomohiro Okazaki, Department of Biochemistry, National Cardiovascular Center Research Institute, Suita, Japan

**Background:** The fetal membrane, which includes amnion and chorion, is considered an ideal source for regenerative medicine, although it is normally discarded after birth. Mesenchymal stem cells (MSC) have been identified in the fetal membrane; however, little information is available regarding the biological difference of MSC derived from different layers of the fetal membrane. We assessed the hypothesis that the different layers of MSC would exert different effects in response to biological stress.

**Methods:** We mechanically and enzymatically separated the human fetal membrane into three layers: amnion and inner and outer layers of chorion, and isolated MSC from each layer. MSC were identified by adherence, surface antigen expression and multi-lineage differentiation. We examined the amount of growth factor from MSC culture and effects of conditioned medium from MSC culture by MTS assay, TUNEL assay and measurement of caspase-3 activity.

**Results:** MSC obtained from all three layers were similar in morphological appearance and surface antigen expression, and comparably differentiated into adipocytes and osteocytes. The amount of growth factor secretion from MSC culture was different according to the origin of MSC: hepatocyte growth factor and insulin-like growth factor-1 were secreted mainly from the inner chorion, while vascular endothelial growth factor was secreted mainly from the amnion. Conditioned media obtained from inner and outer chorion-derived MSC protected against the growth inhibition in endothelial cells and cardiomyocytes, whereas conditioned medium obtained from amnion-derived MSC protected only cardiomyocytes. Moreover, conditioned medium obtained from inner chorion-derived MSC had an anti-apoptotic effect on both endothelial cells and cardiomyocytes under biological stress.

**Conclusions:** MSC can be isolated from three different layers of the fetal membrane, and exert different paracrine effects in response to biological stress. Particularly, inner chorion-derived MSC have potent cytoprotective effects on endothelial cells and cardiomyocytes.

**11:00 a.m.**

**Development of Monitoring Systems for Cardiomyogenic and Endothelial Differentiation**

Seung-Cheol Choi, Ji-Hyun Choi, Chi-Yeon Park, Wan-Joo Shim, Do-Sun Lim, Korea University Medical College, Seoul, South Korea

**Background:** It has been shown that adult stem cells derived from various organs can transdifferentiate into cardiomyocytes and endothelial cells and contribute to myocardial repair. However, the concept of stem cell plasticity has been challenged by recent findings demonstrating cell fusion, but not transdifferentiation. Therefore, questions and controversies regarding the mechanisms of myocardial regeneration still exist. This study is to develop the reporter-vector systems for monitoring stem cells transdifferentiating into cardiomyogenic or endothelial lineage.

**Methods:** For monitoring of cardiomyogenic differentiation, atrial natriuretic factor (785-bp), cardiac troponin I (408-bp), myosin heavy chain (363-bp) and myosin light chain (327-bp) fragment of promoter regions were amplified and cloned into pEGFP vector to monitor endothelial cell differentiation. The reporter vectors were transfected into bone marrow mesenchymal stem cells (BMMSCs) and P19 embryonic stem cells, and cardiac or endothelial differentiation was induced by 5-azacytidine or VEGF treatment.

**Results:** The reporter systems were used to monitor cardiomyogenic or endothelial differentiation confirmed in BMMSCs and P19 embryonic stem cells. The reporter-vector systems based on tissue-specific promoters can be used to monitor stem cells differentiating into cardiac or endothelial lineage. By combining noninvasive molecular imaging technology, these can be used to track stem cell location and fate after transplantation into infarcted myocardium.

**Conclusions:** These results showed that the reporter-vector systems can be used to monitor stem cells differentiating into cardiac or endothelial lineage. By combining noninvasive molecular imaging technology, these can be used to track stem cell location and fate after transplantation into infarcted myocardium.
infarct zone, MI induced nearly 1.8-fold increases (P<0.001) in MMP-9 and MMP-2 (activity and protein) and TIMP-3 protein, nearly 2-fold increases in iNOS, nNOS and eNOS in the ischemic zone and these changes were normalized (P>0.001) by omapatrilat and candesartan. Both drugs also improved the MMP-9/TIMP-3 balance (not MMP-2/TIMP-1) and normalized myeloperoxidase and transforming growth factor β1 in the ischemic zone.

Conclusions: Modulation of MMP-9/TIMP-3 balance, angiotensin II and iNOS with omapatrilat and candesartan induces reverse LV remodeling and limits dysfunction during healing after MI.

**1003-85**

Cell Distribution by both Endomyocardial and Epicardial Injections in Porcine Chronic Myocardial Infarction Model

Dongming Hou, Fernando Tondato, Pendyala Lakshmana, Nic Chronos, Keith Robinson, Saint Joseph's Research Institute, Atlanta, GA

Background: Unrestricted somatic stem cells (USSCs) obtained from human cord blood have intrinsic pluripotent differentiation potential. However the fate of cells transplanted into the chronic infarcted heart has not been extensively studied. We evaluated myocardial distribution of USSCs by both endomyocardial and epicardial injection technique in a swine model.

Methods: Myocardial infarction (MI) was induced by coronary artery embolization in 7 pigs. 28 days after MI, 2x10^6/kg USSCs labeled by 111Iindium (n=7) were delivered either via intramyocardial injection catheter (Endo, n=4), or via thoracotomy direct epicardial injection (Epi, n=3). 20 injections were throughout the infarct and border zones in a grid-like pattern (0.1 ml each site). The Endo delivery was done under intracardiac Echo guidance. Animals were terminated at 24hrs. The radioactive biodistribution in heart and other organs were assessed by γ-emission counting.

Results: Lung, liver, spleen and kidney were weighted and sampled with ~1 cm³ in 3 locations. For hearts, the regions of infarcted, border, and rim of adjacent normal tissue, in addition to remote LV, LA, RV, RA, mital and aortic valves, were also cut out and weighed. Quantitative data showed that average overall cardiac retention was 17±16% for both delivery modalities. The retention rate in the infarction and remote zones were 10±8% and 65±7%, respectively. Epicardial delivery was more variable. The majority of transplanted cells were detected out side the heart, primarily in lung (25±5%) and liver (40±9%).

Conclusions: The majority of delivered USSCs are sequestered into the lungs and liver at 24 hours. The findings support the notion that backstreaming into or outside of ventricular chamber, as well as unintentional injection into intramyocardial veins are significant sources of cell loss by this method. The clinical implications of these findings are potentially significant, as these proangiogenic cells may have undesirable effects if non-target organs and the poor retention efficiency may hinder therapeutic efficacy. Development of improved delivery and retention efficacy is the goal of future study.

**1003-86**

Protein Kinase C-δ inhibitor protects against acute myocardial infarction by intravenous administration either during ischemia or reperfusion

Eiketsu Sho, Jin Dong, Zhen Jin, Yong Sun Lee, Steve Harrison, Dirk Mendel, KAI Pharmaceuticals, South San Francisco, CA

Background: Historical studies have shown that a selective δPKC inhibitor peptide (KAI-9803) reduces reperfusion-induced myocardial damage in a pig acute myocardial infarction (AMI) model when delivered locally into the intracoronary artery at the onset of reperfusion. The goal of this study is to study the therapeutic effects of KAI-9803 administered by intravenous (IV) infusion in a rodent AMI model either during ischemia or reperfusion.

Methods: Transient left coronary artery occlusion was induced in male Sprague Dawley rats for 30min followed by 24hrs of reperfusion. KAI-9803 or saline was administered as a 30-min IV infusion via the femoral vein either starting at the onset of ischemia, the onset of reperfusion, or at 30 min or 90 min after initiation of reperfusion. The infarct sizes were evaluated at 24hrs of reperfusion. Histological studies were performed at the end of IV infusion to evaluate myocyte and capillary protection and early inflammatory reactions following treatment.

Results: Thirty minutes of IV infusion with KAI-9803 both during ischemia and at the beginning of reperfusion resulted in 40% reduction in infarct size after 24hrs of reperfusion. Delayed treatment resulted in a reduced protective effect with a 30% or 23% reduction in infarct size when treatment started at 30 or 90 min of reperfusion, respectively. Histological analysis of the early time course of reperfusion showed KAI-9803 protects against capillary damage (238 ± 234/mm² vs. 139 ± 126/mm² capillary density with treatment during ischemia; 2338 ± 113/mm² vs. 1270 ± 166/mm² capillary density with treatment beginning at reperfusion, p<0.01). This protection was reduced when the treatment started after 90 min of reperfusion. Infarct cell infiltration started ~60-90 min after reperfusion and was limited by treatment with KAI-9803 (246 ± 17/mm² vs. 399 ± 34/mm² infarct cell density at 120-min reperfusion, p<0.01).

Conclusions: IV infusion of KAI-9803 either during ischemia or within 90 minutes of the start of reperfusion can protect against myocardial damage. δPKC inhibition may not only reduce myocyte damage, but can also protect against microvascular damage and limit the acute inflammatory reaction.
Myocardial Ischemia--Basic; Unstable Ischemic Syndrome--Clinical

Sunday, March 30, 2008, 1:00 p.m.-4:30 p.m.
McCormick Place, South Hall

**1010**

**Myocardial Ischemia--Basic; Unstable Ischemic Syndrome--Clinical**

**1010-41**

H2S mediated myocardial preconditioning. Its cytoprotective mechanisms. Therefore, we evaluated several potential mechanisms of H2S mediated cardioprotection. Methods: H2S donor (100 μg/kg), or vehicle was administered intraventricularly to hearts of pigs. Hearts were excised and evaluated for infarct size using 2,3,5-triphenyltetrazolium chloride (TTC) staining. Results: H2S increased the protein expression of the anti-apoptotic, Bcl-2, in both the cytosolic and mitochondrial cellular compartments. However, H2S did not increase the protein levels or activation of eNOS, MnSOD or glutathione. Mice treated with H2S donor also exhibit a 42% reduction (p < 0.001) in infarct size relative to area-at-risk compared to vehicle. Conclusion: These findings suggest that activation of anti-apoptotic signals could be an important mechanism of H2S mediated cardioprotection.

**1010-42**

Delayed Ischemic Preconditioning of the Swine Heart by Gene Delivery of H11 Kinase

Li Chen, You-Tang Shen, Ping Zhang, Stephen F. Vatner, Christophe Depre, Department of Cell Biology and Molecular Medicine, University of Medicine & Dentistry of New Jersey, Newark, NJ

Background: H11 kinase (H11K) is a small heat shock protein expressed predominantly in the heart, the expression of which increases in various forms of ischemic heart disease, both in animal models and in patients. We hypothesized that over-expression of the H11K gene delivered into the potential area-at-risk (AAR) would reduce the extent of irreversible damage upon subsequent ischemia-induced myocardial infarction. Methods: Domestic pigs were instrumented with a left ventricular pressure gauge, catheters and hydraulic occluder around the left circumflex (LCX) coronary artery. An adenovirus harboring the H11K sequence was injected to the potential area-at-risk (n=5). Control pigs were injected with virus expressing LacZ (n=5). Three days after injection, the LCX artery was occluded for 60 min, followed by 3 days of repertusion. A similar protocol was used in 3 pigs injected with H11K and 3 pigs injected with LacZ for comparison in the presence of N-(6-aminohexyl)-5-chloro-2′-deoxyuridine (AIA, a NO synthase inhibitor). Results: The LCX infarct size in the H11K group was significantly smaller than in the LacZ group (29.4+/-5.5 vs. 25.3+/-1.4%) and an increased ejection fraction (EF) (43.8+/-2.4 to 47.0+/-3.5%) in Group-MSC in contrast to controls (EF: 80.0+/-6.2 vs. 88.0+/-7.7 ml, infarct size: 29.5+/-6.2 vs. 30.2+/-1.1%, EF: 43.7+/-5.9 vs. 43.5+/-2.3%). The infarct size was significantly smaller in Group-MSC as compared to controls at 26 days post-MI (p=0.032). Histology confirmed the presence of the viable MSCs (12.9+/-3.4% of the injected cells) in the myocardium 10 days after intramyocardial delivery. Conclusion: Reporter gene imaging enables the non-invasive PET imaging on clinical scanners of the persistence of viable MSCs in the peri-infarcted myocardium at 10 days post-delivery.

**1010-43**

Non-Invasive In Vivo Tracking Of Percutaneously Intramyocardially Injected Autologous Porcine Mesenchymal Stem Cells Modified For Transgene Expression Of PET Reporter Gene Using Serial PET Imaging

Mariani Gnyropylos, Jeronimo Blanco, Terez Marian, Lajos Torn, Ors Petnehazy, Zsolt Petras, Raymon Hemsutersberger, Imre Pavy jr, Dana Krachtman, Johann Wojta, Kurt Huber, Dietmar Gioo, Medical University of Vienna, Vienna, Austria, The Johns Hopkins University, School of Medicine, Baltimore, MD

Background: Reporter gene imaging offers the ability to non-invasively serially track stem cell fate. To-date most studies have been performed in small animals. Methods: Myocardial infarction (MI) was created by percutaneous balloon occlusion of the LAD in farm pigs. Bone marrow (BM) was harvested and mesenchymal stem cells (MSCs) were selected and modified for transgene expression of the fusion protein (lentiviral vector expressing renilla luciferase, red fluorescent protein and herpes simplex truncated thymidine kinase (LV-RL-RFP-ITK) as positron emission tomography (PET) reporter gene. In vitro assays of [18F]FHBG uptake of the LV-RL-RFP-ITK MSCs revealed a minimum number of 0.1 million cells were detectable with PET. Sixteen days after AMI, baseline magnet resonance imaging (MRI) of the heart was performed in all animals and the BM-LV-RL-RFP-ITK MSCs were injected intramyocardially using NOGA guidance in the infarct border zone (total 2.6±0.4 million cells) in 6 pigs, while 7 animals served as control. Thirty hours and 7 days after MSC-LV-RL-RFP-ITK treatment, PET imaging were performed after intravenous injection of 6 mCi [18F]FHBG followed by control MRI. Results: PET demonstrated diffuse distribution of the injected MSC-LV-RL-RFP-ITK in the pig heart in the anterior wall and septum at 30h and decreased tracer activity in the injections sites with pericardial and pleura uptake at 7 days. MRI revealed a trend of a decreased end-diastolic volume (EDV) (82.5+/-6.8 vs. 79.0+/-4.4 ml) and infarct size (29.4+/-5.5 vs. 25.3+/-1.4%) and an increased ejection fraction (EF) (43.8+/-2.4 to 47.0+/-3.5%) in Group-MSC in contrast to controls (EF: 80.0+/-6.2 vs. 88.0+/-7.7 ml, infarct size: 29.5+/-6.2 vs. 30.2+/-1.1%, EF: 43.7+/-5.9 vs. 43.5+/-2.3%). The infarct size was significantly smaller in Group-MSC as compared to controls at 26 days post-MI (p=0.032). Histology confirmed the presence of the viable MSCs (12.9+/-3.4% of the injected cells) in the myocardium 10 days after intramyocardial delivery. Conclusion: Reporter gene imaging enables the non-invasive PET imaging on clinical scanners of the persistence of viable MSCs in the peri-infarcted myocardium at 10 days post-delivery.
Human adipose tissue-derived stem cell preserved heart function in athymic nude rats following permanent ischemia

Living Cai, Brian H. Johnstone, Todd G. Cook, Keith L. March, Indiana Center for Vascular Biology and Medicine, Indianapolis, IN, Kranert Institute of Cardiology, Indianapolis, IN

Background: The use of stem cells for repair of myocardium damaged by cardiac insult has gained much interest as a new therapeutic approach. Previously, we demonstrated that adipose stem cells (ASCs) promote reperfusion and tissue repair in ischemic skeletal muscle.

Methods and Results: ASCs were harvested from human subcutaneous adipose tissue samples obtained following liposaparision. ASCs conditioned media (CM) promote proliferation and migration of mature and progenitor endothelial cells in vitro. Growth and metabolic activity of human microvascular endothelial cells (HMVEC) cultured in growth-factor deficient minimal medium (MM) increased 1.7-fold when supplemented with a 1:1 mixture of ASC CM (p=0.01). Angiogenic formation and migration of HMVECs were enhanced by 2.1- and 2.0-fold, respectively, when ASC CM was added to MM (p=0.01). Intramyocardial injection of ASCs into perforin-inact zone of athymic nude rats hearts following permanent LAD ligation, significantly preserved cardiac function in vivo by serial echocardiography. 28 days after cell treatment, ASC-treated rats exhibited better LV ejection fractions (56.5%±6.78% (mean±SEM), compared to saline control as 37.22±2.96% (p=0.04)). Fractional shortening was also improved, as 32.46±4.71% of ASC-treated rats VS 18.91±1.73% of control (p=0.04). LV volume both at end-diastolic and end-systolic stages were lower in ASC group (311.17±17.29ml and 139.15±20.96ml, respectively) than saline group (390.76±29.80ml and 248.61±26.48µl, p=0.03). Anterior wall thinning was attenuated in ASC group (1.60±0.08mm VS control 1.18±0.17mm, at end-diastolic stage p=0.03). Trichrome staining of heart showed ASC treatment had lowered fibrosis percentage as 33.81±1.75% (VS control 25.97±5.96%, p=0.05). Human ASCs were detected in the border zone of heart by immunofluorescence 28 days after injection.

Conclusion: We demonstrated ASCs have a great potential as cell therapy to preserve heart function following ischemic insult. Given the abundance cell source, this approach may be useful in patients with ischemic heart disease.

Atherosclerosis

The treatment-independent effect of HIV infection on IMT has gained much interest as a new therapeutic approach. Previously, we demonstrated that adipose tissue-derived stem cell preserved heart function in athymic nude rats following permanent ischemia. In conclusion, nonuniform struts distribution which may represent partial strut fracture at the time of DES implantation suggests a new potential mechanism of stent thrombosis.

Nonuniform Struts Distribution as the New Potential Mechanism of Stent Thrombosis After Drug-Eluting Stent Implantation


Background: Relation of nonuniform struts distribution to stent thrombosis (ST) has not been extensively investigated in the setting of ST and control patients. We investigated whether nonuniform struts distribution and stent thrombosis are associated.

Methods: We retrospectively analyzed postprocedural intravascular ultrasound (IVUS) images of 13 patients (14 DES thrombosis lesions) and a control group of 27 patients (30 lesions) matched for history of chronic renal failure and DES type. In addition to standard IVUS measurements the number of visualized struts and the maximum interstrut angles were measured at one millimeter intervals. The nonuniform struts distribution index (SDI) was defined as the maximum interstrut angle divided by the number of struts. Subacute ST was defined during the first 30 days after stent implantation, while late ST after 30 days.

Results: Compared with the control, IVUS studies in the ST group showed a larger mean vessel area (13,33±4,58 vs 12,50±4,07, p=0.014), smaller mean lumen area (5,69±1,32 vs 6,17±1,87, p=0.041) and higher mean vessel area (13,33±3,78 vs 12,40±4,80, p=0.028).

Conclusion: In conclusion, nonuniform struts distribution which may represent partial strut fracture at the time of DES implantation suggests a new potential mechanism of ST in drug-eluting stents.
Background: Chronic obstructive pulmonary disease (COPD) and myocardial infarction (MI) share risk factors and pathophysiological features. Yet, there is limited data on the prevalence of COPD in patients with MI and on its impact on outcome.

Methods: The medical records of all Olmsted County residents with MI defined by standardized criteria (cardiac pain, biomarkers, and Minnesota coding of the ECG) were reviewed to ascertain COPD and evaluate outcomes.

Results: 7,059 incident MIs occurred in Olmsted County between 1979 and 2005 (mean age 68 ± 14, 43% women). A clinical diagnosis of COPD was noted among 406 (13%). The prevalence of COPD increased over time: in 2000-2005 the prevalence of COPD was 16%, twice the prevalence of 8% in 1979-1985, 4% (4% increase/year). After a mean follow-up of 4.8 years, 1436 patients died. Survival at 5 years was markedly reduced among patients with COPD (64% ± 3%) compared to those without COPD (88%, 95% CI 66%-69%), p<0.01 (figure). Adjustments for age, sex, smoking, hypertension, comorbidity, NSTEMI, CK levels, Killip class and treatment of MI, COPD was associated with a large increase in the risk of death (adjusted HR 1.39, 95% CI 1.17-1.64; p<0.01). Among a large, geographically defined community of patients with MI, COPD was frequent and was associated with a large increase in the risk of death. As the prevalence of COPD is increasing over time, its strong association with death underscores the public health impact of this condition among patients with MI.

Conclusions: In OAT, pts who underwent stress testing had better outcomes than pts who did not, likely related to differences in age and LV function. Mild-moderate inducible ischemia was not related to outcomes. The lack of benefit for PCI over MED was consistent regardless of whether stress testing was performed or inducible ischemia was present.

Impact of Stress Testing Prior to PCI or Medical Management on Outcomes of Patients With Persistent Total Occlusion After Myocardial Infarction: Analysis From the Occluded Artery Trial (OAT)

Warren J. Cantor, Gervasio A. Lamas, Eugenia Nikolsky, Camille A. Peart, Vankerpunran S. Srivivas, Sandra A. Forman, Venu Menon, John R. Ross, Sérgio B. Baptista, Peter Meciar, Zygmunt Sadowski, Judith S. Hochman, University of Toronto, Toronto, ON, Canada, New York University School of Medicine, New York, NY

Background: In the Occluded Artery Trial, 2011 pts with an occluded infarct-related artery (IRA) were randomized to percutaneous coronary intervention (PCI) or medical treatment (MED). There was no difference in the primary endpoint of death, re-MI or heart failure (CHF). We examined the prognostic impact of pre-randomization stress testing.

Methods: Stress testing was required by protocol except for pts with single vessel disease and akinesia/dyskinesia of the infarct zone. Severe inducible ischemia was an exclusion criterion regardless of whether stress testing was performed or inducible ischemia was present.

Among pts with inducible ischemia, outcomes were similar for PCI and MED (all p>0.1). Conclusions: In OAT, pts who underwent stress testing had better outcomes than pts who did not, likely related to differences in age and LV function. Mild-moderate inducible ischemia was not related to outcomes. The lack of benefit for PCI over MED was consistent regardless of whether stress testing was performed or inducible ischemia was present.

Adaptive Remodeling of Culprit Artery Following Sirolimus Eluting Stent Implantation in Acute Myocardial Infarction: Its Effect on Late Stent Malapposition

Mitsunori Harada, Soichiro Kumagai, Shinya Mikono, Atsushi Tanaka, Shinya Kamiya, Takayuki Saijo, Yui Yamakana, Toshioh Osabayashi, Kariya Yoyota General Hospital, Kariya, Japan

Background: Late stent malapposition (LSM), which is mainly caused by chronic positive remodeling of the vessel, occurs in one third of cases following sirolimus eluting stent (SES) implantation in acute myocardial infarction (AMI). Recent intravascular ultrasound (IVUS) study has shown that positive remodeling is a predominant pattern of lesion remodeling in AMI. However, it remains unknown whether acute positive remodeling of the culprit artery causes LSM following SES implantation in patients with AMI. Methods: Adiponectin and resistin were measured in 397 consecutive patients (age: 62 ± 12 years, male: 72%) with acute MI. Methods: We investigated preinterventional IVUS images of 40 consecutive patients with AMI who underwent IVUS-guided SES implantation (stent to artery ratio ≥ 1). IVUS analysis included qualitative and quantitative measurements of external elastic membrane (EEM), lumen and plaque area at reference and lesion. Positive remodeling was defined as lesion/reference EEM > 1.0. LSM was defined as separation of at least 1 stent strut from the intima, with evidence of blood flow behind the strut, where post-stent implantation IVUS had revealed complete apposition of the stent to the vessel wall. Twenty nine patients with positive remodeling were enrolled in this study. Serial IVUS analysis was performed at baseline and 8-month follow-up. Results: Soft plaque with spotty calcification was more frequent in patients with positive remodeling than in those without (75.9% versus 40.0%, p=0.04). No difference was seen between lumen area immediately after stenting and that at follow-up (9.6±2.8mm² versus 9.5±2.4mm², p=N.S). EEM and plaque area decreased significantly (23.9±4.8mm² to 19.4±4.1mm², p=0.04, 14.4±3.2mm² to 9.8±2.1mm², p=0.003, respectively). There was a good correlation between EEM and plaque area (r=0.866, p<0.0001). LSM occurred in 4 patients (13.8%) at follow-up. Conclusion: The infarct-related artery with positive remodeling shrank in response to plaque regression to adapt itself to the implanted SES. Acute positive remodeling did not increase LSM following SES implantation in patients with AMI probably due to adaptive remodeling of the culprit artery.
Comparison of Clopidogrel Responsiveness between Chronic Renal Failure Patients and Normal Renal Function Subjects Using VerifyNow(TM) P2Y12 Assay

Weon Kim, Sang-Hyun Park, Won-Yu Kang, Sun-Ho Hwang, Wan Kim, Cardiovascular Center, Gwangju veterans Hospital, Gwangju, South Korea

BACKGROUND: Effective antiplatelet regimen is an emerging issue in the drug-eluting stent (DES) era. Stent thrombosis was increased in chronic renal failure (CRF) which may be attributed to poor response to clopidogrel. The mechanisms leading to poor clopidogrel effects are not fully elucidated and are likely multifactorial.

METHODS: We conducted a prospective, randomized, open-label trial to evaluate the difference of clopidogrel responsiveness according to clopidogrel dose in CRF patients. 23 normal renal function patients with standard dose clopidogrel 75mg daily (Group 1, 63% 66 years) and CRF subjects (63.7 years) divided into two groups according to clopidogrel dose (Group 2: 18 subjects with 75mg, Group 3: 19 subjects with 150mg daily) were enrolled. All patients were administered clopidogrel for 30 days. The primary efficacy variable was mean PRU (P2Y12 Reaction unit) and % inhibition difference between each group within 90 days of hospitalization for NSTEACS, in the province of Alberta, Canada, from 2000 to 2004. Subjects were identified using the Alberta Provincial Project for Outcome Assessment in Coronary Artery Disease (APPRAOCH) database. Patients who underwent emergency CABG were excluded. The time to CABG was defined as the number of days from initial hospital admission to CABG surgery, and was categorized as being within: 3-7 days (group 1); 8-14 days (group 2); or 15-60 days (group 3). The primary outcome was all-cause mortality, both short term (at 30 days) and long term.

RESULTS: There were no significant PRU difference between each three groups (239±87 PRU in group 1, 307±86PRU in group 2, 302±95PRU in group 3, p= 0.056). But, comparing normal subject group with CRF group, significantly increased in CRF group (239±87 in control, 304±89 PRU in CRF, p=0.016). There was good positive correlation between serum creatinine and PRU (r=0.438, p=0.03) and no fair negative correlation between serum creatinine and % platelet inhibition (r=-0.334, p=0.025). And, the duration of dialysis and PRU were correlated positively (Spearman’s rho=0.320, p=0.03).

CONCLUSION: The clopidogrel resistance was more increased in CRF patients than non-CRF patients. The PRU and % platelet inhibition were correlated with serum creatinine level and the duration of dialysis. More increased in CRF patients than non-CRF patients.

Time of Coronary Artery Bypass Grafting Following Non-ST-Elevation Acute Coronary Syndrome and Mortality

Marc W. Dewey, Jianguo Zhang, David B. Ross, William A. Ghali, Brenda Hemmelgarn, University of Calgary, Calgary, AB, Canada, University of Alberta, Edmonton, AB, Canada

Background: Despite advances in management of non-ST-segment elevation acute coronary syndromes (NSTEACS), there is little data regarding optimal timing of coronary artery bypass surgery (CABG) following NSTEACS. The purpose of this study was to determine the association between time to CABG following NSTEACS and short and long-term mortality. Methods: The cohort consisted of all patients who underwent isolated CABG within 90 days of hospitalization for NSTEACS, in the province of Alberta, Canada, from 2000 to 2004. Subjects were identified using the Alberta Provincial Project for Outcome Assessment in Coronary Artery Disease (APPRAOCH) database. Patients who underwent emergency CABG were excluded. The time to CABG was defined as the number of days from initial hospital admission to CABG surgery, and was categorized as being within: 3-7 days (group 1); 8-14 days (group 2); or 15-60 days (group 3). The primary outcome was all-cause mortality, both short term (at 30 days) and long term (follow-up to December 31st, 2005). Logistic regression and Cox proportional hazards models were used to determine the association between time to CABG and short and long-term mortality, respectively, adjusting for comorbidities and severity of CAD. Results: A total of 1454 patients were included with 213 (14.6%) in group 1, 637 (43.8%) in group 2 and 707 (46.8%) in group 3. Median follow-up was 3.7 years. In the final adjusted models there was a non-significant trend towards increased mortality at 30 days in group 1 (odds ratio 2.62, 95% confidence interval 0.66, 7.53), using group 3 as a reference. However, there were no significant differences in mortality between the three groups with long-term follow-up, with hazard ratios (95% confidence interval) for death of 0.69 (0.35, 1.35) for group 1 and 0.99 (0.71, 1.37) for group 2. Conclusions: We found no association between timing of CABG after NSTEACS and mortality. There was no evidence of increased mortality associated with CABG performed early after presentation with NSTEACS.

Recent Trends of Gender-age Interaction and Its Relation to In-hospital Mortality in Patients with Acute Myocardial Infarction - Analysis of 30 Years of Data from a Single Center

Yoritsuka Otsuka, Nobuaki Kobuk, Takuya Taniguchi, Nobuhito Yagi, Yoichiro Kasahara, Yu Kataoka, Mitsuru Abe, Yui Yasuga, Atsushi Kawaamura, Hiroyuki Yokoyama, Yoichi Goto, Hiroshi Nonogi, Hitonobu Tsuchi, National Cardiovascular Center, Saita, Japan

Background: The longevity of the Japanese women is world’s highest and further increasing. Such a constant aging and westernization of life style should affect the morbidity and mortality of the ischemic heart disease. However, little is known about recent trends of gender-age interaction in patients with acute myocardial infarction (AMI). We investigated recent trends of gender-age interaction and its relation to in-hospital mortality in patients with AMI using a 30-year database of National Cardiovascular Center.

Methods: Consecutive patients (n = 4,766) admitted due to AMI to this hospital from 1977 to 2006 were divided into 3 groups (Group A; n = 1,740 from 1977 to 1989, Group B; n = 1,735 from 1990 to 1999, and Group C; n = 1,291 from 2000 to 2006). The data of these 3 groups were analyzed.

Results: The mean age of both men and women with AMI increased from year 1977 to 2006 (men; 61.7 years for Group A vs 64.0 years for Group B vs 65.8 years for Group C, women; 67.8 years vs 69.8 years vs 72.6 years, p < 0.05). The proportion of women with AMI increased in the same time frame (20.1 % vs 21.8% vs 27.8%, p < 0.05). Particularly, the ratio of elderly women (≥ 80 years old) was significantly higher than that of elderly men (men vs women; 4.2% vs 9.7% for Group A, 6.9% vs 17.9% for Group B, 11.6% vs 27.9% for Group C). Although in-hospital mortality of both men and women decrease by reperfusion therapy with passage of time, in-hospital mortality for elderly women (≥ 80 years old) with AMI (14.6%) was still higher than that for elderly men (8.4%), younger men (< 80 years old) (3.1%), and younger women (5.2%) with AMI in Group C (the most recent years of admission).

Conclusions: These data show that there are steady trends towards higher mean age and greater proportion of elderly women in Japanese patients with AMI in recent 30 years. In-hospital mortality of elderly women with AMI remains high and additional strategies may be needed for these patients.
Conclusions Although coronary revascularization itself was associated with lower mortality and fewer myocardial infarctions, no benefit of an early invasive strategy was observed. The conclusion that an early invasive strategy leads to a better outcome than a selective invasive strategy cannot be drawn from the observation that revascularized patients have an improved prognosis in non-randomized studies.

3:00 p.m.

**TO10-59**

NO IMPROVEMENT IN TIME TO TREATMENT OF ACUTE MYOCARDIAL INFARCTION IN RURAL NATIVE AMERICAN PATIENTS: TEMPORAL TRENDS 1999-2006

Eric A. Brody, Andrew C. Duarte, Adeline June-Tsosie, Justin L. Sewell, Beth R. Malasky, James Ranger-Moore, Elizabeth Custiel, Phyllis Sanderson, Neil S. Freund, University of Arizona, Tucson, AZ

Background: Acute myocardial infarction (AMI) is a leading cause of morbidity and mortality in Native American (NA) communities. Time to presentation in NA with AMI in a large national database is minimally longer than in the general U.S. population but does not reflect the rural population served by the Native American Cardiology Program (NACP). This prospective study was designed to examine the time to treatment (T2T) of rural NA patients and any longitudinal trends in T2T over an 8 year period.

Methods: Three hundred twenty-two NA patients with AMI were evaluated at rural facilities and transferred to NACP from February 1999 through June 2006. Data obtained included T2T (symptom onset to arrival at initial treatment facility) measured continuously for patients presenting within 12 hours, and as a count of patients arriving after 12 hours. Three longitudinal trends were evaluated: T2T among patients arriving at <12 hours, and proportion of patients presenting <6 vs. >6 and <12 vs. >12 hours.

Results: T2T information was available on 293 patients. The overall median and mean times to presentation were 360 and 572 minutes. Cox proportional hazards model suggested no significant changes in T2T by year (p = 0.880) in the cohort presenting under twelve hours. Binary logistic regression indicated no significant changes in the proportions of patients coming in <6 vs. >6 (p = 0.993) or <12 vs. >12 (p = 0.868) hours over the eight years of the study.

Conclusions: Based on the above data, time to presentation in rural NA patients with AMI is longer than nationally reported and has not improved. This T2T delay places NA patients at risk for worse outcomes and increased mortality. Public education about the importance of rapid clinical presentation and symptoms of AMI would reduce the burden of AMI in NA communities.

3:00 p.m.

**TO10-60**

Dramatic Time-to-Treatment Delay in Rural Native Americans with Acute Myocardial Infarction

Eric A. Brody, Andrew C. Duarte, Adeline June-Tsosie, Justin L. Sewell, Beth R. Malasky, James Ranger-Moore, Elizabeth Custiel, Phyllis Sanderson, Neil S. Freund, James M. Galloway, University of Arizona, Tucson, AZ

Background: National database studies have reported a significant but minor delay in presentation of Native American (NA) patients with acute myocardial infarction (AMI). The Native American Cardiology Program (NACP) experience is a strong clinical impression of a markedly greater delay in rural NA patients. In order to clarify the magnitude and causes of this delay for potential intervention, the NACP prospectively studied rural NA patients and their connections to emergency facilities.

Methods: Three hundred twenty-two NA patients with AMI were evaluated at rural facilities and transferred to NACP from February 1999 through June 2006. Data obtained included demographics, ECG findings, patient symptoms, complications, laboratory findings and reasons for delayed presentation if applicable.

Results: Time to treatment (T2T) data was available for 293 patients. One hundred six patients (36%) presented greater than 12 hours (delayed) following onset of symptoms. Of these delayed patients, 64% presented greater than 24 hours after symptom onset. The overall median and mean times to presentation were 360 and 572 minutes respectively. Only 11% of the total cohort presented within the first hour after symptom onset. Distance traveled to medical facilities did not contribute to treatment delay (21.6 miles for delayed patients versus 21.2 miles for those presenting within 12 hours) although travel over unimproved roads was more common in the delayed group. Diabetes mellitus and advanced age predicted delayed presentation. The most common reason cited for delayed presentation was the patient’s own misunderstanding of symptoms (69% of delayed patients). Other potential causes of delay (traditional healer consultation, road conditions, telephone access, and EMS availability) were investigated and much less frequently reported.

Conclusions: This analysis reveals a dramatic delay in presentation of rural NA patients with AMI. Misinterpretation of symptoms was confirmed to be the predominant cause of patient delay. These findings clearly underscore the need for community-based education among rural NA’s in an effort to increase thrombolytic eligibility and to improve cardiovascular outcomes.

3:00 p.m.

**TO10-61**

Reduced Benefit of Delayed Coronary Artery Bypass Graft Surgery in Acute Coronary Syndromes

Jerme M. P. Ferreira, Carlos Aguiar, Ana Almeida, Jose Santos, Luis Santos, On Behalf of Investigators of Portuguese Registry ACS, Hospital Santa Cruz, Camafe, Portugal

Background: In pts with ACS, early coronary revascularization is increasingly used, but the optimal timing remains uncertain, especially in pts eligible for CABG. A clinical registry of ACS revealed that many Pts submitted to coronaryography and with a suitable coronary anatomy, do not proceed to CABG during the initial hospitalization and are discharged with a planned procedure. We aimed to evaluate the benefit of this unresolved delayed CABG (Cases = Planned CABG after discharge), in comparison with Pts submitted to CABG during the initial hospitalization (Controls).

Methods: A clinical registry of ACS with 44 centres prospectively enrolled 18,543 Pts since 2002. Our study included 612 Cases and 385 Controls after exclusion of Pts with cardiogenic shock and cardiac rupture. Baseline characteristics, in-hospital medications, LV function and angiographic features were similar in both groups except for recurrent angina (Cases 9% vs Controls 19%, p<0.001) and left main disease (Cases 14% vs Controls 31%, p<0.001). The study endpoint was death or MI at 6 months.

Results: CABG was performed in 61% of Cases with a median time delay of 37 d (vs 10 d in Controls, p<0.001). Mortality after CABG was similar in both groups (3.5% in Cases and 3.3% in Controls). Cumulative MI free survival at 6 months was 83.3% in Cases and 92.1% in Controls (p<0.01).

Conclusions: Our study demonstrates a reduced benefit of a post-discharge surgical coronary revascularization practice in comparison with an earlier in-hospital procedure.

3:00 p.m.

**TO10-62**

Impact of the Degree of Platelet Function on Thrombin Generation Profiles in Patients with Type 2 Diabetes Mellitus

Dominick J. Angiolillo, Bhalko Desai, Yoshie Suzuki, Lidimaria Rozum, Ronald Charton, Steven B. Shocmaker, Mohammed Aslam, Binu Jacob, Piera Capranzano, Martin Z. Zenni, Marco A. Costa, Luis A. Guzman, Theodore A. Bass, University of Florida College of Medicine-Jacksonville, Jacksonville, FL

Background: Although antiplatelet agents reduce platelet activation and aggregation processes, there is a broad interindividual variability in the effects achieved and elevated platelet activity is associated with risk of thrombosis. Activated platelets not only participate in the formation of aggregates, but also play a pivotal role in triggering the coagulation cascade by inducing thrombin generation. The aim of this study was to evaluate if the presence of elevated platelet reactivity despite the use of dual antiplatelet therapy is associated accelerated thrombin generation.

Methods: Type 2 diabetes mellitus (T2DM) patients are characterized by hyper-reactive platelets and were selected to assess the study aim. A total of 50 T2DM patients with documented coronary artery disease in a steady state (>1 month) maintenance phase of aspirin (100mg/day) and clopidogrel (75 mg/day) treatment were studied. Peak platelet aggregation was assessed using light transmittance aggregometry in platelet rich plasma following 20µmol/L adenosine diphosphate stimuli. Patients were divided in to 2 groups according to the degree of platelet reactivity: Group A (>50% aggregation) and Group B (<50% aggregation). The onset of thrombin induced platelet-fibrin clot formation, a marker of the speed of thrombin generation, and the time to the maximum rate of thrombin generation were determined by thrombelastography.

Results: Platelet aggregation was 54±15% in the overall diabetic population. Group A and Group B were composed of 30 and 20 patients, respectively. Peak platelet aggregation was significantly higher in Group A than Group B (66±8% vs 39±8%; p<0.001). The speed of thrombin generation (5.6±1.4 min vs 7.2±1.8 min; p=0.002) and the time to the maximum rate of thrombin generation (6.8±1.6 min vs 8.7±2.2 min; p=0.001) were significantly accelerated in Group A compared to Group B patients.

Conclusions: T2DM patients with elevated platelet reactivity are characterized by accelerated rates of thrombin generation. These findings may contribute to the enhanced thrombotic risk of patients who persist with elevated platelet reactivity despite the use of standard dual antiplatelet treatment regimens.

3:00 p.m.

**TO10-63**

Chronic Kidney Disease is an Early Independent Predictor of In-Hospital Death in Patients with Acute Myocardial Infarction even that with preserved left ventricular function

Rudrinay Azevedo, José Marcioni de Souza, Marcos D. Ferreira, Aurelia Musili, Edison Stefani, Antonio Carlos C. Carvalho, Federal University of Sao Paulo, Sao Paulo, Brazil

Background Chronic kidney disease (CKD) is an independent predictor of events after acute myocardial infarction (AMI). The purpose of this study was to assess renal dysfunction after AMI in a real world situation and to examine the influence of ejection fraction (EF) on the relationship CKD and in-hospital death.

Methods Our study population consisted of 613 consecutive patients with AMI (with or without ST segment elevation), evaluated within 24 hours after the onset of symptoms, mean age 61.9 (±13) years, admitted to the risk of the University Hospital from lead to the 1999 to December 2004. Previous diseases, medication in use and coronary risk factors were recorded. The Modification of Diet in Renal Disease (MDRD) study equation was
Sex-Based Differences in Mortality Following Acute Coronary Syndromes


Background: There is conflicting information about whether sex-differences modulate short-term mortality following acute coronary syndromes (ACS). We investigated the relationship between sex and mortality using a large database spanning the full spectrum of ACS.

Methods: Data from patients in 11 independent randomized ACS trials from 1993 to 2006 were pooled. This included 136,247 patients, of whom 38,046 (28%) were women. There were 102,004 (72% women) with ST-segment elevation myocardial infarction (STEMI), 14,486 (29% women) with non-STEMI (NSTE-MI), and 19,777 (40% women) with unstable angina (UA).

Results: The relationship between sex and mortality using a large database spanning the full spectrum of ACS.

Conclusions: The relationship between sex and mortality using a large database spanning the full spectrum of ACS.

A194 ABSTRACTS - Myocardial Ischemia and Infarction
Prognosis and Treatment of Acute Coronary Syndrome in Patients With No In-Hospital Coronary Angiography: Six Months Follow-up in the EMMACE-2 Prospective Cohort Study

Raifaele Bazzarri, Christine Morrell, Rajiv Das, Julian H. Barth, Alistair S. Hall, EMMACE-2 Investigators, Leeds Institute for Genetics Health and Therapeutics, Leeds, United Kingdom, University of Bologna, Bologna, Italy

Background: Patients with acute coronary syndrome (ACS) do not necessarily undergo coronary angiography. The size, medical treatment and prognosis of this group has not been assessed in a contemporary prospective cohort. Our objective therefore was to investigate the above variables among patients admitted with ACS from a U.K. community area.

Methods: The Evaluation of Methods and Management of Acute Coronary Events (EMMACE-2) registry enrolled patients hospitalized with unstable angina and myocardial infarction during a month period in 11 adjacent districts in the West Yorkshire region.

The in-hospital administration of evidence based therapy (aspirin, beta-blocker, statins and ACE-inhibitors) was compared between patients who did and did not undergo cardiac catheterization. The effect of therapy on 6-month mortality was evaluated with logistic regression models.

Results: The cohort consisted of 1,883 patients without cardiac catheterization and 601 patients with cardiac catheterization. Aspirin (71.8% vs 82.8%, p <0.001), beta-blockers (55.1% vs 77.0%, p <0.001), statins (71.1% vs 98%, p <0.001) and ACE-inhibitors (58.9% vs 64.4%, p <0.006) were less likely to be administered to patients with no-cardiac catheterization than to those with cardiac catheterization. The rate of death over a 6-month period for patients who did not undergo cardiac catheterization was remarkably higher than that of patients who underwent cardiac catheterization (23.7% vs 4.3%, p <0.001).

The risk reduction of evidence based therapies on 6-month mortality was of greatest magnitude and statistical significance (p <0.001) in those patients with no-cardiac catheterization [aspirin: OR 0.48 (95% CI: 0.36-0.63); beta-blocker: OR 0.41 (95% CI: 0.31-0.50); statins: OR 0.43 (95% CI: 0.33-0.58); ACE-inhibitor: OR 0.46 (95% CI: 0.39-0.60)].

Conclusions: We observed that patients who did not undergo cardiac catheterization are also much less likely to be treated with evidence based therapies for ACS. Simplicistically, aggressive medical treatment must be applied more consistently to patients identifiable by the active clinical decision not to investigate with cardiac catheterization.

Genetic Polymorphisms and the Cardiovascular Risk of Cyclooxygenase-2 Inhibitors

Christine St.George, Germaine Hanley, Peter Bogaty, Lucy Boyer, Jamie C. Engert, James M. Brophy: McGill University, Montreal, QC, Canada

Background The cardiovascular safety of cyclooxygenase-2 (COX-2) selective non-steroidal anti-inflammatory drugs (NSAIDs) is of concern, although the majority of users remain free of adverse outcomes. A gene-drug interaction may contribute to the variation in individual response to COX-2 inhibitors.

Methods In a case-only study of 460 patients selected from a cohort admitted for myocardial infarction or unstable angina, we genotyped 84 tagging single nucleotide polymorphisms (SNPs) spanning seven candidate genes plus 21 additional SNPs of cyclooxygenase-1 (COX-1) gene. We identified 115 exposed patients who reported treatment with rofecoxib (n=43), celecoxib (n=49) and the matched unexposed subjects (n=276), the association between coxib exposure and genotype strengthened and remained free of adverse outcomes. A gene-drug interaction may contribute to the variation in individual response to COX-2 inhibitors.

Results We observed statistically significant gene-drug interactions between NSAID exposure and 16 SNPs. Furthermore, the study group was limited to subjects exposed to rofecoxib (n=43) or celecoxib (n=49) and the matched unexposed subjects (n=276), the association between coxib exposure and genotype strengthened and remained significant for 4 SNPs. Using the homozygous major allele as a reference, the homozygous minor allele yielded statistically significant case-only odds ratios for a SNP in the C-Reactive Protein (CRP) gene [OR=3.6, 95% confidence interval (CI): 1.6 - 7.9, p <0.001] as well as two SNPs in the cyclooxygenase-1 (COX-1) gene [OR=6.9, 95% CI: 1.5 - 35.7; p=0.02 and OR=6.9; 95% CI, 1.3 - 35.6; p=0.02]. Within the Klotho gene, the heterozygote of one SNP yielded a statistically significant case-only odds ratio of 2.3 (95% CI: 1.4-4.0, p=0.02).

Conclusions Genetic polymorphisms within the COX-1, CRP and Klotho genes are associated with increased risk of cardiovascular events and death in patients exposed to COX-2 inhibitors. Further studies are warranted to elucidate optimal indications for EI strategy for ACS.
Results: Baseline TIMI grade on 1-month mortality in 1,168 NSTEMI patients treated with early invasive strategy.

Conclusions: In NSTEMI patients treated with early invasive strategy, baseline TIMI grade is an independent predictor of 1-month mortality.
1010-77
An Invasive Management Strategy is the Only Therapeutic Intervention Associated with Improved Survival in Acute Coronary Syndrome complicated by Hemodynamic Compromise

Benjamin K. Dunston, Luan T. Huynh, Stephen G. Worthing, Ashish Soman, David B. Brieger, Derek P. Chew, University of Adelaide, Adelaide, Australia, Flinders University, Adelaide, Australia

Introduction: The presentation of Acute Coronary Syndrome (ACS) is commonly complicated by heart failure or other hemodynamic compromise. Therapeutic trials targeting such high risk patients remain limited however: We sought to assess the impact of contemporary management strategies on clinical outcomes in ACS complicated by hemodynamic compromise.

Methods: The Australian Collaborative Acute Coronary Syndrome Prospective Audit (ACACIA, n=3402, PML0051) is a prospective, multi-centre registry of ST-segment elevation myocardial infarction and intermediate- to high-risk non-ST-segment elevation ACS patients from 39 Australian metropolitan and rural sites. ACS patients presenting with Hemodynamic Compromise (HC) (defined as Killip Class ≥2, Systolic Blood Pressure <100mmHg) were the focus of this investigation. Patient characteristics, management and clinical outcomes were assessed. Results: 647 patients fulfilled the pre-specified analysis criteria. Patients with HC were older (mean 69.8 vs 63.2yrs, p<0.0001), with a higher prevalence of diabetes (31.9 vs 21.2%, p<0.0001) and renal impairment (mean eGFR 64.1 vs 73.3mL/min, p<0.0001). The presence of HC at hospital presentation was associated with markedly increased in-hospital (HR 6.3, 95% CI 2.9-9.4 p<0.0001) and 12-month (HR 5.1, 3.8-6.8 p<0.0001) mortality, with incremental Killip Class predicting worsening survival (p<0.03). After multivariate adjustment, survival was only revealed to be an independent management strategy was the only therapy associated with improved in-hospital (HR 0.41, 0.22-0.74 p=0.003) and 12-month survival (HR 0.43, 0.31-0.60 p=0.001), with benefit seen across all Killip grades. Conclusion: In this large real-world study, an invasive management strategy was the only therapeutic intervention associated with improved outcomes in ACS complicated by HC at hospital presentation. Further efforts are necessary to improve the provision of recommended therapies in such high-risk ACS patients.

3:00 p.m.

1010-78
Abnormal glucose metabolism in acute myocardial infarction - association with NT-proBNP and prognosis

Dan E. Høfsten, Brian B. Løgstrup, Jacob E. Møller, Kenneth Egstrup, Department of Medical Research, Fonden Hospital, Svendborg, Denmark, Department of Cardiology, Rigshospitalet, Copenhagen, Denmark

Background: Abnormal glucose metabolism is common in patients with acute myocardial infarction (MI), and is associated with impaired prognosis, particularly to post-MI congestive heart failure (HF). We hypothesized that increased neurohumoral activation, expressed by elevated levels of N-terminal B-type natriuretic peptide (NT-proBNP) could signal an important pathophysiological pathway. Methods: NT-proBNP levels were assessed in 197 consecutive patients during admission for acute MI. Values were log-transformed for statistical analysis. Using echocardiography, we also assessed left ventricular systolic function by using a regional 16-segment wall motion score index (WMSI), and diastolic function using early to late diastolic mitral annulus velocity (E/e'). Patients without a previous diagnosis of diabetes (DM), underwent a standardized 75g oral glucose tolerance test and were, using glucose metabolism independently predicted outcome in multivariable survival analysis (P<0.01 for both variables). Conclusions: In acute MI, abnormal glucose metabolism is associated with increased neurohumoral activation beyond what can be explained from estimates of left ventricular dysfunction and wall motion signs of HF. However, estimates of glucose metabolism and NT-proBNP both provide independent additional prognostic information in such patients.

3:00 p.m.

1010-79
Plaque rupture and morphological characteristics of the culprit lesion in acute coronary syndromes without significant angiographic lesion: analysis by intravascular ultrasound

Marie-Jeanne ALIBELLI-CHEMARIN, H o r m a O U D O Z E I N, Jr., Remy CAGNAC, Jr., Jerome Roncalli, Br, Didier CARRE, Sr, Jacques PUEL, Sr, Meyer ELBAZ, Sr., Federation of Cardiology Rangueil Hospital, Toulouse, France

Background: The main purpose of this study was to assess the morphological characteristics of the culprit lesion with plaque rupture, by intravascular ultrasound (IVUS), after acute coronary syndrome (ACS) without significant angiographic stenosis (≤50%). The second purpose was to quantitatively assess the culprit lesion and the arterial remodeling.

Methods: IVUS was performed in 68 patients (46.8 years +/- 11.9) after ACS (21 ST + and 47 ST-) without significant angiographic lesion (% stenosis: 31% +/- 15%). IVUS was performed 12 days after ACS, before any interventional procedure, if the plaque was identified as a cavity within plaque, communicating with the arterial lumen and having an overlying residual fibrous cap fragment. At the culprit lesion, qualitative analysis has defined the type of plaque and quantitative analysis has evaluated plaque plus media area, plaque volume, plaque burden, total plaque area, positive remodeling index, and clinical outcomes were assessed.

Results: Patients were divided into 2 groups: Group I with plaque rupture and Group II without rupture. After qualitative analysis of plaque, we studied plaque plus media, plaque volume, plaque burden and remodeling index. Results: Patients were divided into 2 groups: Group I with rupture (25 patients 36.8%), Group II without rupture (43 patients 63.2%). All patients with rupture showed soft or mixed plaque but no calcified plaque. The average length of plaque was 19.3 ± 9.0 in Group I vs 17.6 ± 8.9 mm (ns). In Group I, plaque rupture was associated with a larger plaque burden (48.9% ± 12.3 vs 39.8% ± 12.0, p=0.005), a more significant plaque plus media area (7.44 mm² ± 2.9 vs 5.24 mm² ± 2.4, p=0.001), a greater plaque volume (151.9 mm³ ± 103.4 vs 99.2 mm³ ± 81.6 p=0.007) and a higher ratio of plaque volume over length (8.0 mm³/mm ± 3.8 vs 5.8 mm³/mm ± 3.7, p=0.003). In group I, positive remodeling was more frequent than intermediate remodeling (p=0.03) or negative remodeling (p=0.005). In group II, there was no significant difference between the 3 types of remodeling. Conclusions: The plaque ruptures responsible for ACS frequently appear on voluminous plaques with a large plaque burden and positive arterial remodeling.

3:00 p.m.
Prehospital Wireless Transmission of STEMI Electrocardiograms to a Cardiologist Reduces Door-to-PCI Times to Less than Half of the ACC/AHA Guidelines

Benjamin A. Lee, George L. Adams, Paul T. Campbell, Janet Patterson, Charles Maynard, Galen S. Wagner, Duke University Medical Center, Durham, NC

Background: Percutaneous coronary intervention (PCI) for STEMI reduces morbidity and mortality if performed rapidly. However, the ACC/AHA <90 minute goal for door-to-PCI time is infrequently accomplished.

Methods: The Timely Intervention in Myocardial Emergency • NorthEast (TIME-NE) study enrolled 422 STEMI patients during three two-year phases: 1) pre-intervention - transmission of electrocardiograms (ECGs) unavailable, 2) intervention - study of wireless ECG transmission to a cardiologist’s hand-held computer, and 3) follow-up - ECG transmission available in routine clinical practice. This study tests the hypothesis that pre-hospital ECG transmission to a cardiologist reduces door-to-PCI time not only during the study period, but also into follow-up routine clinical practice.

Results: A pre-hospital ECG transmission system at NorthEast Medical Center reduced door-to-PCI times for both EMS-transport and self-transport patients. The door-to-PCI times were significantly lower for the ECG Transmission group vs. the No ECG Transmission group (<0.0001 and p<0.0001) in both the pre-treatment and follow-up phases. Despite fewer ECG transmissions during the follow-up phase than during the intervention phase, a median time reduction of 25 minutes was maintained (Transmission vs. No transmission).

Conclusion: Pre-hospital ECG transmission to a cardiologist reduces door-to-PCI time for patients with STEMI to less than half of the ACC/AHA recommended goal of 90 minutes.

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Pre-intervention</th>
<th>Intervention</th>
<th>Follow-up</th>
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<tbody>
<tr>
<td>2001-2003</td>
<td>105</td>
<td>106</td>
<td>82</td>
</tr>
<tr>
<td>2003-2005</td>
<td>73</td>
<td>37</td>
<td>38</td>
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<tr>
<td>2005-2007</td>
<td>38</td>
<td>31</td>
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A198 ABSTRACTS - Myocardial Ischemia and Infarction

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Conclusion: Pre-hospital ECG transmission to a cardiologist reduces door-to-PCI time for patients with STEMI to less than half of the ACC/AHA recommended goal of 90 minutes.
Methods: In this single center cohort study, 1206 STEMI patients underwent primary PCI between 2000 and 2005. STR was defined as the relative difference (in %) of the summed ST deviation between the 12-lead electrocardiogram (ECG) recorded on admission and the 12-lead ECG recorded immediately prior to PCI. TIMI flow through the culprit vessel was determined at first angiographic film of the infarct related coronary artery. Coronary artery occlusion was defined as TIMI flow 0 or 1. Results: Coronary artery occlusion was observed in 911 patients (75.5 %) at coronary angiography preceding primary PCI. The ROC-curve revealed that STR was predictive for TIMI flow prior primary PCI (area under the curve = 0.72; p < 0.0001). Figure 1 shows the percentage of patients with pre-procedural occlusion as a function of the degree of STR (p for trend < 0.0001). Conclusions: It is apparent that although STR is associated with TIMI flow prior primary PCI, it is an imperfect, non-invasive measure of spontaneous reperfusion. Therefore, adequate STR should not restrain from performing coronary angiography in STEMI.
cardiac biomarker positivity calculated as previously published (1). Mortality rates across TRACS score categories by upstream vs. downstream (cath lab) use of GP2b3a agents were ascertained.

Results: Overall GPI were used in 1,376 (40%) pts of which “upstream” use was in 543 (15.7%) pts (294 (8.5%) in ER, 249 (7.2%) in CCU or chest pain unit). Upstream GPI use was strongly associated with survival benefit (OR 0.47, p<0.04, 95% CI 0.22-0.89). This survival benefit was seen to be greater in the patients with higher categories of the TRACS score (Figure 1).

Conclusions: There was a strong survival benefit seen with upstream GPI use in this prospective registry. This survival benefit was greater across higher categories of the previously published TRACS score. The TRACS score may be used to guide early, upstream initiation of GPI agents.

11:00 a.m.

1017-44 The Relationship between ECG Computer Interpretation and Catheterization Laboratory Activation Time in Patients with Suspected ST Elevation Myocardial Infarction

Muhammad Arias, James K. McCord, Akshay Khandelwal, Steven Mast, Karthik Iyer, Glenn Tokarz, Nabi Khoury, Aaron Kugelmann, Henry Ford Heart and Vascular Institute, Detroit, MI

Background: The benefit of primary angioplasty for treatment of ST Elevation Myocardial Infarction (STEMI) is highly time dependent. Many primary angioplasty centers rely on computer-generated ECG interpretation for initial patient triage. We sought to determine the relationship of different computer ECG interpretations on emergency department arrival time to CLA in patients presenting with suspected STEMI.

Methods: We included consecutive patients with suspected STEMI from 9/2003-6/2006 who had ECG changes that met criteria for reperfusion therapy and had subsequent CLA at our institution. ECG computer interpretation results were categorized into 5 groups: acute MI, Left Bundle Branch Block (LBBB), MI of unknown onset, normal and other.

Results: 392 patients were analyzed in the study. Overall, the computer interpretation was acute MI in 277 (71%) of cases. The different door to activation time during different ECG groups is listed in the table below. Overall, there was a significant time difference between the acute MI group vs. all other patients (12 ± 13 vs. 46 ± 74 minutes; 95% CI: 10-14 vs. 33-60, p < 0.0001).

Conclusions: Physician based ECG interpretation lead to CLA in 29% of patients in whom the computer based interpretation did not identify as acute MI. This resulted in significant delays in door to initiation time in this group of patients with suspected STEMI. A new protocol to overcome the limitation of this approach is currently being implemented and studied.

<table>
<thead>
<tr>
<th>ECG Group</th>
<th>Number of patients</th>
<th>Door to activation time (minutes)</th>
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<tbody>
<tr>
<td>Acute MI</td>
<td>277</td>
<td>12 ± 13</td>
</tr>
<tr>
<td>MI unknown onset</td>
<td>69</td>
<td>43 ± 51</td>
</tr>
<tr>
<td>LBBB</td>
<td>9</td>
<td>14 ± 10</td>
</tr>
<tr>
<td>No change</td>
<td>6</td>
<td>17 ± 20</td>
</tr>
<tr>
<td>Other</td>
<td>31</td>
<td>46 ± 115</td>
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</table>

11:00 a.m.

1017-45 Implications of History of Clinical Coronary Heart Disease on Incident Heart Failure in the Elderly

Andreas Kalogeropoulos, Vasiliki Georgiopoulou, Syed A. Agha, Nicolas Rodondi, Melissa Garcia, Douglas Bauer, Suzanne Sattlerfield, Anne Newman, Andrew Smith, Tamara Harris, Stephen Kritchevsky, Javed Butler, for the Health ABC Study, Emory University, Atlanta, GA

Background: Although clinically manifest coronary heart disease (CHD) is a major risk factor for heart failure (HF), many elderly subjects may develop HF in the absence of a coronary event, often ascribed to age-related ventricular changes. The epidemiologic and clinical significance of incident HF in the elderly with and without CHD is not well described.

Methods: We compared clinical characteristic and outcomes between 477 participants with CHD at baseline (age 74.0 ± 2.8 years, 38% females, 40% blacks) and 2320 participants with new HF without baseline CHD, 35 (22.8%) were hospitalized for MI and 39 (25.5%) for angina prior to new HF development; overall 66/153 (43%) developed a coronary event prior to HF whereas 87/153 (57%) developed HF without any preceding coronary event. In the 2.4 ± 1.1 year follow-up period post-HF development, participants with prior coronary event had higher mortality as compared to those who died (26% vs. 13% per year, p<0.013 unadjusted, p<0.070 after adjustment for gender, race, and age), and similar re-hospitalization rate (68% vs. 59%, p<0.030). In comparison, participants with baseline CHD who developed HF had 18% per year mortality by 1 year and 79% re-hospitalization rate.

Conclusions: Although prevalent CHD is a major risk factor for incident HF, subjects who develop HF without an intervening coronary event may have at a higher mortality risk, underscoring the need to study this group further.

11:00 a.m.

1017-46 Evaluation of Coronary Artery Disease in Women Using Magnetocardiography

Amelia Young, Indraneil Ray, David Gallegos, Melissa Silvka, Jana Williams, Margo Minnaska, Theresa Polk, C. Noel Baiery, Merz, Robert Siegel, Kirsten Tolstrup, Cedars-Sinai Medical Center, Los Angeles, CA

Background: Women have an increased death rate from coronary heart disease (CHD) compared to men, partly due to delays in diagnosis. Magnetocardiography (MCG) is a rapid, noninvasive scan that has the ability to detect ischemia without exposure to radiation using an automated analysis that collects, processes, and analyzes the magnetic field generated by the heart’s electrical activity.

Methods: A 6 minute resting MCG scan (9-channel CMI 2406) was performed in 35 women presenting with chest pain (study group), and 19 normal controls (control group). Automated MCG analysis of cardiac repolarization was performed and results were available immediately. All patients were angina free at the time of scanning. Sensitivity, specificity, and predictive values were calculated for typical or atypical angina secondary to CHD as determined after noninvasive and invasive work up.

Results: The mean age for women in the study group was 61 ± 13 years. The prevalence of cardiovascular risk factors was high: hypertension 60%, diabetes 32%, hyperlipidemia 71%, smoking 32%, family history 37%, prior infarct 23%, and prior CABG 6%. The control group women included in this study had no cardiac risk factors, and had normal ECG. In the study group, 12-lead ECG was normal in 80%, and 88% had normal troponin I. An abnormal MCG was significantly associated with the presence of myocardial ischemia (p<0.0001). The specificity, sensitivity, positive and negative predictive values for the ECG for ischemia were 40%, 88%, 57%, and 79%, respectively, compared to 100%, 80%, 67% and 100%, respectively for MCG. In comparison, the sensitivity, specificity, positive and negative predictive values for single photon emission computed tomography scan were 83%, 83%, 71% and 91%, respectively.

Conclusion: Magnetocardiographic scanning detects CHD in women with high diagnostic accuracy. These results suggest that MCG scanning may be useful for the early diagnosis of myocardial ischemia and thus may facilitate timely interventions and treatment in women.

11:00 a.m.

1017-47 Carotid Plaque Inflammation in Patients with Acute Coronary Syndrome Assessed by 18F-fluorodeoxyglucose Positron Emission Tomography

Jin Won Kim, Sung Eun Kim, Soon Yang Suh, Cheol Ung Choi, Jin Oh Na, Eung Joo Kim, Seung-Woon Rha, Chang Gyu Park, Hong Seog Bae, Dong Joo Oh, Cardiovascular Center Korea University, Guro Hospital, Seoul, South Korea, Nuclear Medicine, Korea University Guro Hospital, Seoul, South Korea

Background: A systematic plaque instability is suggested in patients with acute coronary syndrome. Plaque inflammation could be assessed by 18F-fluorodeoxyglucose Positron Emission Tomography (18FDG PET). We investigated whether carotid plaque inflammation could be related to coronary plaque instability using 18FDG-PET.

Methods: In 50 (male 14, 48±7.7 yrs) patients who were newly diagnosed as acute coronary syndrome (28 patients, male 6, 46±7.9 yrs) or stable angina (22 patients, male 13, 49.5±9.8 yrs), the co-registration of PET and contrast enhanced computed tomography (CT) images was performed within 1 week after percutaneous coronary intervention. Regional (neck) PET/CT imaging at 1 hour (early scan) and additional scan at 2 hours (delayed scan) after 555 MBq of 18FDG injection and the multi-slice CT angiogram were acquired at 180 min on the Philips GEMINI TF scanner with 16 slice CT. The maximum standardized uptake values (SUV) of individual plaques were measured in individual plaques. Results: In all patients, carotid plaque with increased 18FDG uptake was observed in the fused PET/CT images. Age and gender-adjusted SUV of FDG on delayed scan was significantly higher in the carotid plaques of patients with acute coronary syndrome than those of patients with stable angina (mean 4.13±1.24 (3.9 to 5.27) vs. 2.87±0.98 (2.2 to 4.25, p<0.0003). There were no differences of risk factors between two groups.

Conclusions: The patients presenting with acute coronary syndrome demonstrate simultaneous increase of inflammatory activity of the carotid plaque, supporting a potential causal role of inflammation regarding widespread plaque destabilization associated with acute coronary syndrome.
Nationwide trends in the incidence of acute ST elevation myocardial infarction (STEMI) in the United States

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) in a very large data base from 1988 to 2004.

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 STEMI were used to compile the data. Patient demographic data was also 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. The mean age for these patients was 66.06 ± 14.69 years old. Male has almost twice adjusted STEMI rate than female (male: 62.4%, female: 37.6%). From 1988 the age-adjusted rate for acute STEMI remained steady for 8 years (108.32 per 100,000 (95%CI=99.06-117.58) in 1988 and 102.56 per 100,000 (95%CI=94.70-110.42) in 1996). However, from 1997, the age-adjusted incidence of STEMI steeply declined to half of the incidence of previous 8 years (50.06 per 100,000 (95%CI=46.59-53.53) by the year 2004 (P<0.01)(see figure).

Conclusion: The incidence of STEMI was stable from 1988 to 1996 with steady linear decline to half by the year 2004. The cause of steady decline in STEMI rate is not known. It is most likely reflecting the advancement in the prevention and treatment of atherosclerosis risk factors.
Low Molecular Weight Dalteparin As An Adjunct In Treatment Of Acute Myocardial Infarction: A Meta-Analysis
Amol A. Bahekar, Rohit Arora, Sarabjeet Singh, Ahmad Khalediat, Janos Moinar, Param Prasad Singh, Sandeep Khosla, Rosalind Franklin University/Chicago Medical School, North Chicago, IL

Background: Aim of the current study is to evaluate the effectiveness of short-term and long-term dalteparin in preventing new cardiovascular (CV) events after an episode of acute myocardial infarction (AMI).

Methods: A systematic review of the literature revealed 3 randomized controlled trials comparing short-term dalteparin with unfractionated heparin (UFH) and 4 randomized controlled trials comparing long-term dalteparin with placebo in AMI. Heterogeneity of the studies was assessed by Cochran’s Q test. The Mantel-Haenszel fixed-effect model was used to calculate combined relative risks (RR) for those outcomes where the studies were homogeneous and the random effect model was used when the studies were heterogeneous.

A two-sided alpha error of <0.05 was considered to be statistically significant.

Results: No significant difference was seen in the 7 day mortality, revascularization and risk of bleeding when dalteparin was compared to UFH. The risk of death or infarction was significantly reduced with long-term (up to 45 days) dalteparin as compared to placebo group (RR: 0.76; CI: 0.627-0.920). There was an increased risk of minor hemorrhage (RR: 1.912; CI: 1.308-2.796) but no major hemorrhage (RR: 1.411; CI: 0.417-4.776) with dalteparin. The rate of revascularization was decreased with dalteparin use as compared to placebo (RR: 0.819; CI: 0.713-0.941).

Conclusions: Long-term dalteparin lowers CV endpoints in AMI when compared to placebo, but it is not superior to UFH in short-term treatment of AMI.

Primary Percutaneous Coronary Intervention Performed During Nightshift Hours Was Associated With Increased In-Hospital Mortality in Patients With ST Elevation Myocardial Infarction. Results From EUROTRANSFER Registry
Zbigniew Sudak, Tomasz Rakowski, Artur Dzieriew, Wojciech Zasada, Michal Brezinski, Magnus Janzoon, Ralf Birkemeyer, Dariusz Dudek, Department of Interventional Cardiology, Krakow, Poland

Background: Scattered evidence suggest that there might be a trend towards poorer outcome of ST-Elevation Myocardial Infarction (STEMI) patients treated by Primary Percutaneous Coronary Intervention (PCI) during night hours.

Methods: Consecutive 1,650 STEMI patients treated with PCI were enrolled in 7 European countries in the setting of hospital networks from November 2005 to January 2007. Two patients who died during transport to cathlab were excluded from the analysis. Patients were divided into two groups according to their time of admission to cathlab, from 8 am - 5.59 pm (Dayshift) and from 6 pm - 7.59 am (Nightshift). Shift cut-off points were chosen based on daily schedules of the participating centers.

Results: There were 985 patients admitted during Dayshift and 663 during Nightshift. Patients in both groups did not differ in baseline demographics and clinical status. Overall time from chest pain onset to balloon inflation was similar in Dayshift and Nightshift respectively (301±223 vs 296±225 minutes). Infarct related artery patency (TIMI 2+3) in baseline angiography was similar (27% in both groups). Nightshift admission was an independent predictor of in-hospital death in multivariate regression analysis model (OR 1.47, 95%CI 1.11-1.94, p=0.007).

Conclusions: Performing PCI for STEMI patients in the setting of hospital networks during night hours is an independent predictor of poorer immediate clinical outcome of these patients, namely higher in-hospital mortality.

randomized trial of early vs. late abximab administration in patients undergoing primary angioplasty: infarct size assessment with magnetic resonance imaging (the Myocardial Perfusion Study)
Anna S. Petronio, Marco De Carlo, Alessandra Mazzoni, Elisabetta Strata, Federica Castellano, Roberto Gistri, Nicola Ciabatti, Giovanni D. Aquaro, Umberto Pandosso, Gabriele Borelli, Maria Grazia Delle Donne, Massimo Lombardi, Sergio Berti, University of Pisa, Pisa, Italy, Institute of Clinical Physiology, Massa, Italy

Background: Abciximab improves outcome in patients undergoing primary percutaneous coronary intervention (PCI). Our aim was to demonstrate that early abciximab (before transfer from remote hospital to cath lab) compared to late abciximab (during PCI) enhances myocardial salvage, as assessed by magnetic resonance imaging (MRI).

Methods: At present, a total of 107 patients (out of 120 intended) admitted <6 hours to remote hospitals with anticipated delay to PCI >45 minutes, were prospectively randomized to either Early (57 pts) or Late (50 pts) abciximab administration. Four days after PCI, contrast-enhanced MRI was performed (99 patients) to assess perfusion defects (identified by delayed enhancement, DE). Cardiac MRI was repeated after 6 months to assess myocardial salvage (48 patients). Complete data will be presented.

Conclusions: Performing PPCI for STEMI patients in the setting of hospital networks during night hours is an independent predictor of poorer immediate clinical outcome of these patients, namely higher in-hospital mortality.

Medications and Clinical Outcome
Medications pre-cathlab Dayshift(n=985) Nightshift(n=663) p value
Aspirin 94.7% 93.7% 0.365
Epicardial loading dose > 300 mg 59.1% 34.1% 0.169
Thrombolyis 3.1% 7.8% <0.0001
Early abximab 43.7% 44.7% 0.719
Outcome Parameters
Death in-hospital 3.1% 5.3% 0.022
Death+reMI in-hospital 3.8% 5.9% 0.044
Death at 30 days 4.6% 6.5% 0.089
Major bleeding requiring transfusion 1.9% 1.8% 0.653

Bypassing the Emergency Room After Pre-Hospital ECG Transmission as a Major Contributor to Reduced Door-to-Ballooon Times in Patients With Acute ST-Elevation Myocardial Infarctions
Donnsta Aehrensnn, Karl-Henich Schorr, Holger Dudaial, Rolf Nitsche, Georg von Knobelsdorff, Reinhard Hilgers, Friedrich Keyling, St. Bernard Hospital, Hildesheim, Germany, University of Vermont, Burlington, VT

Background: Streamlining diagnosis and treatment of patients with ST-elevation myocardial infarction (STMI) reduces time to revascularization. We prospectively examined the effects of a strategy to bypass the emergency room in those patients in whom the diagnosis was established pre-hospital with a transmitted 12-lead ECG.

Methods: All patients with STEMI transported by ambulance to a center with 24-hour primary PCI capability in semirural Germany over an 18-month period (1/2006 to 6/2007) were included. Patients transferred from other hospitals were excluded. All ambulances serving the hospital were equipped with portable 12-lead ECG machines capable of wireless transmission. The previously established protocol for diagnosing, transporting and treating patients with STEMI included the goal of transmitting a 12-lead ECG (tele-ECG) for every patient suspected of having an acute MI. Time sheets were used to prospectively assess time points from first patient contact to balloon inflation and to record whether a tele-ECG was performed.

Results: During the study period, 130 patients presented to the PCI center with STEMI. A tele-ECG was obtained and transmitted in 107 patients (82%). The mean contact-to-balloon time was 101 min (median 96 min) in patients without tele-ECG as compared to 76 min (median 75 min) in those with tele-ECG (p=0.0001). A significant reduction in mean door-to-balloon time from 66 min (median 54 min) to 34 min (median 29 min) was observed in patients with tele-ECG transmission (p=0.0005). Of those patients receiving a tele-ECG, 82% (77%) bypassed the emergency room with a direct handoff from the emergency response team to the catheterization lab staff. In this group of patients, mean door-to-balloon time was 28 min (median 26 min) as compared to 53 min (median 50 min) in patients with tele-ECG not bypassing the ER (p=0.0001). Thus, most of the time savings seen in the group of patients who received a tele-ECG were attributable to the subgroup who bypassed the emergency room.

Conclusion: Bypassing the emergency room on the way to the catheterization laboratory is associated with a marked reduction in time to revascularization in those patients with STEMI who receive a pre-hospital ECG.
Percutaneous Coronary Intervention with Off-site Cardiac Surgery Backup for Acute Myocardial Infarction as a Strategy to Reduce Door-to-Balloon Time

Victor A. Umanz, Hans O. Peels, Hans de Swart, Raymond Haudwast, Medical Center Alkmaar, Alkmaar, The Netherlands

Background: We sought to determine whether primary percutaneous coronary intervention (PCI) for patients admitted with an acute ST-segment elevation myocardial infarction (STEMI) can be performed more rapidly and with comparable outcomes in a community hospital vs. a tertiary center with cardiac surgery. Method: We studied the first 514 PCI with off-site surgery program in the Netherlands in 2002 and reported the results of 739 consecutive pts. Results: In the safety phase, 199 pts presenting with STEMI were randomly assigned to treatment at our off-site center vs. a more distant cardiac surgery center. In the confirmation phase, 540 consecutive patients were treated in the off-site hospital. Safety and efficacy endpoints were the rate of angiographically successful PCI procedure (diameter stenosis <50% and TIMI 3 flow) in the absence of major adverse cardiac and cerebrovascular events (MACCE) at 30 days. The randomization phase showed a significant decrease of 37 minutes in door-to-balloon time (p<0.001) with comparable procedural and clinical success (91% TIMI-3 flow in both groups). In the confirmation phase, the 30-day MACCE-free rate was 95%. None of the 739 patients in the study required emergency surgery for failed primary PCI. Conclusion: PCI at hospitals with off-site cardiac surgery backup can be considered as one of the needed strategies to improve access to primary PCI for a larger segment of the population basis, and can be delivered with a very favorable safety profile.

Impact of Spontaneous Reperfusion in Diabetics with Acute Myocardial Infarction

Kevin R. Raeymaekers, Yuling Fu, Christopher B. Granger, Christian W. Hamm, David R. Holmes, Jr., William W. O'Neill, Ricardo Seabra-Gomes, Matthias E. Pfisterer, Frans Van de Werf, Paul W. Armstrong, APEX AMI Investigators, University of Alberta, Edmonton, AB, Canada

Background: Spontaneous(498,418),(658,428)reperfusion (SR) in STEMI is known to improve clinical outcome, yet its incidence and impact among diabetics is unclear. Accordingly, in the APEX AMI study we report a systematic analysis of SR in the 15.5% of diabetics versus non-diabetic patients. Methods: A total of 4,944 patients undergoing primary PCI in APEX AMI whom both core lab ECG and investigator determined TIMI flow grade data were studied. Results: Overall, SR defined as pre-PCI TIMI 3 flow occurred in 11.5% of patients. SR was less common in diabetics (9.2%, 70/764) as compared to non-diabetics (11.9%, 498/4180, p=0.031). The table shows angiographic, ECG, baseline glucose and 90 day outcomes comparing presence or absence of SR in the total patient population, diabetics, and non-diabetics.

Conclusion: These data indicate that while SR is less common in diabetics, it is associated with comparable subsequent epicardial flow post PCI to non-diabetics and improved clinical outcomes in contrast, diabetics without SR have achieve diminished epicardial patency with impaired microvascular perfusion post PCI likely contributing to their worse clinical outcomes.

ABSTRACTS - Myocardial Ischemia and Infarction

Incidence and Bleeding Outcomes of Excess Unfractionated Heparin Dosing Among Patients with ST-Segment Elevation Myocardial Infarction Undergoing Fibrinolysis

Tracy Y. Wang, Anita Y. Chen, Eric D. Peterson, Karen P. Alexander, E. Magnus Ohman, W. Brian Gibler, Matthew T. Roe, Duke Clinical Research Institute, Duke University Medical Center, Durham, NC, USA

Background: Practice guidelines recommend heparin therapy for patients (pts) with ST-segment elevation myocardial infarction (STEMI) undergoing fibrinolysis, yet an associated increased bleeding risk is well known. Methods: We examined the incidence of excess unfractionated heparin dosing and subsequent bleeding complications among 964 STEMI pts treated with fibrinolics in the CRUSADE initiative (2004-2006). Excess dosing was defined as a bolus dose >60 U/kg or an infusion dose >12 U/kg/hr, and was stratified into mild and major (bolus >70 U/kg or infusion >15 U/kg/hr) excess. Generalized estimating equations method was used to compare bleeding risk among groups. Results: A total of 758 fibrinolytic-treated STEMI pts (79%) received adjunctive unfractionated heparin therapy. Among these, 49% received an excess dose while 16% received a major excess dose. Female sex and low body mass were significantly associated with excess dosing (ORs 2.17 [1.32, 3.56] and 2.65 [2.03, 3.47], respectively). Pts who received major excess dosing had higher unadjusted rates of bleeding and transfusion compared with pts without excess dosing (Table). After adjustment, a trend persisted for the association with higher transfusion risk. Conclusion: Almost half of STEMI pts treated with fibrinolics received excess heparin dosing that was associated with increased bleeding. Careful attention to dosing may limit the compounded bleeding risk when heparin is used in conjunction with fibrinolytic agents.

The Smoker’s Paradox with a Clopidogrel Twist: Insights from CLARITY-TIMI 28

Nilan R. Desai, Jessica L. Mega, Wei Guo, Christopher P. Cannon, Marc S. Sabatine, TIMI Study Group, Cardiovascular Division, Brigham and Women’s Hospital, Boston, MA, USA

Background: Clopidogrel is a prodrug that needs to be converted into its active metabolite by cytochrome P450 enzymes. One of these enzymes, CYP1A2, is potently induced by cigarette smoking and has a half-life of 1.6d. We hypothesized that acute therapy with clopidogrel would be especially effective in smokers. Methods: We examined the effect of clopidogrel on outcomes in CLARITY-TIMI 28, a randomized trial of clopidogrel vs placebo in STEMI patients undergoing fibrinolysis. Patients were stratified by smoking intensity. Formal interaction terms in logistic regression models were used to test for effect modification by smoking on clopidogrel. Results: 1,732 patients were not current smokers and 1,697 were, the latter consisting of 206 light (1-9 cigs/d, median=5), 364 moderate (10-19 cigs/d, median=10), 715 heavy (20-29 cigs/d, median=20), and 422 very heavy smokers (30+ cigs/d, median=40). Current smokers were younger and less likely to have hypertension or diabetes, present with an anterior MI, and get a fibrin-specific lytic. The benefit of clopidogrel on angiographic and clinical events was greater in higher intensity current smokers, even after adjusting for differences in baseline characteristics (Fig). Conclusion: A greater benefit of clopidogrel was observed in >20 cigs/d current smokers. A potential explanation is increased CYP1A2 activity and hence greater ADP-receptor antagonism. The differential effects of clopidogrel based on current smoking status merits further exploration.
Constraining ex Vivo and In Vitro Effects of Pexelizumab on Complement Activation and Cell Apoptosis in Patients With ST-Stage Elevation Myocardial Infarction Undergoing Primary PCI: A Substudy of The APEX-AMI Trial

Catherine Martel, Benoît Labarthé, Jacinthe Rivard, Marta Ghitescu, Arnaud Bonnetoy, Pierre Thérioux, Montreal Heart Institute, Montreal, QC, Canada, University of Montreal, Montreal, QC, Canada.

Background: Complement (C) activation and apoptosis are involved in the pathophysiology of STEMI. Yet, Pexelizumab (PEX), a mAb to C5 designed to prevent activation of terminal complement (Term C), failed to benefit STEMI patients enrolled in the APEX-AMI trial. We therefore explored why and examined C activation and cell apoptosis in patients treated with PEX or placebo.

Methods: Blood was obtained from 45 patients enrolled at MH1 before the initiation of PEX and PCI, and 24 hours later before drug discontinuation. C activity was measured ex vivo in serum and in vitro in the supernatant formed after incubation of the serum for 72 hours on HUVEC monolayers, C4a, C3a, Ib, and MBL (proximal C), and C5b-9, sC5b-9 and HUVEC-bound C5b-9 (Term C), were assessed by CBA, ELISA and flow cytometry. Apoptosis was quantified as % of HUVEC with DNA fragmentation after membrane permeabilization, and by cells positive to propidium iodide and/or annexin V. Analyses were performed blinded to treatment allocation.

Results: Baseline levels of all parameters were similar in PEX and placebo groups. At 24 hours, proximal C remained unchanged in the 2 study groups in both the ex vivo and in vitro studies. An increase at 24 hours in C4a levels in serum from 6.24 to 8.85 ng/ml in placebo patients (p=0.031) was abrogated with PEX (5.6 to 6.2 mg/ml; NS); sC5b-9 values, however, increased more with PEX (743 to 1893 ng/ml; p=0.003) than with placebo (858 to 1473 ng/ml). In cell cultures, PEX strikingly inhibited C5a (26.3 to 2.0 ng/ml vs. 32.5 to 38.7 ng/ml with placebo; p=0.002), sC5b-9 (3235 to 743 mg/ml vs. 3505 to 4259 mg/ml, p=0.033), and HUVEC-bound C5b-9 (3.27 to 0.6 % vs. 3 to 3.2%, p=0.002). Despite a positive correlation at baseline between HUVEC-bound C5b-9 and HUVEC apoptosis (r=0.628, p=0.033), PEX had no detectable effects on apoptosis. Conclusions: PEX in the early hours of STEMI blunts C5a activation in serum but tends to promote formation of sC5b-9 in cell culture. It blocked C5b-9 and sC5b-9 formation in supernatant and C5b-9 assembly on cells, with no impact on apoptosis. The reasons for these paradoxical effects ex vivo and in vitro remain to be investigated; they could help understand why PEX failed to prevent ischemic events.
Remote Ischemic Preconditioning in Humans Attenuates Procedure-Related Cardiac Troponin-I Release After Elective Percutaneous Coronary Intervention: A Single-Center Randomized Controlled Trial

Stephen Hoole, Patrick Heck, Sada Khan, Linda Sharples, Cameron Densmore, Sarah Clarke, Leonard Shapiro, Peter Schofield, Michael O’Sullivan, David Dutka, Papworth Hospital, Cambridge, United Kingdom, Addenbrooke’s Hospital, Cambridge, United Kingdom

Background: Endogenous “early” protection by remote ischemic preconditioning (remote IPC) attenuates myocardial ischemia-reperfusion injury in animals, but translation into clinical benefit has been slow. We hypothesized that remote IPC may prevent procedure-related cardiac troponin (cTnI) release during elective percutaneous coronary intervention (PCI).

Methods: We randomized 180 patients undergoing elective PCI to either remote IPC (n = 92); three 5-minute blood pressure cuff inflations to 200mmHg around the upper arm with 5-minutes of cuff deflation between, or control (n = 88); a deflated cuff throughout, before PCI. Patients taking nicorandil or glibenclamide were excluded. Baseline and 24-hour post-PCI serum cTnI levels, creatinine and CRP were measured and compared.

Results: PCI was successful in 84% in both groups with similar cTnI release (p = 0.07). There was no difference in post-PCI cTnI levels between the two groups. This difference was significant for the incidence of myocardial infarction and normal cTnI after PCI (Figure). There was no difference in 24-hour creatinine or CRP levels between the two groups.

Conclusion: Remote IPC attenuates procedure-related cTnI release after elective PCI, which may have prognostic significance. It is feasible in normal clinical practice.
These SNPs in CYP genes on the clinical efficacy of clopidogrel. bleeding (Pinteraction >0.50 for each).

Results: 465 patients were genotyped for 5 commonly studied SNPs: CYP1A2*1F and rs1277806, which tags CYP2C19*2 (r2=1.0). There were no significant interactions between the evaluated genotypes and the effect of clopidogrel on either the primary efficacy endpoint (occluded infarct-related artery, death, or recurrent MI) or the composite between the evaluated genotypes and the effect of clopidogrel on either the primary efficacy endpoint (occluded infarct-related artery, death, or recurrent MI) or the composite.

Background: The most recent (2005) ACC/AHA/SCAI guidelines for percutaneous coronary intervention (PCI) state that, when performing primary PCI for acute myocardial infarction (AMI) with multi-vessel disease, "Elective PCI should not be performed in a non-infarct-related artery at the time of primary PCI of the infarct-related artery in patients without hemodynamic compromise." However, this guideline is based only on expert opinion and not on scientific evidence. With the advancement of PCI technology, multi-vessel PCI might safely be performed during primary PCI, thus eliminating the need for staged interventions. However, evidence for this approach is also lacking.

Methods: We evaluated 227 consecutive AMI patients admitted to a single institution who were diagnosed with multi-vessel CAD at the time of primary PCI. Of these, 190 underwent guidelines-directed staged PCI within 3 months and 37 underwent multi-vessel PCI at the same time as primary PCI. Logistic regression was used to determine odds ratios (OR) corrected for baseline characteristics to determine differences in death and MI at 6-months and 1-year.

Results: Patients averaged 63.6±12.2 years, 73% were males, left ventricular ejection fraction was 52.3±12.2% and 41.5% of staged PCIs were performed during the same hospitalization. Both groups were similar in baseline characteristics. By 6-months, 5.3% of patients undergoing staged PCI and 17.9% undergoing non-staged PCI were deceased (multivariable OR=2.22, p=0.005) and 13.3% and 5.1% respectively had experienced non-fatal AMI (multivariable OR=2.97, p=0.15). By 1-year, 6.6% of patients undergoing staged PCI and 17.9% undergoing non-staged PCI were deceased (multivariable OR=2.98, p=0.02) and 16.0% and 5.1% respectively had experienced a non-fatal AMI (multivariable OR=4.50, p<0.05). Conclusions: In this series of AMI patients with multi-vessel disease undergoing primary PCI, those receiving guidelines-directed staged PCI fared significantly better at both 6-months and 1-year follow-up than those undergoing multi-vessel PCI at the same time as primary PCI. This study provides evidence supporting the existing guidelines regarding this issue.

Impact of the Absence of Significant Changes on the Electrocardiogram Throughout the Hospital Phase in Patients With Non ST Segment Elevation Myocardial Infarction: Data From the RICO Survey

Background: From a large contemporary population-based cohort of patients with acute MI, we analysed the respective impact of waist circumference (WC) and body mass index (BMI) on mortality.

Methods: One-year mortality was evaluated in 2225 consecutive acute MI patients. Patients were classified into normal, overweight, obese and very obese (BMI<25, 25 to 29.9, 30 to 34.5 and >35) and to Abdominal Obesity (AO, WC >88 cm [women] >102 cm [men]). Results: Only 660 patients had a normal BMI, half were overweight (n=1044), and 1/4 were obese or very obese (n=397 and n=128, respectively). Patients with overweight or obesity were younger than patients with a normal BMI (p<0.001). AO was present in half of the patients (n=1110) and associated with older age (71.58-79 vs 65.53-75 y). An increased BMI was associated with reduced mortality, with a 5% risk reduction for each increase in BMI unit (HR<0.93-0.98, p<0.001). Conversely, AO was associated with a 30% increase in mortality. Diagonal stratification of mortality identified patients with AO but normal BMI as high risk patients (Figure). When adjusted for baseline predictors of mortality (age, Nt-ProBNP), neither BMI nor AO were independent predictors of mortality.

Conclusion: WC and BMI have opposite relations with mortality after acute MI, the former being associated with increased and the latter with reduced mortality. Moreover, our findings show that these relations are largely explained by differences in baseline predictors of mortality.

Mortality

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<th>Normal</th>
<th>Overweight</th>
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<td>22%</td>
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Are Staged Interventions Really Necessary in Patients Presenting With Acute Myocardial Infarction and Multi-Vessel Disease and Treated With Primary Percutaneous Coronary Intervention?

Background: The former being associated with increased and the latter with reduced mortality. Moreover, our findings show that these relations are largely explained by differences in baseline predictors of mortality.

Conclusion: WC and BMI have opposite relations with mortality after acute MI, the former being associated with increased and the latter with reduced mortality. Moreover, our findings show that these relations are largely explained by differences in baseline predictors of mortality.

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Sequence Variations in CYP Metabolism Genes and Cardiovascular Outcomes in following Treatment With Clopidogrel: Insights From the CLARITY-TIMI-28 Genomic Study

Methods: CLARITY-TIMI-28 randomized STEMI patients undergoing fibinolysis to clopidogrel (300 mg loading dose, then 75 mg daily) or placebo. Patients were to undergo coronary angiography at 48-192 h and were followed for 30 d for clinical events. Genotyping was performed using Illumina GoldenGate Assay.

Results: 465 patients were genotyped for 5 commonly studied SNPs: CYP1A2*1F (rs762551), CYP2CZ3*3 (rs1057910), CYP3A4*1B (rs7240574), CYP3A5*3 (rs776746), and rs1277806, which target CYP2C19*2 (rs1277806). There were no significant interactions between the evaluated genotypes and the effect of clopidogrel on either the primary efficacy endpoint (occluded infarct-related artery, death, or recurrent MI) or the composite of cardiovascular death, MI, or urgent revascularization by 30 d (F). Likewise, there was no observed heterogeneity for the relationship between genotype, treatment, and bleeding (Printeraction =0.50 for each).

Conclusions: Whereas genetic sequence variations have been associated with clopidogrel responsiveness in ex vivo platelet studies, in this cohort, we did not observe an impact of these SNPs in CYP genes on the clinical efficacy of clopidogrel.

Impact of the Absence of Significant Changes on the Electrocardiogram Throughout the Hospital Phase in Patients With Non ST Segment Elevation Myocardial Infarction: Data From the RICO Survey

Methods: Between the 1st of January 2001 and the 1st of September 2005, from the French regional RICO survey, all the consecutive NSTEMI patients who benefited from coronary angiography <48h were included. Patients were categorized into 2 groups based on either the presence (ECG+) or absence (ECG-) of significant changes on ECG recordings. ECGs were continuously monitored during the first 48h after admission and then once a day until discharge. Significant ECG changes were defined by the presence of Q waves (Q), atrial fibrillation (AF), atrial flutter (AFL), or ST segment (ST)-, T wave (T)-, or U wave (U)- deviation.

Results: Among the 829 patients included, 85 (10%) were ECG -. Patients from the ECG- group were younger than patients with a normal BMI (p<0.001). AO was present in half of the patients (n=1110) and associated with older age (71.58-79 vs 65.53-75 y). An increased BMI was associated with reduced mortality, with a 5% risk reduction for each increase in BMI unit (HR<0.93-0.98, p<0.001). Conversely, AO was associated with a 30% increase in mortality. Diagonal stratification of mortality identified patients with AO but normal BMI as high risk patients (Figure). When adjusted for baseline predictors of mortality (age, Nt-ProBNP), neither BMI nor AO were independent predictors of mortality.

Conclusion: WC and BMI have opposite relations with mortality after acute MI, the former being associated with increased and the latter with reduced mortality. Moreover, our findings show that these relations are largely explained by differences in baseline predictors of mortality.
Methods: We analyzed non-transfer patients with STEMI presenting between July 2005 and May 2007 at UPMC Presbyterian Hospital. Beginning in September 2006, a multi-departmental effort including the following elements was implemented: 1) Commitment from leadership of involved departments to make improvement of D2B highest priority; 2) Empowerment of emergency physician to directly activate cardiac cath team; 3) Single call activation system for in-house cardiology, cardia lab staff, interventional fellow and attending; 4) Defining time expectations for triage to ECG time, decision to activate cath lab, time to ECG, and time to D2B; 5) Detailed real time feedback of each component of D2B to all caregivers involved.

Results: Elderly pts showed a higher prevalence of female gender (36% vs 15%, p<.0001), and a lower recovery of EF and WMSI were found in elderly (from baseline to 6-month, p=.05), as compared to the younger pts, and they showed a lower peak creatine kinase (2475±1938 vs 2915±2303, p=.040). The 6-month prevalence of LV remodeling was higher in elderly pts as compared to younger pts (34% vs 25%, p=.041), and a lower recovery of EF and WMSI were found in elderly (from baseline to 6-month, p=.0002 for both by ANOVA analysis). The incidence of 6-month HF was 2-fold higher in elderly (17% vs 8%, p=.002) as compared to younger pts. By stepwise multivariate logistic regression analyses, the independent predictors of LV remodeling were: infarct size (OR 1.43, 95% CI 1.31 to 1.54), baseline LV EDV (OR 0.79, 95% CI 0.72 to 0.85) and WMSI (OR 1.23, 95% CI 1.11 to 1.34). Whereas, the independent predictors of 6-month HF were: infarct size (OR 1.29 95% CI 1.18 to 1.41), age (OR 1.18, 95% CI 1.08 to 1.28), WMSI (OR 1.13, 95% CI 1.02 to 1.24), anterior location of MI (OR 1.11, 95% CI 1.01 to 1.21), and diabetes (OR 1.09, 95% CI 1.00 to 1.18).

Conclusions: Our results suggest that as primary PCI aging is associated with an increased risk of HF, but not of LV remodeling. Factors other than LV remodeling may play a significant role in the development of HF in elderly pts.

9:45 a.m.

Improving Door-to-Balloon Time in ST-Elevation Myocardial Infarction
Sun K. Soo-Jae, Joon S. Lee, Suresh Mulatoril, Vincent N. Moseso, Donald M. Yealy, Charles R. Pacella, Kathleen Zell, UP garn Presbyterian Hospital, Pittsburgh, PA.

Background: Prompt percutaneous coronary intervention (PCI) guided reperfusion therapy in the management of ST-elevation myocardial infarction (STEMI) improves patient outcomes. Despite consensus guidelines recommending a door-to-balloon time (D2B) of ≤90 minutes, this is not achieved less than 50% of the time. We sought to determine the effect of a multidisciplinary collaborative effort involving emergency medicine, cardiology, pre-hospital, and nursing departments to improve D2B performance.

Methods: We analyzed non-transfer patients with STEMI presenting between July 2005 and August 2006, and we compared these to 31 consecutive patients between July 2005 and August 2006, and we compared these to 31 consecutive STEMI patients enrolled after protocol implementation. Performance data are described in mean +/- SD or frequencies, and analyzed using paired t tests and Fischer’s Exact test, alpha set at 0.05.

Results: Mean D2B decreased from 108±34.7 to 72±23.6 minutes (p<0.00001) after the new protocol was implemented. D2B goal of ≤90 minutes improved from 28.6% of patients in the baseline group to 87.1% in the group after protocol implementation (p<0.00001).

Conclusions: Our protocol mirrors the AHA/ACC Guidelines Applied in Practice-Door to Balloon (P2B) project, which was launched in November 2006. At our institution, a constant feed back system and commitment from multiple disciplines must be established in order to maintain a well-orchestrated chain of activation in the face of STEMI.
Background: Fibrinolytic therapy is the most widely used reperfusion strategy in patients with STEMI. The clinical characteristics and in-hospital outcomes of patients that require percutaneous coronary intervention (PCI) for ongoing or recurrent myocardial ischemia (rescue angioplasty) are largely limited to small studies. In-hospital outcomes data for patients undergoing rescue PCI were assessed and compared with patients undergoing primary PCI.

Methods: Clinical outcomes data for these “real-life” rescue PCI patients are clinically useful.

Methods: The study population consisted of all patients undergoing primary or rescue PCI in 484 hospitals contributing to NCDR from 1/1/04-3/31/06. Clinical characteristics and in-hospital outcomes of patients undergoing rescue PCI were assessed and compared with patients undergoing primary PCI.

Results: Of a total 309,351 PCI procedures, 2829 STEMI patients underwent rescue PCI and 30,650 patients underwent primary PCI. Of the rescue PCI cohort 89.8% of patients received aspirin, 57.4% received a Gp IIb/IIIa inhibitor and 64.7% received a thienopyridine.

Conclusion: When compared to the primary PCI cohort, rescue PCI patients were at higher risk for bleeding and CHF, largely due to their shared predictors. These outcomes, therefore, should not be viewed in isolation when selecting treatments for this population.

### Table 1: Clinical characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Primary PCI (n=30690)</th>
<th>Rescue PCI (n=2829)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61±13</td>
<td>59±12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>21620(70)</td>
<td>2102(74)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Caucasian</td>
<td>26469(86)</td>
<td>2496(88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>28.7±6</td>
<td>29.1±6</td>
<td>0.03</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6452(21)</td>
<td>568(20)</td>
<td>0.03</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>2096(6.8)</td>
<td>146(5.2)</td>
<td>0.005</td>
</tr>
<tr>
<td>Peripheric Vascular disease</td>
<td>2011(6.6)</td>
<td>144(5.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Smoking</td>
<td>2042(6.65)</td>
<td>1982(70)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>52(17)</td>
<td>42(15)</td>
<td>0.005</td>
</tr>
<tr>
<td>ABP</td>
<td>5333(11)</td>
<td>572(13)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>UVEF</td>
<td>45.1±12.7</td>
<td>45.2±12.4</td>
<td>0.04</td>
</tr>
</tbody>
</table>

### Table 2: In-hospital outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Primary PCI (n=30690)</th>
<th>Rescue PCI (n=2829)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>1570(5.35)</td>
<td>1706(6.2)</td>
<td>0.006</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>959(3.3)</td>
<td>1244(5)</td>
<td>0.14</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>136(3.8)</td>
<td>236(3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>176(0.67)</td>
<td>54(0.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Tamponade</td>
<td>108(0.4)</td>
<td>55(0.3)</td>
<td>0.47</td>
</tr>
<tr>
<td>Post procedure TIMI 3 flow</td>
<td>2840(90.27)</td>
<td>2583(91.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>No reflow phenomenon</td>
<td>343(3.3)</td>
<td>1565(5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Acute closure</td>
<td>317(11)</td>
<td>47(1)</td>
<td>0.008</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1585(5.2)</td>
<td>1586(5.7)</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Age, BMI, and LVEF are presented as mean ± STD. The remainder are presented as frequency (percentage).
Arterial Access and Door-to-Ballooning Times for Primary Percutaneous Coronary Intervention in Patients Presenting with Acute ST-Elevation Myocardial Infarction

Rick A. Henderson, Ian Glchrist, Steven M. Ettinger, Penn State College of Medicine, Hershey, PA

Background: The radial approach for cardiac catheterization and PCI (r-PCI) is an alternative to the femoral artery approach (f-PCI). Survival following STEMI is directly related to reperfusion times (door-to-ballooning, D2B). For patients undergoing primary PCI for acute STEMI, potential benefits of r-PCI compared to f-PCI in reducing D2B times have not been fully studied.

Methods: Consecutive patients presenting with an STEMI at the M.S. Hershey Medical Center were enrolled in the Penn State Heart & Vascular Institute - Heart Alert program (HA) and were included in our analysis. Specific time parameters were measured including time from ECG to-ha activation, activation-to-cath lab team arrival, patient arrival to cath lab-to-arterial access, and arterial access-to-balloon inflation. Groups were stratified according to the arterial access approach (r-PCI vs. f-PCI). Times are reported as medians.

Results: Of 131 total patients, 107 underwent successful PCI (n=72 r-PCI; n=60 f-PCI), 4 patients underwent emergent surgery. 16 patients had non-obstructive disease, 3 patients were medically managed, and 1 patient could not be treated (failure to cross lesion with guidewire). No significant difference was observed in the pre-cath lab times (door-to-ECG, ECG-to-ha activation, ha activation-to-cath lab team arrival). Case start times for r-PCI took significantly longer (11min vs. 10min; p=0.005) due to patient preparation. Once arterial access was obtained, balloon inflation occurred faster in the r-PCI group (17min vs 24min; p=0.004). Total time from patient arrival to the cardiac cath lab to PCI was reduced in the r-PCI group (31min) as compared to the f-PCI group (34min) but did not reach statistical significance (p=0.10). There was no difference in D2B time (r-PCI 83min vs. f-PCI 84min). Less diagnostic catheters were required in the r-PCI group (1.8) compared to the f-PCI group (2.2). (p=0.001). Fluoroscopy times were similar (r-PCI 12.3min vs. 14.3min) as was the used r-PCI (168 vs. f-PCI 169c).

Conclusion: Patients presenting with STEMI can undergo successful PCI via a radial artery approach without compromise in D2B times as compared to a femoral artery approach.

Long-term Outcome of Primary Angioplasty Compared with Fibrinolysis across Age Groups: A DANAMI-2 substudy

Emil L. F波st, Jens J. Thune, Herning Kelbaek, Herning R. Andersen, Kari Saunamäki, Torsten T. Nielsen, Brian M. Mortonson, Lars Kober, Morten Hojgaard, Heart Centre, University Hospital of Copenhagen, Rigshospitalet, Copenhagen, Denmark

Background: Primary angioplasty in patients with acute ST-elevation myocardial infarction has been shown to be superior to fibrinolysis. Whether elderly patients have the same long-term benefit from angioplasty compared to fibrinolysis as younger patients is unknown.

Methods: The effect of angioplasty versus fibrinolysis was investigated in 1572 patients from the Danish Multicenter Randomized Study on Fibrinolytic Therapy Versus Acute Coronary Angioplasty in Acute Myocardial Infarction (DANAMI-2) study across age groups. Endpoints were total mortality and a composite endpoint of death, reinfarction, or disabling stroke, which was defined as three years.

Results: Increasing age was associated with mortality (adjusted hazard ratio [HR]=2.51 per 10 year increment, 95% confidence interval [CI]=1.83-3.45, p=0.001) and composite event rate (adjusted HR=1.47, CI=1.23-1.75, p<0.0001). The long-term superiority of angioplasty over the combination of fibrinolysis and aspirin was independent of age: HR=0.73 (CI=0.41-1.31), HR=0.83 (CI=0.52-1.33), HR=0.71 (CI=0.48-1.04) and HR=0.83 (CI=0.59-1.17) for patients <65, 65-75, >75 respectively (p=0.006 for overall treatment effect and p=0.5 for interaction between age and treatment). There was no long-term effect of angioplasty versus fibrinolysis on mortality and no interaction with age (p=0.5 and p for interaction=0.6).

Conclusions: The effect of primary angioplasty compared to fibrinolysis in patients with ST-elevation myocardial infarction is not affected by age.
Among subjects presenting by EMS, median first medical contact to balloon time was shorter, with a pre-hospital ECG (89 min [70, 112] vs. 102 min [79, 128], p < 0.0001).

There was no difference in in-hospital death among groups.

Conclusion: Fewer than one fifth of STEMI patients were being evaluated with a pre-hospital ECG in contemporary U.S. practice even though more than half of STEMI patients receiving reperfusion therapy are transported to the ED via EMS. Moreover, when a pre-hospital ECG is available, time to reperfusion is more rapid. Equipping all EMS ambulances with pre-hospital ECG capabilities should markedly shorten the average times to reperfusion.

11:00 a.m.

1017-37 A novel cardioprotective medication after an acute ST-elevated myocardial infarction decreases proinflammatory response and stimulates vascular endothelial growth factor release

Sergey Kozhukhov, Alexander Parkhomenko, National Scientific Center “Institute of Cardiology”, Kiev, Ukraine

Background: Myocardial damage is associated with an inflammatory response and leads to complement activation and free radical generation, triggering a cytokine cascade and chemokine upregulation. Prognosis after AMI has been linked to the infarct size and detection of left ventricular enlargement. In order to evaluate efficacy of the i.v. form of bioflavonoid Quercetin 91pts with successful reperfusion (PCI or TLT) within the first 6 h of AMI were randomized to two groups identical as regard baseline clinical, hemodynamic characteristics and concomitant medication.

Methods: Dynamic 2-D echocardiography, infarct size measurement by serial serum CK-MB assessment were used during the first 10 days of AMI. Leukotriene C4 was measured at the admission and on day 3. CRP, von Willebrand factor and VEGF were measured at the admission and on day 10 and differences (in %) were calculated.

Results: are presented in the table (Mm±). [* < 0.05 compared with the 1st day value; ESVI, EF - changes in end-systolic, end-diastolic volume indices and ejection fraction; CK-MB time of peak - time from AMI onset to peak value of CK-MB isoenzyme; N time - normalization time of CK-MB; SI - infarct size index).

Conclusions: These findings suggest that intravenous form of lipoxigenase inhibitor Q in AMI pts with successful reperfusion will decrease final infarct size and improves heart function. Obtained cardioprotective effect of Q was accompanied by decreases proinflammatory activation and induces VEGF expression.

1017-38 Dose-effect of clopidogrel reloading in patients on 75mg maintenance dose (The RELOAD study)

Antoine Landivier, Jean-philippe collet, Johanne Silvain, Guillaume Cayla, Marie-Laure Tanguy, Farzin Beggai, Olivier Barthélémy, Raphaelle Dumaune, Nicolas Vignolles, Delphine Bruger, Sophie Gallier, Gilles Montalescot, Hôpital Pitié-Salpêtrière Institut de Cardiologie, Paris, France

Background: The most appropriate loading strategy with clopidogrel in patients on a maintenance dose of 75mg of clopidogrel scheduled for coronary angiography and eventually ad-hoc percutaneous coronary intervention remains unknown.

Aim: To evaluate 3 different strategies of administration of a loading dose of 900 mg of clopidogrel in patients already on chronic clopidogrel therapy.

Methods: Patients on chronic maintenance dose of 75 mg/day and aspirin 75 mg/day were to be randomized to receive either 300 mg, 600 mg or 900 mg of clopidogrel as initial loading dose. Four hours later, a second loading dose was administered (600, 300 or nothing respectively) to achieve a final loading dose of 900 mg in all patients. Platelet aggregation (PA) was evaluated at baseline, 4 hours after the initial load (and before second load) and at 24 hours using light transmission aggregometry with 20 μM ADP. The primary objective of the study was to evaluate the % of inhibition of late PA (ILPA) in the three groups at H4. ILPA was calculated as LPA at H0-LPA at H4/LPA at H0. ILPA at 24 hours was also evaluated as well as the rate of suboptimal response at 4 hours defined as ILPA>10%.

Results: We included 166 consecutive patients with either ACS (45%), stable angina (42%) or scheduled catheterization/PCI (11%). Baseline characteristics were similar in the three dose groups. There was a significant stepwise increase in ILPA assessed at baseline and at 4 hours in patients who received 300, 600 and 900 mg, respectively (p<0.0024). Differences in ILPA at 4 hours were significant between 600mg and 900mg, and between 300mg and 900mg. ILPA at 24 hours after all patients received 900mg did not differ between the three loading regimens. The rates of suboptimal response (ILPA<10% at H4) were 23.6% vs 20.4% vs 5.3%, in patients who received 300, 600 and 900 mg, respectively (p<0.01 for all). The rate of slow responders (variation of maximum aggregation>10%) was 63.6% vs 53.7% vs 38.6%, respectively (p=0.028).

Conclusion: Reloading with 900mg of clopidogrel patients on a maintenance dose of 75mg of clopidogrel is more effective than 600mg or 300mg to inhibit ADP induced PA, prevent slow response and/or poor response to clopidogrel.

11:00 a.m.

ACC.ORAL CONTRIBUTIONS
JACC March 11, 2008

806 Contemporary Therapy in Acute Chronic Ischemic Disease

Monday, March 31, 2008, 1:00 p.m.-2:45 p.m.
McCormick Place, Room E352

1:00 p.m.

806-4 One Year Follow Up Results of the FINESSE Trial of Facilitated PCI

Stephen G. Ellis, Michael Tendera, Mark A. De Belder, Ad J. van Boven, Petr Widimsky, Luuk Janssens, H.R. Andersen, Amadeo Betriu, Stefano Savonitto, Jerzy Adams, Jan Z. Peruga, Maciej Kosmider, Olivier Katz, Thomas Neunteufl, Julia Jorgova, Maria Dorobantu, Liliana Grinfeld, Paul Armstrong, Bruce Brodie, Howard C. Herrmann, Gillies Montalescot, Franz-Josef Neumann, Mark B. Effron, Elliot S. Barnathan, Eric J. Topol, Cleveland Clinic Foundation, Cleveland, OH

Background: The hypothesis that early facilitation with a combination of hale dose reteplase + abciximab prior to primary PCI (combination-facilitated PCI) would be superior to PCI with abciximab in the cath lab (primary PCI) for patients with ST elevation MI <6 hours duration, with expected delays to the cath lab of 1-4 hours was evaluated in the FINESSE trial. A second active treatment group received abciximab alone immediately after randomization (abciximab/cellciate-c-PCI).

Methods: 2452 patients from 20 countries (age = 62+/11 years, 26% female, 48% anterior MI, median door to balloon time = 2.2 [interquartile range, 1.8-2.8] hours were randomized in a 1:1:1 fashion. The primary endpoint was evaluated at 90 days with mortality follow up through 1 year. All cause mortality at one year was a pre-specified secondary endpoint.

Results: The composite primary outcome of all cause mortality, cardiogenic shock, heart failure, or ventilatory intubation > 48 hours after MI was seen in 9.8% of the combination-facilitated, 10.5% of the abciximab-facilitated and 10.7% of the primary PCI groups, respectively (p=NS). ST segment resolution at 60-90 minutes, pre-PCI TIMI flow and infarct size by CK curve analysis, however, were improved with combination therapy compared with primary PCI (all p<0.01), whereas indices of bleeding worsened. After discharge, 88%, 85% and 77% of patients were treated with statins, beta-blockers and ac inhibitors/angiotensin receptor blocker agents, respectively.

Conclusion: Whether or not measures of improved early flow and reduction of infarct size might favorably impact long-term survival will be ascertained with this analysis. All one-year follow up visits are expected to be complete by the end of 2007. Final data will be available for presentation at the ACC meeting.

“Abstract withdrawn by author"
Background: SR123781A, a synthetic hexadecasaccharide, is a potent antithrombin-dependent inhibitor of factor Xa and Xa with strong antithrombotic activity in animal models.

Methods: A randomized double-blind, dose-ranging trial was conducted in patients presenting with NSTEACS for whom catheterization and percutaneous coronary intervention (PCI) within 48 hrs was planned. Patients were randomized to receive a fixed daily dose of subcutaneous SR123781A (0.25, 0.5, 1, 2 or 4 mg) for 5 days or to hospital discharge or intravenous (IV) UFH. An additional IV dose of SR123781A was administered immediately before PCI. Abciximab was used during PCI in the UFH arm. The primary outcome was a composite of all-cause mortality, myocardial infarction or urgent repeat target vessel revascularization within 7 days. Bleeding and procedural outcomes were analyzed.

Results: A total of 1,243 patients were treated (ITT population). Due to excess catheter-related thrombotic events, the three lowest dose arms were stopped and a 5,000 U bolus of UFH was used in the SR123781A arms immediately prior to PCI. Similar rates of the primary outcome and bleeding were observed for all doses when compared to control (Table). PCI thrombotic complications were not increased in the high-dose groups.

Conclusions: SR123781A in doses of 2 to 4 mg/day may provide similar protection against ischemic events as UFH and abciximab, without an apparent increased bleeding risk. Lack of dose response suggests further dose optimization is necessary.

### Efficacy and Safety Outcomes in SHINE

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>ITT population (n=1,243)</th>
<th>PCI population (n=775)</th>
<th>TIMI Major Bleeding (p=0.75)</th>
<th>TIMI Minor/Proximal Bleeding (p=0.04)</th>
<th>PCI thrombotic complications (p&lt;0.003 for dose effect)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>SR123781A (N=115)</td>
<td>SR123781A (N=116)</td>
<td>5.2%</td>
<td>3.4%</td>
<td>11.9%</td>
</tr>
<tr>
<td>2nd</td>
<td>SR123781A (N=122)</td>
<td>SR123781A (N=128)</td>
<td>4.1%</td>
<td>3.7%</td>
<td>11.3%</td>
</tr>
<tr>
<td>3rd</td>
<td>SR123781A (N=230)</td>
<td>SR123781A (N=288)</td>
<td>3.4%</td>
<td>4.3%</td>
<td>6.6%</td>
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<tr>
<td>4th</td>
<td>SR123781A (N=305)</td>
<td>SR123781A (N=356)</td>
<td>3.9%</td>
<td>3.8%</td>
<td>5.8%</td>
</tr>
<tr>
<td>5th</td>
<td>UFH/abciximab (N=297)</td>
<td>UFH/abciximab (N=356)</td>
<td>4.9%</td>
<td>5.9%</td>
<td>2.4%</td>
</tr>
</tbody>
</table>

### ABSTRACTS - Myocardial Ischemia and Infarction

#### Intracoronary Compared with Intravenous Bolus Abciximab Application in Patients with ST-Elevation Myocardial Infarction Undergoing Primary Coronary Intervention

Hoelger Thiele, Kathrin Schindler, Josef Friedenberger, Ingo Eitel, Georg Furrnau, Eigk Grebe, Dietmar Kivelitz, Gerhard Schuler, University of Leipzig - Heart Center, Leipzig, Germany

Background: Abciximab reduces major adverse cardiac events in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention (PCI). Intracoronary bolus application of abciximab results in high local drug concentrations and may be more effective than standard intravenous bolus application for reduction of infarct size, no-reflow and improvement in perfusion.

Methods: Patients undergoing primary PCI were randomized to either intracoronary (n=77) or intravenous (n=77) bolus administration of abciximab with subsequent 12 hour intravenous infusion. Primary endpoint was infarct size and extent of microvascular obstruction assessed by delayed enhancement magnetic resonance. Secondary endpoints were ST-resolution at 30 minutes, Thrombolysis in Myocardial Infarction (TIMI)-flow and perfusion grade post PCI, and the occurrence of major adverse cardiac events within 30 days.

Results: The primary endpoint infarct size could be reduced by absolute 7% (17.7% i.e. versus 24.7% i.e. p<0.005). Similarly, the extent of microvascular obstruction was significantly smaller in i.c. patients in comparison to i.v. patients (p=0.02). Myocardial perfusion measured as early ST-segment resolution was significantly improved in i.c. patients with an absolute ST-resolution of 76±23% versus 64±31% (p<0.009). The TIMI flow after PCI was not different between treatment groups (p=0.51), but there was a trend towards an improved perfusion grade (p<0.12). There was a trend towards a higher major adverse cardiac event rate after intravenous versus intracoronary abciximab application (15.6% versus 5.2%, p=0.06; relative risk 3.00; 95% confidence intervals 0.94-10.80).

Conclusions: Intracoronary bolus administration of abciximab is superior to standard intravenous treatment with respect to infarct size, extent of microvascular obstruction, and perfusion in primary PCI. An adequately powered trial for major adverse cardiac event reduction is warranted.

#### Decline in the Use of Drug-Eluting Stents for Patients With Non-ST-Segment Elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention: Results From the CRUSADE and ACTION Registries

Matthew T. Roe, Christopher P. Cannon, Anita Y. Chen, Sunil V. Rao, John S. Rumsfeld, Lloyd W. Klein, E. Magnus Ohman, W. Brian Gibler, Eric D. Peterson, Duke Clinical Research Institute, Duke University Medical Center, Durham, NC

Background: Relative risks and benefits of drug-eluting stents (DES) vs. bare-metal stents (BMS) have been scrutinized recently given concerns regarding the risk of stent thrombosis in patients receiving DES. How the controversy surrounding DES use has impacted patterns of stent use in patients with acute myocardial infarction (MI), an off label indication for DES, is unclear.

Results: Data were collected from 153 CRUSADE hospitals and 185 ACTION hospitals. There was a slight increase in the percentage of patients undergoing PCI over the 1.5-year period. Among PCI patients, there was a progressive decline in the use of DES vs. BMS (Table).

Conclusions: Over a 1.5-year period, the proportion of NSTEMI patients undergoing PCI who received a DES declined from 92% to 63%, despite a slight increase in the proportion of patients who underwent PCI. These findings suggest that off-label DES use patterns have been rapidly affected by the recent controversy regarding the risk of stent thrombosis associated with DES.

<table>
<thead>
<tr>
<th>Quarter and Year</th>
<th>CRUSADE</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 06</td>
<td>5505</td>
<td>3533</td>
</tr>
<tr>
<td>Q2 06</td>
<td>5602</td>
<td>4654</td>
</tr>
<tr>
<td>Q3 06</td>
<td>6602</td>
<td>6563</td>
</tr>
<tr>
<td>Q4 06</td>
<td>5333</td>
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### Abstract withdrawn by author
The CRUSADE Bleeding Score to Assess Baseline Risk of Major Bleeding in Non-ST-Segment Elevation Myocardial Infarction

Sumeet Subherwal, Richard G. Bach, Anita Y. Chen, Brian F. Gage, Sunil V. Rao, Tracy Y. Wang, W. Brian Gibler, E. Magnus Ohman, Eric D. Peterson, Matthew T. Roe, Karen P. Alexander, Washington University in St. Louis School of Medicine, St. Louis, MO, Duke Clinical Research Institute, Durham, NC

Background: Major bleeding adversely affects outcomes in non-ST-segment elevation myocardial infarction (NSTEMI). Early identification of those at high risk of bleeding could improve outcomes by guiding treatment, but estimation of baseline risk is limited by including treatment variables in existing models.

Methods: Using the NSTEMI population in CRUSADE, we performed logistic regression to identify baseline predictors of bleeding in a derivation cohort (n=71,277); the model was tested in a validation cohort (n=17,857). A major bleed was defined as hematocrit (HCT) drop >12%, intracranial hemorrhage, witnessed retroperitoneal bleed, any RBC transfusion when baseline HCT >28%, or baseline HCT <28% with witnessed bleed; post-CABG bleeding was censored. A scoring system (range 1-100) was developed by assigning a weighted integer based on the coefficient of each predictor.

Results: Independent predictors of bleeding included glomerular filtration rate, SBP (mm Hg), heart rate, weight, baseline HCT, peripheral vascular disease, signs of CHF, diabetes, and female sex. The regression model (derivation C=0.72 and validation C=0.71), and scoring system (derivation C=0.70 and validation C=0.69) had good discriminative power overall and across treatment subgroups. The patient’s risk of bleeding is predicted by the score (Figure).

Conclusions: The CRUSADE bleeding score identifies a patient’s baseline risk for major bleeding. Its potential to guide management may improve safety and outcomes in NSTEMI.

ACC.Poster Contributions

ACC.Poster Contributions

1024

Acute Myocardial Infarction--Therapy; Unstable Ischemic Syndrome

Monday, March 31, 2008, 1:00 p.m.-4:30 p.m.
McCormick Place, South Hall

1024-41

What is the Effect of Late Revascularization of a Totally Occluded Infarct-Related Artery?

Andrew N. Rassi, Anthony A. Bavy, Michael L. Sarkees, Arman T. Askari, Deepak L. Bhatt, Duke University Medical Center, Durham, NC, Cleveland Clinic, Cleveland, OH

Background: Although there is benefit to early revascularization of the infarct-related artery in ST-elevation myocardial infarction, there is conflicting data on how best to treat patients who present late for revascularization.

Methods: We conducted a Medline search for clinical trials that randomized patients who presented greater than 12 hours after the onset of symptoms with ST-elevation myocardial infarction to percutaneous revascularization versus medical therapy. We included trials where there was angiographic evidence of total occlusion of the infarct-related artery at randomization. We excluded trials that performed surgical revascularization, studies that included stenosed arteries, and those without available clinical outcomes.

Results: In all, there were 7 trials with 2,678 patients available for analysis. On average, patients were randomized 8.5 days after symptom onset with 99.9% demonstrating TIMI 0-1 flow. At a weighted mean follow-up of 44 months, the incidence of all-cause mortality was 7.6% in the revascularization group, compared with 8.0% in the medical group (risk ratio [RR] = 0.98, 95% confidence interval [CI] 0.75 to 1.27, p = 0.86). Similarly, cardiovascular mortality was 5.1% and 5.2% (RR = 1.00, CI 0.72 to 1.41, p = 0.98), heart failure was 4.0% and 5.2% (RR = 0.59, CI 0.29 to 1.22, p = 0.18), non-fatal myocardial infarction was 5.1% and 3.8% (RR = 1.36, CI 0.96 to 1.97, p = 0.097) and subsequent revascularization was 16.4% and 19.2%, respectively (RR = 0.85, 95% CI 0.72 to 1.00, p = 0.051). At the extent of follow-up, ejection fraction was noted to be 53.5% in the revascularization group compared to 50% in the medical group (p = 0.06). While the incidence of persistent occlusion was 18.4% versus 74.3%, respectively (RR = 0.30, 95% CI 0.17 to 0.54, p < 0.0001).

Conclusions: Late revascularization of an occluded infarct related artery after an acute coronary syndrome reduces persistent occlusion and the need for subsequent revascularization procedures. Despite these benefits, available data does not indicate that this therapy reduces death or myocardial infarction.
activity measured by soluble P-selectin (sP-selectin). Methods: In a biomarker substudy to ESTEEM, a phase II study for safety and efficacy of the oral direct thrombin inhibitor ximelagatran, 518 patients with acute MI were within 14 days randomized to treatment with one of four doses (24-60 mg twice daily) of ximelagatran or placebo for 6 months. All patients received aspirin 160 mg once daily. SP-selectin was analyzed at randomization, after 1 week and 6 months on study treatment. Results: Results describe change of sP-selectin from the levels at randomization. Conclusions: There is an increase in sP-selectin levels up to six months after an acute MI despite treatment with aspirin. This might indicate increased platelet activity after symptom onset.

1005 pts (61.9±13.5 yrs; m±SD; 71.3±28.7 %) presenting with acute STEMI, 59.6% (n=617) underwent PPCI. If PPCI could not be offered within 90 min of 1st medical contact TT was performed (n=277, 26.8%). The median time from onset of symptoms to treatment was 205 min in the PPCI group and 120 min in the TT group. One-year mortality in the PPCI group was 11.8% and in the TT group 11.9%. In 141 pts (13.6%) no reperfusion therapy was offered due to long presentation delays or contraindication against both reperfusion strategies. One-year mortality was 34.8% in patients treated with 2 hours after symptom onset was lower compared to mortality rates of patients treated later in both reperfusion groups. (PPCI: vs. TT: 10%: vs. >2 hrs 12.1%: TT < 2 hrs: 5.7% vs. vs. >2 hrs 18.2%) with a trend in favour of TT observed in the very early treatment period (p=0.238). Conclusion: One-year mortality in both treatment groups, was time-dependent and lowest when treatment was offered within 2 hrs of onset of symptoms without significant differences between PPCI and TT. Accordingly, pts presenting with acute STEMI of ≤2 hrs duration should be treated with the earliest available reperfusion method while PPCI should be the preferred method in all other pts.

3:00 p.m.

The Gender Gap in Door-to-Treatment Time and Outcomes in Acute ST Segment Myocardial Infarction

Elizabeth 2. Greg, Norman L. Thiessen, Timothy D. Henry, Denise Widenburg, Catherine A. Pastorius, Sus Duval, Joseph Decker, Robert G. Hauser, Minneapolis Heart Institute Foundation, Minneapolis, MN

Background: Gender differences exist in the treatment and outcomes of acute ST segment elevation myocardial infarction (STEMI). The aim of this study was to assess clinical variables in women and men undergoing emergency percutaneous coronary intervention (PCI) or surgical revascularization (CAB) for STEMI at our institution.

Methods: The records of consecutive STEMI patients treated by us with emergency PCI or CAB as part of our Level 1 acute STEMI program were reviewed. These patients presented to our hospital or to 30-PCI capable community hospitals within 210 miles from March 2003 and July 2007. Patients received half-dose thrombolytic therapy if their transfer for PCI was delayed or if the community hospital was more than 60 miles from the center.

Results: Of the 1,665 patients, 28% (n=463) were women whose average age was 66.8±14.6 years vs. 59.7±13.8 years for men (p<0.001); 27% of women and 10% of men were >80 years. In addition to being older, women were more likely to have hypertension (women:45%; men:58%, p=0.001), diabetes (women:33%, men:42%, p=0.0006), and more men had a family history of premature coronary artery disease (women:40%, men:47%, p=0.010). The median door-to-needle time was 96 minutes for men and 103 minutes for women (p=0.002), and more women had cardiogenic shock (women:16%, men:11%, p=0.005). The 30-day mortality for was 7.6% for women vs 4.6% for men (p=0.02) and the 1-year mortality was 11.0% for women and 6.4% for men (p=0.002). The stroke rate at 30 days was 1.9% for women vs 0.7% for men (p=0.02).

Conclusions: Women who suffer STEMI are at greater risk for death and stroke at 30 days and death at 1 year than men. These outcomes appear to be related to older age and delays in treatment despite a standardized Level 1 STEMI protocol. The higher incidence of cardiogenic shock in women implies that a significant delay exists between symptom onset and arrival at a health care facility. Thus women are disadvantaged by age and lags in presentation and treatment.

3:00 p.m.

Predictors of Prehospital Delay Time in Acute ST-Elevation Myocardial Infarction

Carlos T. Aguier, Jorge S. Ferreira, Investigators of the Portuguese Registry of Acute Coronary Syndromes, Centro Nacional de Colheita de Dados de Cardiologia, Coimbra, Portugal

Background: In patients (Pts) suspected of acute myocardial infarction (MI), an excessive delay between symptom onset and initial clinical evaluation - prehospital delay - may impede the administration and compromise the efficacy of life-saving therapies. The relation between time to reperfusion and survival benefit of reperfusion is particularly strong in the first 2 hrs after symptom onset. The aim of this study is to identify predictors of prehospital delay time.

Methods: We studied 2,827 Pts with STElevation MI included in a nationwide registry and explored the relation between prehospital delay and age, gender, body mass index, hour of day (0-8 vs. 8-24) and day (working vs holiday/week-end) of symptom onset, risk factors, and prior history of angina, MI, revascularization, peripheral arterial or cerebrovascular disease. The effects of prehospital delay on frequency of administration of reperfusion therapy and all-cause hospital mortality were also evaluated.

Results: Median prehospital delay was 184 min. Prehospital delay was >2 hrs for 1925 Pts (68.1%) and >12 hrs for 466 (18.3%). Independent predictors of prehospital delay >2 hrs were age (OR 1.02; 95% CI, 1.02-1.03), symptom onset at night (OR 1.32; 95% CI, 1.08-1.61), diabetes (OR 1.44; 95% CI, 1.41-1.81), and prior history of angina (OR 1.35; 95% CI, 1.06-1.71). Age >60 years more accurately discriminated Pts presenting >2 hrs after symptom onset. Reperfusion therapy was delivered to 64% of all Pts and 74.1% of those presenting in first 12 hrs. Among Pts eligible for reperfusion, prehospital delay >2 hrs was associated with a higher likelihood of receiving this treatment: 81.3% vs 69.6% when prehospital delay was >2 hrs (OR 1.49; 95% CI, 1.10-2.02).

Conclusions: Prehospital delay for STElevation MI is far from being optimal and is particularly long in the elderly, diabetic, and Pts with prior history of angina or for whom symptoms began during the night. Strategies aimed at improving prognoses of ST-
Our study demonstrates that the preservation of good myocardial viability in patients with acute myocardial infarction (AMI) can be predicted by myocardial viability assessment (MVA) using 18F-fluorodeoxyglucose positron emission tomography (FDG-PET). We analyzed the data from 47 patients with AMI who underwent MVA using FDG-PET in acute phase of AMI. The patients were divided into two groups; good viability group: VS> 2 (n=23), and good viability group: VS<2 (n=14). We used the 5-point score system (no uptake=0, best uptake=4) to evaluate the FDG-PET uptake for infarcted areas (VS). VS is derived from the mean value of score of FDG-PET uptake for infarcted areas.

Results: We found that the patients with VS>2 had significantly higher uptake of FDG-PET compared to patients with VS<2 (p<0.001). We also found that patients with VS>2 had better functional outcome compared to patients with VS<2 (p<0.001). We concluded that FDG-PET in acute phase of AMI can be a predictor of cardiac events in patients with AMI.

Conclusion: Our study demonstrates that FDG-PET in acute phase of AMI can be a predictor of cardiac events in patients with AMI. The results of our study suggest that MVA using FDG-PET can be used to predict cardiac events in patients with AMI.
The OAT randomized trial (n=2201) found that percutaneous coronary revascularization (PCI) of an occluded infarct related artery after recent infarction was not associated with superior clinical outcomes compared to medical therapy alone (MED). Aims: To assess the impact of collaterals on clinical outcomes and potential interaction with assignment to PCI or MED.

Methods: Core laboratory TIMI collateral scores were available for 1087 and 1086 pts in the PCI and MED groups respectively. Presence of collaterals to the infarct related artery was associated with reduced risk of heart failure at 60 months in both treatment groups. There was a strong trend towards interaction between treatment assignment and collateral flow for heart failure, but not for the primary, or other secondary endpoints.

Conclusion: In the OAT trial, angiographically-visible collaterals subtending the infarct territory were associated with a lower rate of heart failure, regardless of treatment assignment. In patients without collaterals, the trend towards benefit of PCI was not detectable when fatal events were factored in.
The Benefit of an Invasive Strategy in Diabetic Versus Non-Diabetic Subjects With Non-ST-Elevation Acute Coronary Syndromes: A Collaborative Meta-Analysis of Randomized Trials

Michelle O'Donohue, William E. Boden, Christopher P. Cannon, Tim C. Clayton, Robert J. de Winter, Keith AA Fox, Bo Lagerqvist, Peter A. McCullough, Sabina A. Murphy, Rudolf Speedack, Eva Swahn, Lars Wallentin, Fons Windhauser, Marc S. Sabatine, Massachusetts General Hospital, Boston, MA, Brigham and Women's Hospital, Boston, MA

Background: Patients with diabetes mellitus (DM) have a worse prognosis after ACS than do non-diabetic patients. Whether DM patients derive particular benefit from an invasive (INV) vs. conservative (CONS) strategy in non-ST-elevation (NSTE) ACS remains unclear.

Methods: We conducted a collaborative meta-analysis of randomized trials of INV vs. CONS in NSTE ACS stratified by DM. Odds ratios (OR) from each trial were combined using a random-effects model.

Results: Across 8 trials, 1722 subjects had DM and 7736 did not. The OR for death, MI or ACS for INV vs. CONS was similar in DM (OR 0.95, 95% CI 0.61-1.03) and non-DM (OR 0.82, 95% CI 0.64-1.05). INv reduced recurrent ACS to a similar extent in DM (OR 0.67, 0.52-0.87) and non-DM (OR 0.71, 0.56-0.89). INV reduced recurrent MI in DM (OR 0.75, 95% CI 0.53-0.95), but had no significant effect in non-DM (OR 0.93, 95% CI 0.72-1.21; P=0.62). INV did not reduce mortality in DM (OR 0.97, 0.73-1.28) or non-DM (OR 0.94, 0.74-1.19). In non-DM, the benefit of INV tended to be greater in those with elevated biomarkers (OR 0.72, 0.53-0.97) vs. those with (OR 0.92, 0.66-1.29, P interaction=0.29). DM patients benefited from INV irrespective of biomarker status (OR 0.75, 0.56-1.01; OR 0.76, 0.53-1.08).

Conclusion: An INV strategy reduces death, MI or ACS to a similar extent in DM and non-DM patients, but the former tend to have a greater reduction in recurrent MI. Regardless of biomarker status, DM patients have a comparable benefit from INV as high-risk biomarker positive non-DM patients.

Decreasing Coronary Heart Disease Mortality Over Two Decades: Prevention or Postponement? (A New Jersey Statewide Study)

William J. Kostis, Yu-Hsuan Shao, Abel E. Moreyra, Alan C. Wilson, John B. Kostis, For the Myocardial Infarction Data Acquisition System (MIDAS) Study Group, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ

Background: Over the last two decades, there has been a marked decrease in age-adjusted coronary heart disease (CHD) mortality. However, it is unclear whether this decrease is due to prevention or postponement of CHD deaths.

Methods: We studied admissions for acute myocardial infarction (N=344,659) and total CHD deaths (N=356,572) in New Jersey over the 19-year period 1986-2004 and examined differences in trends of crude and age-adjusted rates.

Results: In the years under consideration, there was a decrease in age-adjusted CHD mortality observed in non-DM patients. Different risk groups had a positive trend of mortality in the 19-year period studied. The decrease in the crude CHD death rate was less pronounced (640 to 360 [44%] in men and 537 to 349 [35%] in women). The difference between the crude and age-adjusted death rates increased progressively over time intervals 1986-89 and 2001-04, respectively. The decrease in the crude CHD death rate was less pronounced (640 to 360 [44%] in men and 537 to 349 [35%] in women). The difference between the crude and age-adjusted death rates increased progressively over the years studied. Of the 301 per 100,000 decrease in age-adjusted mortality in men, 280 deaths per 100,000 annually appear to have been truly prevented and 21 (7%) postponed to an older age during the 19-year period studied. In women, 228 per 100,000 deaths appear to have been truly prevented and 18 (7%) postponed.

Conclusions: Despite increased use of an invasive strategy, compared to younger patients, the elderly and very elderly remain significantly less likely to undergo coronary angiography/ revascularization, with an associated worse outcome. Future studies should determine whether more aggressive treatment of these high-risk patients improves outcome.

The Divergent Effect of Age on Functional and Mortality Outcomes Post-Myocardial Infarction

Suzanne V. Arnold, Karen P. Alexander, Frederick A. Masoudi, P. Michael Ho, Alpesh A. Amin, John A. Spertus, Mid America Heart Institute, Kansas City, MO

Background: Age is a well-established and powerful risk factor for death after AMI, even after adjusting for comorbidities and disease severity. Among patients who survive, it is not known whether increasing age is associated with functional decline, a similarly important, patient-centered outcome.

Methods: PREMIER, a 19-site US registry of post-MI pts, was analyzed to identify patients who had a decline in function at 1 year, as defined by either a >5 point decrease in SF-12 Physical Components score from baseline or if the patient reported being “too ill” to provide a follow-up interview at 1 year. The proportion of those with functional decline was compared across age in 10-year increments using the Cochran-Armitage Trend Test. One year mortality was also compared across age groups.

Results: Of 1789 patients who survived to 1 year and were able to be assessed for functional decline, 524 (29%) experienced decline. While age was strongly associated with 1-year mortality (p for trend<0.001), there was no association between age and 1-year functional decline among survivors (p for trend=0.39; Figure). Conclusion: While age remains strongly associated with post-MI death, there does not appear to be a significant relationship between age and functional decline among AMI survivors. More investigation is needed to understand the mechanisms behind this observed disassociation between functional and survival outcomes by age.
High Density Lipoprotein Cholesterol Is a Strong Independent Predictor of All-Cause Mortality in the Non-ST Segment Elevation Acute Coronary Syndrome

Alon Yarkoni, Nicholas Kalayeh, Yusel Kahn, Francisco J. Gonzalez, Aki Loli, Frank Cardello, Robert E. Halligan, Jr., Richard Gerkin, Kenneth B. Desizer, Nathan Laufer, Banner Good Samaritan/Veterans Affairs Medical Center Cardiology Fellowship Program, Phoenix, AZ

Background: High density lipoprotein cholesterol (HDL) has been shown to have specific anti-inflammatory activity. Although HDL is used in combination with other markers such as low density lipoprotein cholesterol (LDL) and total cholesterol, the significance of HDL alone is unclear. We hypothesized that HDL alone is an independent predictor of all-cause mortality in patients with the non-ST segment elevation acute coronary syndrome (ACS).

Methods: A total of 6881 patients who presented during 2000-2003 with non-ST segment elevation ACS had fasting lipid panels collected within the first 24 hours of admission. Patients were divided into quintiles based on values of each of the following lipid profiles: HDL level alone, triglyceride (TG)/HDL ratio, and low density lipoprotein cholesterol (LDL)/HDL ratio. The patient population with the lowest expected risk was selected as reference group for comparison. Isolated HDL as well as the ratios of TG/HDL and LDL/HDL were analyzed as predictors of all-cause mortality.

Results: After adjustment for coronary risk factors, isolated HDL and both TG/HDL and LDL/HDL ratios were statistically significant predictors of all-cause mortality, with HDL being the strongest. The hazard ratio among patients with HDL levels < 31 mg/dl was 2.11 (95% CI 1.79-2.4, p < 0.005). Patients with low HDL levels had increased all-cause mortality in the first 120 days following discharge. Kaplan-Meier Survival curves showed wide and significant separation between the first and fourth quintiles of HDL levels (log rank test p < 0.01).

Conclusions: HDL, TG/HDL and LDL/HDL were all found to be independent predictors of all-cause mortality in the non-ST segment elevation ACS, with HDL alone being the strongest predictor. Strategies to increase LDL levels may play a pivotal role for overall cardiac protection in this population. These findings contradict conventional opinion regarding the influence of isolated HDL levels as an independent predictor of survival in patients with ischemic heart disease.

Sex and Race Are Associated with the Finding of Non-Obstructive Coronary Artery Disease in Patients with Acute Coronary Syndromes

Neil P. Chokshi, Rachel L. Berger, Judith S. Hochman, Norma M. Keller, Frederick Feit, Michael J. Attubato, James N. Slater, Ivan Pena-Sing, Anvar Babaev, Harmony R. Reynolds, NYU School of Medicine, New York, NY

Background: A substantial minority of patients with acute coronary syndromes (ACS) are found to have no obstructive CAD (No-CAD) at angiography. The prevalence of this finding varies in the literature. We one pooled the frequency of No-CAD in ACS in a diverse patient population to better understand factors predisposing patients to this disease entity.

Methods: We reviewed the results of all angiograms from 5/1996 - 9/2006 at one private (NYU Medical Center, N=431) and one public (Bellevue, N=92) urban academic medical center. Charts were reviewed for indication for and results of angiography and current antiplatelet therapy. We identified no obstructive coronary disease as a finding on angiography and examined data from these patients to identify risk factors. Results: Overall, 32% of angiograms performed for variations indicated showed No-CAD, and the cohort included 947 pts with ACS, 52% of whom had confirmed MI by cardiac marker elevation. No-CAD was found at angiography in 20% of ACS pts overall and in 18% of those with MI. Women were more likely to have No-CAD than men in the overall ACS group (31% vs. 14%, p<0.001) and in the subset with MI (30% vs. 11%, p<0.001). See Table for distribution of No-CAD by race/ethnicity among 528 ACS pts for whom race/ethnicity was recorded.

Conclusions: The rate of No-CAD at angiography was high in this multi-ethnic sample of patients with ACS. No-CAD was particularly common among women and African-Americans.

Incidence and Impact of Acquired Thrombocytopenia Among Patients With Acute Coronary Syndromes

Tracy Y. Wang, Fang-Shu Ou, Matthew T. Roe, E. Magnus Ohman, Brian Gibler, Charles V. Pollack, Jr., Eric D. Peterson, Duke Clinical Research Institute, Durham, NC, University of Cincinnati College of Medicine, Cincinnati, OH

Background: Therapies used to manage acute coronary syndromes (ACS) can contribute to the risk of developing thrombocytopenia. However, the incidence and impact of varying severities of thrombocytopenia in contemporary practice are not well known.

Methods: We stratified 42,580 ACS patients (pts) with normal admission platelet counts (>150x10^9/L) in the CRUSADE initiative (2004-2006) into 3 groups based on nadir platelet counts: normal >150, mild 100-150, and moderate/severe thrombocytopenia <100 x10^9/L. A generalized estimating equations method was used to compare outcomes among these groups after adjusting for baseline characteristics.

Results: A total of 6168 (15%) pts developed mild thrombocytopenia and 1542 (4%) had moderate/severe thrombocytopenia. Thrombocytopenic pts were older and more likely to have lower body mass, diabetes, and renal insufficiency than pts without thrombocytopenia. Unfractionated heparin therapy was more commonly used in the thrombocytopenic groups (normal 56% v mild 60% v moderate/severe 62%, p<0.0001). Higher risks of bleeding, transfusion, and mortality were observed with increasing severity of thrombocytopenia (Figure). Notably, even thrombocytopenia was associated with increased adverse outcomes.

Conclusions: Approximately 1 in 5 pts treated with contemporary ACS therapies developed new thrombocytopenia that was associated with increased bleeding and mortality. Even mild thrombocytopenia is of clinical significance and warrants further evaluation.
bleeding, p=0.10). CRP levels were similar between patients with and without transfusion (median CRP 15.3 v. 16.9 mg/dL respectively, p=0.79). CRP levels fell rapidly in time in all groups (Figure) and there was no difference in CRP levels among patients with and without bleeding/transfusion or by bleeding severity at 1, 4, or 8 months.

Conclusion: Although CRP levels may be acutely elevated among patients with a bleeding event, this elevation in inflammatory markers resolved rapidly. There does not appear to be a persistent pro-inflammatory state as assessed by CRP among patients with a bleed, suggesting that inflammation per se does not contribute to the excess long-term mortality associated with bleeding.

**Myocardial Ischemia and Infarction**

**3:00 p.m.**

**1024-66**

### Myeloperoxidase Levels Associated With Risk of Cardiovascular Death and Heart Failure After Non-ST Elevation Acute Coronary Syndrome

**Benjamin M. Sirica, Marc S. Sabatine, Petr Jarolim, Sarah Sloan, Sabina A. Murphy, James L. de Lemos, David A. Morrow, TIMI Study Group, Boston, MA, Brigham and Women’s Hospital, Boston, MA**

#### Background:

Myeloperoxidase (MPO) is released from leukocytes and implicated in the pathophysiology of ACS. Initial studies demonstrated an association of higher MPO with poor cardiovascular (CV) outcomes but prospective evaluation together with contemporary biomarkers is still needed.

#### Methods:

4516 pts randomized in MERLIN-TIMI 36 with NSTEACS had baseline samples obtained within 48hrs of last symptoms. MPO, cTnl (99%ile = 0.07), and NT-proBNP were measured (Dade Behring Dimension) and MPO was categorized by quartiles and a cutpoint of 670 pM (based on prior work). Median follow-up was 1-year.

#### Results:

MPO was >670 pM in 1938 pts(43%). Increasing quartiles of MPO were associated with greater risk of CV death/heart failure (HF) (Figure). Elevated MPO (>670pM) was associated with increased risk of CV death (adjHR 1.2, p=0.001) and CV death/HF after adjusting for baseline risk factors and biomarkers (adjHR 1.7, p=0.001). (Figure) This relationship was consistent in pts with normal cTnl (adjHR 1.9, p=0.001) or elevated cTnl (Adj HR 1.7, p=0.002). Elevated MPO was associated with CVD/MI at 30d (adjHR 1.3, p=0.06).

#### Conclusions:

Elevated MPO, a marker of leukocyte activation, is associated with a substantially higher risk of cardiac events in pts with ACS. This relationship is independent of other biomarkers and suggests that MPO offers additive information regarding cardiovascular outcomes.

**1024-67**

### The Effect of Intended Duration of Clopidogrel Use on Early and Late Mortality and Major Adverse Cardiac Events in Patients With Drug-Eluting Stents

**Michelle J. Butler, David Eccleston, David J. Clark, Andrew E. Ajan, Nick Andrianopoulou, Angela Brennan, Alexander Black, Chris Reid, Anthony Dart, Stephen J. Duffy, Melbourne Interventional Group, Alfred Hospital, Melbourne, Australia, Monash University, Department of Epidemiology and Preventive Medicine, Melbourne, Australia**

#### Background:

The optimal duration of clopidogrel use for prevention of stent thrombosis with drug-eluting stent (DES) use is uncertain.

#### Methods:

We analysed data from 2860 patients who underwent percutaneous coronary intervention (PCI) in a large registry who had 15-month follow-up; 1669 (56.0%) with DES implantation and 1311 (44.0%) with bare-metal stents (BMS). We compared outcomes at 30 days and 12 months in 3 patient groups according to planned duration of clopidogrel use: ≤3months, 6 months and ≤12 months.

#### Results:

Procedural success was similar among the 3 patient groups, irrespective of stent type used. Among patients receiving a DES, 30-day follow up demonstrated no difference in mortality (p=0.32) or overall MACE (p=0.55) between the groups. In patients who received a DES, 12-month mortality was significantly lower in the group of patients with a longer (≥12 months) planned duration of clopidogrel when compared with a shorter (≤6 months) planned duration (2.8% vs. 5.3%, p=0.012). However, 12-month myocardial infarction (6.4% vs. 6.6%, p=0.82), target-vessel revascularization (7.1% vs. 6.5%, p=0.61), and overall MACE (14.3% vs. 14.8%, p=0.76) were similar in the longer- and shorter-duration clopidogrel strategies. In contrast, mortality at 12 months was similar among the 3-clopidogrel-duration strategies in patients receiving a BMS, as was 12-month myocardial infarction, target-vessel revascularization and overall MACE.

Kaplan-Meier analysis demonstrated improved cumulative survival with planned clopidogrel use of ≥12 months (log rank p=0.017). Premature cessation of clopidogrel in patients receiving a DES was documented in 5.2% of patients alive at 30-day follow up and these patients had increased 12-month mortality (10.6% vs. 1.4%, p=0.0001) and MACE (22.4% vs. 12.0%, p=0.005).

#### Conclusions:

These data suggest that in patients treated with DES, longer (≥12 months) planned duration of clopidogrel results in significantly higher event rates. Randomized studies are urgently needed to address this issue.

**3:00 p.m.**

**1024-68**

### Impact of Anemia on Long-term Mortality in Patients with Acute Coronary Syndrome

**Umeesh U. Tamhane, Irlan Hameed, Daniel Montgomery, Krishna Aragam, Garry Ng, Saagar Sanghvi, Eva Kline-Rogers, Kim A. Eagle, Hilinder S. Gurum, University of Michigan Medical Center, Ann Arbor, MI**

#### Background:

Anemia is an independent marker of short-term mortality in patients with acute coronary syndromes (ACS). We investigated the role of anemia as a prognostic marker of long-term mortality in unselected patients with ACS. Further, we assessed the incremental value of adding hemoglobin (Hb) to Global Registry of Acute Coronary Events (GRACE) risk model.

#### Methods:

We analyzed 3078 consecutive patients with ACS admitted to the University of Michigan between December 1998 and October 2004 with complete follow-up data. Admission Hb was available for 3052. Patients were divided into two groups based on whether they had anemia according to WHO criteria (Hb <13.0g/dL [male] / <12.0g/dL [female]). Primary endpoint of our analysis was all-cause mortality. Kaplan-Meier curve was used to plot the survival of anemic and non-anemic patients. A Multivariate model was used to assess the additive value of anemia beyond that provided by the GRACE risk score.

#### Results:

There were 171 deaths on follow-up. Anemic patients had a significantly higher risk of death (p<0.001). After adjusting for GRACE risk score, anemia remained an independent predictor of mortality (OR=2.42; 95% CI 1.74-3.35, p<0.001). Anemia was an independent predictor of mortality (OR=2.42; 95% CI 1.74-3.35, p<0.001). Unadjusted OR=3.40. Adding Hb into the GRACE model modestly improved the prediction of six-month mortality (C statistic 0.78 versus 0.77).

#### Conclusion:

Lower Hb level is a significant predictor of long-term mortality. This readily available marker added value to established independent risk predictor models.

**3:00 p.m.**

**1024-69**

### Low Responsiveness to CLopidogrel and Sirolimus-or Paclitaxel-Eluting StEnt Thrombosis (RECLOSE) Trial: the Long-Term Mortality

**Piergiovanni Buonamici, Angela Migliorini, Guia Moschi, Ruben Vergara, Rossella Marucci, Gian Franco Gensini, Rosanna Abbate, David Antonucci, Careggi Hospital, Florence, Italy**

#### Background:

The RECLOSE trial showed that non-responsiveness to clopidogrel is associated with reduced 12-month mortality, and that premature cessation of clopidogrel results in significantly higher event rates. Randomized studies are urgently needed to address this issue.

#### Methods:

4516 pts randomized in MERLIN-TIMI 36 with NSTEACS had baseline samples obtained within 48hrs of last symptoms. MPO, cTnl (99%ile = 0.07), and NT-proBNP were measured (Dade Behring Dimension) and MPO was categorized by quartiles and a cutpoint of 670 pM (based on prior work). Median follow-up was ~1-year.

#### Results:

MPO was >670 pM in 1938 pts(43%). Increasing quartiles of MPO were associated with greater risk of CV death/heart failure (HF) (Figure). Elevated MPO (>670pM) was associated with increased risk of CV death (adjHR 1.2, p=0.001) and CV death/HF after adjusting for baseline risk factors and biomarkers (adjHR 1.7, p=0.001). (Figure) This relationship was consistent in pts with normal cTnl (adjHR 1.9, p=0.001) or elevated cTnl (Adj HR 1.7, p=0.002). Elevated MPO was associated with CVD/MI at 30d (adjHR 1.3, p=0.06).

#### Conclusions:

Elevated MPO, a marker of leukocyte activation, is associated with a substantially higher risk of cardiac events in pts with ACS. This relationship is independent of other biomarkers and suggests that MPO offers additive information regarding cardiovascular outcomes.
Does the Pattern of Serial Values of C-Reactive Protein Predict Outcome in Patients With Acute Coronary Disease? The RISCA Study

Peter Bogaty, Luce Boyer, Serge Simard, Franz Dauwe, Robert Dupuis, Benoît Verret, Thao Hoang, Fernand Bertrand, Gilles R. Dagenais, James M. Brophy, Quebec Heart Laval/Laval Hospital/Laval University, Quebec, QC, Canada

Background: The predictive value of serial measurements of the inflammatory marker, C-Reactive Protein (CRP), in the follow-up of patients with acute coronary syndromes is undefined.

Methods: We prospectively measured CRP at admission, hospital discharge, and 1 month later in 1210 patients with acute myocardial infarction (MI; 64%) or unstable angina (UA; 36%). Patients were followed for 1 year and were classified into 5 patterns of serial CRP values: high plateau; high plateaus; falling values; rising values; and no pattern. High values and low values were those in the top and bottom tertiles, respectively, at that sampling time point. We evaluated the odds ratios (OR) and 95% confidence intervals (CI) of each pattern for occurrence at 1 year of the primary composite endpoint of death, MI, and UA with ECG changes.

Results: Mean age was 62 ± 12 years, 75% were men, 20% had diabetes, 28% previous MI, 6% coronary vessel disease, and 6% previous heart failure. From hospital discharge to 1 year, there were 37 deaths (3.1%), 59 nonfatal MI (5.0%) and 26 UA with ECG changes (2.2%). The primary endpoint occurred in 109 patients (9.2%) at 1 year. ORs with 95% CI of the 5 patterns for the occurrence of the primary endpoint are shown in Table.

Table: 30-day Clinical Outcomes and Costs

<table>
<thead>
<tr>
<th>CRP pattern</th>
<th>OR (95% CI) for primary endpoint of patterns of admission &amp; discharge</th>
<th>OR (95% CI) for primary endpoint of patterns of admission, discharge, and 1 month CRP values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Plateau (n=236)</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>High Plateau (n=193)</td>
<td>1.25 (0.64, 2.43)</td>
<td>1.59 (0.52, 4.91)</td>
</tr>
<tr>
<td>Rising Values (n=140)</td>
<td>0.96 (0.53, 1.73)</td>
<td>0.93 (0.63, 1.39)</td>
</tr>
<tr>
<td>Falling Values (n=141)</td>
<td>1.16 (0.55, 2.43)</td>
<td>0.60 (0.15, 2.47)</td>
</tr>
<tr>
<td>Low Plateau (n=193)</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
</tr>
</tbody>
</table>

Conclusion: Neither low nor high plateaus nor rising or falling values predicted occurrence of the primary endpoint at 1 year. This large prospective study does not support the clinical utility of measuring serial CRP values to predict outcome in patients with acute coronary disease.

Economic Evaluation of Bivalirudin With or Without Glycoprotein IIb/IIIa Inhibition Versus Heparin With Routine Glycoprotein IIb/IIIa Inhibition for Early Invasive Management of Acute Coronary Syndromes

Duane S. Pinto, Gregg W. Stone, Meghan York, Matthew R. Reynolds, Brent T. McLaurin, David A. Cox, Elizabeth A. Schneider, Chunhuei Shi, Joshua Walczak, David A. Machon, Ronna H. Berezin, Roxana Mehran, Ebrahim Ohman, A. Michael Lincoff, David J. Cohen, Beth Israel Deaconess Medical Center, Boston, MA, Cardiovascular Research Foundation, Columbia University, New York, NY

Background: The ACUITY trial demonstrated that in ACS pts enrolled under invasive management, bivalirudin (BIV) monotherapy yields similar ischemic complication rates and less bleeding compared to regimens that include glycoprotein IIb/IIIa receptor inhibitors (GPI).

Methods: We performed a prospective economic analysis of US pts enrolled in ACUITY (n=7851) who were randomized to receive heparin (UFP or LMWH) + GPI, BIV + GPI or BIV alone. Resource utilization data were collected through 30 days and costs were estimated using resource-based accounting, hospital (HOSP) billing data and the Medicare fee schedule.

Results: At 30 days, ischemic event rates were similar for all groups, but major bleeding was significantly lower with BIV alone (3.4% vs. 8.4% and 9.3%, respectively; p<0.001). Although anticoagulant costs were lowest for heparin + cath lab GPI, initial HOSP costs were lowest with BIV alone compared to either heparin + upstream GPI or heparin + cath lab GPI (p=0.001) with similar findings at 30 days. Regression modeling demonstrated that savings with BIV were primarily due to lower major and minor bleeding (incremental cost = $86856 and $22928/event).

Conclusions: Among US ACUITY patients, BIV monotherapy compared to heparin + GPI, resulted in similar rates of ischemic events, reduced bleeding and shorter LOS. Despite higher drug costs, aggregate HOSP and 30 day costs were lowest with BIV alone. BIV is thus an economically attractive alternative to GPI in pts with moderate-high risk ACS.

Coronary flow reserve is related to extension and transmural entity of myocardial necrosis and predicts functional recovery after acute myocardial infarction. A study performed with contrast-enhanced magnetic resonance

Roberta Montisci, Massimo Ruscucchio, Francesco Tona, Francesco Cortebert, Cristiano Saras, Sara Portarolfo, Lusia Cacciavillani, Ramoado Angelo, Luig Meloro, Sabino Ilcic, Clinical Cardiology, Cagliari, Italy, Clinical Cardiology, Padova, Italy

Background: In humans, few studies have examined the effect of the transmural entity of myocardial necrosis on coronary microcirculation and its related role in predicting functional recovery. The aim of this study was to examine the influence of infarct size and gadolinium contrast-enhanced cardiac magnetic resonance (GE-MRI) derived structural determinants of coronary flow reserve (CFR) after anterior myocardial infarction (AMI), and their predictive value on regional functional recovery.

Methods: CFR by transfemoral schoenography and GE-MRI were studied in 37 patients with AMI, who underwent coronary revascularization with coronary angioplasty. The wall motion score index in left descending anterior coronary artery territory (A-WMSI) was calculated at admission and follow-up (FU). Recovery of regional left ventricular(LV) function was defined as the difference in A-WMSI at admission and FU.

The necrosis score index (NSI) and transmurality score index (TSI) by GE-MRI were calculated in the risk area.

Results: Bivariate analysis indicated that the CPK peak (P<0.001), Tropinin I peak (P<0.003), heart rate (P=0.03), NSI (P=0.001) and TSI (P=0.001) were related to CFR and that CFR (P=0.001), NSI (P=0.01), TSI (P=0.001), microvascular obstruction at GE-MRI (P=0.001) and heart rate (P=0.03) are all related to functional recovery. Multivariable analysis revealed that TSI (P=0.001) was the only independent determinant of CFR and that CFR (P=0.001) was the only independent predictor of A-WMSI.

Conclusions: Preservation of microvascular function after AMI is related to the transmural entity of myocardial necrosis, and is an important factor influencing regional LV recovery.

Major Bleeding Is Associated With Increased One-Year Mortality and Ischemic Events in Patients With Acute Coronary Syndromes: Results From the ACUITY Trial

Steven V. Manoukian, Frederick Feit, Steven R. Steinbuch, Michele D. Vozel, George D. Dangas, Ramin Ebrahimi, Roxana Mehran, Gregg W. Stone, Emory University School of Medicine, Atlanta, GA

Background: Major bleeding (MB) is associated with increased short-term mortality and ischemic events in acute coronary syndromes, although its long-term impact is less clear. We evaluated the relationship between MB and rates of one-year mortality and ischemic events in patients with acute coronary syndromes.

Methods: The ACUITY Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial is a randomized comparison of unfractionated heparin or enoxaparin (H) + glycoprotein IIb/IIIa inhibition (GPI), bivalirudin (BIV) + GPI and BIV alone in 13,819 patients with moderate and high-risk acute coronary syndromes undergoing an early invasive strategy. MB (non-coronary artery bypass surgery-related) was defined as intracranial, intradural or retroperitoneal access site with intervention, hematoma ≥5 cm, hemoglobin drop ≥3 g/dL with source ≥49 g/dL without source or transfusion within 30 days. The impact of MB on one-year mortality and ischemic events was assessed using a time-updated covariate-adjusted Cox model.

Results: Of 13,819 patients, 645 (4.7%) had MB. Patients with MB were more likely to be older, female and have lower body weight, diabetes, hypertension, reduced creatinine clearance and elevated biomarkers. They were more likely to receive GPI and less likely to have had prior percutaneous coronary intervention, smoke and have hypertension (all p<0.05). MB was less frequent for BIV vs. H+GPI (3.0% vs. 5.7%, p<0.001), and similar for BIV-GPI vs. H+GPI (p=0.9). Mortality at one year was higher in patients with vs. without MB (14.4% vs. 3.3%, p<0.001). Composite ischemic event rates at one year
were also higher in patients with vs. without MB (32.7% vs. 14.9%, p<0.0001). MB was an independent predictor of one-year mortality (hazard ratio [95% confidence interval] = 2.89 [2.54-3.27], p<0.0001).

Conclusion: MB is an independent predictor of one-year mortality and is associated with increased rates of ischemic events at one year in patients with acute coronary syndromes. MB rates are lower in patients treated with BIV (vs. H+GPI) and similar in regimens containing GPI.

**Transfusion Is Associated With Increased One-Year Mortality and Ischemic Events in Patients With Acute Coronary Syndromes: Results From the ACUITY Trial**

Steven V. Manoukian, Michele D. Voeltz, Frederick Felt, Sunil V. Rao, Steven R. Steinshlub, George D. Danas, Roxana Mehran, Gregg W. Stone, Emory University School of Medicine, Atlanta, GA

Background: Blood product transfusion is associated with increased rates of short-term mortality and ischemic events in patients with acute coronary syndromes. Whether transfusion adversely affects long-term outcomes is not well-studied. We assessed the relationship between transfusion and rates of one-year mortality and ischemic events in patients with acute coronary syndromes.

Methods: The Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial is a randomized comparison of bivalirudin (BIV), heparin or enoxaparin (H) + glycoprotein IIb/IIIa inhibition (GPI) and BIV+GPI in 13,819 patients with moderate and high-risk acute coronary syndromes undergoing an early invasive strategy. Transfusion was defined as the administration of any blood product, including whole blood, packed red blood cells, platelets or fresh frozen plasma within 30 days. The association between transfusion and rates of one-year mortality and composite ischemic events (death, myocardial infarction and unplanned revascularization) was assessed using a time-updated covariate-adjusted Cox model.

Results: Of 13,819 patients, 319 (2.3%) received a transfusion. Transfusion rates were significantly lower in patients treated with BIV vs. H+GPI (1.6% vs. 2.7%, p=0.0003) but similar in patients treated with BIV+GPI vs. H+GPI (2.6% vs. 2.7%, p=ns). Composite ischemic event rates at one year were higher in transfused vs. nontransfused patients (40.1% vs. 15.1%, p<0.0001). Mortality at one year was also higher in transfused vs. nontransfused patients (21.9% vs. 3.4%, p=0.0001). Transfusion was an independent predictor of one-year mortality (hazard ratio [95% confidence interval] = 3.89 [2.88-5.25], p<0.0001).

Conclusion: Blood product transfusion is an independent predictor of one-year mortality and is associated with increased one-year ischemic event rates in patients with acute coronary syndromes. Transfusion rates are lower in patients treated with BIV compared to those treated with H+GPI. These data suggest that BIV may have a beneficial effect on mortality in part due to a reduction in the risk of transfusion in patients with acute coronary syndromes.

**Anemia Is Associated With Increased One-Year Mortality and Ischemic Events in Patients With Acute Coronary Syndromes: Results From the ACUITY Trial**

Steven V. Manoukian, George D. Danas, Michele D. Voeltz, Frederick Felt, Roxana Mehran, Gregg W. Stone, Emory University School of Medicine, Atlanta, GA

Background: Anemia is associated with increased rates of short-term mortality and ischemic events in patients with acute coronary syndromes. Whether anemia adversely impacts long-term outcomes is less clear. We assessed the relationship between anemia and rates of one-year mortality and ischemic events in patients with acute coronary syndromes.

Methods: The Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial is a randomized comparison of bivalirudin (BIV), heparin or enoxaparin (H) + glycoprotein IIb/IIIa inhibition (GPI) and BIV+GPI in 13,819 patients with moderate and high-risk acute coronary syndromes undergoing an early invasive strategy. Transfusion was defined as the administration of any blood product, including whole blood, packed red blood cells, platelets or fresh frozen plasma within 30 days. The association between transfusion and rates of one-year mortality and composite ischemic events (death, myocardial infarction and unplanned revascularization) was assessed using a time-updated covariate-adjusted Cox model.

Results: Of 13,819 patients, 319 (2.3%) received a transfusion. Transfusion rates were significantly lower in patients treated with BIV vs. H+GPI (1.6% vs. 2.7%, p=0.0003) but similar in patients treated with BIV+GPI vs. H+GPI (2.6% vs. 2.7%, p=ns). Composite ischemic event rates at one year were higher in transfused vs. nontransfused patients (40.1% vs. 15.1%, p<0.0001). Mortality at one year was also higher in transfused vs. nontransfused patients (21.9% vs. 3.4%, p=0.0001). Transfusion was an independent predictor of one-year mortality (hazard ratio [95% confidence interval] = 3.89 [2.88-5.25], p<0.0001).

Conclusion: Blood product transfusion is an independent predictor of one-year mortality and is associated with increased one-year ischemic event rates in patients with acute coronary syndromes. Transfusion rates are lower in patients treated with BIV compared to those treated with H+GPI. These data suggest that BIV may have a beneficial effect on mortality in part due to a reduction in the risk of transfusion in patients with acute coronary syndromes.

**ST Segment Deviation Resolution Predicts Long-Term Mortality in Patients With Acute Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention**

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

Background: Because the predictive value of ST segment deviation resolution (STR) originates from the fibrinolysis era, we evaluated whether STR is predictive for long-term mortality in patients with ST Elevation Myocardial Infarction (STEMI) patients undergoing primary Percutaneous Coronary Intervention (PCI).

Methods: In this single center cohort study, 1572 STEMI patients underwent primary PCI between 2000 and 2005. Mean clinical follow-up was 2.5 years (SD ± 1.3 years). STR was defined as the relative difference (in %) of the summed ST deviation between the pre-PCI and the immediately post-PCI 12-lead electrocardiogram. We discriminated between 687 anterior MI and 885 non-anterior MI patients.

Results: During follow-up, 83 patients with anterior MI and 82 with non-anterior MI died. Among patients with non-anterior MI, there was an inverse relationship between STR and mortality. Compared to patients with STR ≥ 70% (reference), patients with STR between 70 and 30% showed a hazard ratio (HR) of 3.0 (95% confidence interval (CI), 1.5 - 6.1; p = 0.002), and patients with STR < 30% showed a HR of 4.9 (95% CI, 2.4 - 9.8; p = 0.0001). Among anterior MI patients, mortality was solely higher in patients with STR < 30% compared to patients with STR ≥ 30% (HR 2.0; 95% CI, 1.2 to 3.3; p = 0.005) (see table).

Conclusions: STR immediately post procedure is a strong predictor of long-term mortality in STEMI patients undergoing primary PCI. Different cut-off points should be used for anterior versus non-anterior MI.

**Chronic Kidney Disease, Cardiovascular Outcomes, and Treatment Disparities following Non-ST Elevation Myocardial Infarction**

Jessica L. Mega, Benjamin M. Scirica, Jie Qin, C. Michael Gibson, David A. Morrow, Brigham & Women’s Hospital, Boston, MA

Background: Chronic kidney disease (CKD) is associated with an increased risk of death and CV events following an MI. There is concern regarding underutilization of medical and interventional therapies in this population.

Methods: MERLIN-TIMI 36 randomized NTSE ACS patients to ranolazine or placebo, and the study did not exclude subjects based on renal dysfunction (except dialysis). Glomerular filtration rate (GFR, ml/min/1.73 m2) was estimated using MDRD in 6,557 patients. Results: Patients with worse renal function were older and more likely to have a history of DM, DM, prior revascular, and heart failure (P<0.0001 for each). Lower GFR was associated with a striking increase in risk of CV death and MI through 1 year (Fig), despite adjustment for baseline variables (GFR <30 vs. >90: HR 2.10, 95% CI 1.32-3.35). During the hospitalization, patients with lower GFRs were found to have a greater extent of coronary disease on angiography and worse LV function (P<0.0001 for each); however, they were less likely be treated with evidence-based medicines (including aspirin, clopidogrel, heparin, GPIIb/IIIa receptor inhibitors, P<0.04 for each) and undergo an early invasive management strategy (Fig).

Conclusions: There was a strong graded relationship between worse renal function and cardiovascular events, and patients with lower GFR were less likely to be treated with evidence-based medications and an early invasive treatment strategy. Continued efforts to modify the high risk of this CKD population are warranted.
1024-78  
Prognosis of Elderly Patients after Acute Myocardial Infarction and Coronary Revascularization Procedure  
Nicolaos Manessoglou, Rémy Pilière, Alain Beauchet, Thierry Joseph, Franck Digne, Pascal Lacolme, Olivier Dubourg, AP-HP, Hôpital universitaire Ambroise Pare, Boulogne, France

The aim of this study was to assess the prognosis of pts ≥ 80 years referred to a cath-lab for acute myocardial infarction (MI).

Methods: Over an 10-year study period, we analyzed the data of 1687 pts referred to our cath-lab for acute MI. We divided the data into two groups: group 1 (pts ≥ 80 years of age) and group 2 (pts < 80 years). Follow-up was established by phone contact with the pts, their families or their physicians. Results: Global in-hospital mortality was 7%: 11% in pts ≥ 80 years versus 5.5% in pts in group 2 (p < 0.0001). Among pts presenting with cardiogenic shock (18 pts in group 1 and 60 pts in group 2), the in-hospital mortality was 83% versus 62% (p = 0.07). In pts without initial cardiogenic shock, in-hospital mortality was 10% in group 1 versus 2% in group 2 (p < 0.0001). Follow-up was obtained in 97.4% in group 1 (30 ± 28 months) and 96.5% in group 2 (63 ± 49 months). Kaplan-Meier analysis showed an early increased mortality of pts ≥ 80 years at one year (p < 0.0001, Fig), whereas the rate of mortality among pts ≥ 80 years at one year but after the initial hospitalization following acute MI was low (4% versus 3% in group 2, p = 0.58). Long-term follow-up (> 10 years) reveals that elderly patients died, as expected.

Conclusions: This study demonstrates that elderly patients presenting with acute MI had an early increased risk of mortality. Interestingly, once the acute phase passed, prognosis at one year is excellent and is comparable with younger patients.

1024-80  
Is Right Ventricular Involvement A Predictor Of Long-Term Mortality In Patients With Acute Inferior ST Elevation Myocardial Infarction?  
Stamatis Makrygiannis, Michael Zairis, Giorgios Z Tsagakis, Dionisis Xenos, Anastasios Theodosios-Georgias, Evdikti Gogusoueta, Petros Smilakos, Joseph Papadopoulos, Konstantinos Garefalakis, Nikolas Tellis, Konstantinos Katsaras, Stephanos Foussas, Tzanio Hospital, Piraeus, Greece

Background: It is well known that right ventricular (RV) myocardial involvement carries an increased risk of early fatal and non-fatal complications in patients (pts) who are hospitalized due to an acute inferior ST elevation myocardial infarction. However, there is scant data concerning the long term impact of RV myocardial involvement in this setting.

Methods: The study cohort comprised 1208 consecutive pts (mean age=64.5±10.3 yrs, 79.2% males) who survived to hospital discharge after hospitalization for acute inferior ST elevation myocardial infarction. The cohort was divided into two groups according to the presence (459 pts) or no (749 pts) of RV involvement, defined as ST-segment elevation ≥ 1mm in V4R, in admission ECG. Cardiac death by 3 years was the prespecified primary study endpoint. Results: There were no significant differences in baseline characteristics, medical history and medical therapy during the study period between the 2 groups. By 3 years, the incidence of the primary endpoint was similar in both groups (17.6% and 16.8% for pts with or without RV involvement, respectively; RR=1.1, 95%CI=0.8–1.4; p=0.73). Conclusion: In patients who survived to hospital discharge following hospitalization for acute inferior ST elevation myocardial infarction, right ventricular involvement does not portend any increased risk for long term mortality.
Myocardial Ischemia and Infarction

Methods: In a prospective study, EECP was performed for 1 hour each day for 35 days in 47 patients, mean age 61 ± 8 years, with prior coronary revascularization who had chronic refractory angina despite antianginal drugs and who were not candidates for further coronary revascularization. The effect of EECP on symptoms, quality of life, 6-minute walking distance, and LV systolic and diastolic function measured by 2-dimensional and Doppler echocardiography was investigated after 35 days of EECP and at 1 year after EECP.

Results: Compared to baseline values, EECP significantly improved anginal symptoms, dyspnea on exertion, and quality of life after 35 days of treatment (p < 0.001) and at 1 year-follow-up (p < 0.001). Compared to the baseline value of 653 ± 249 feet, EECP significantly improved the 6-minute walking distance to 1,025 ± 234 feet after 35 days of treatment (p < 0.001) and to 1,040 ± 221 feet at 1-year follow-up (p < 0.001). However, EECP did not significantly affect LV ejection fraction, LV end-diastolic and end-systolic volumes, LVEF, deceleration time measured by 2-dimensional and Doppler echocardiography.

Conclusions: EECP caused a significant improvement in symptoms and in exercise tolerance after 35 days of therapy and at 1 year follow-up in patients who were candidates for refractory angina pectoris who were not candidates for further coronary revascularization. However, EECP did not improve any measurements of LV systolic function or LV diastolic function.

Do Different Healthcare Systems Impact Major Outcomes in Stable Coronary Disease Patients Enrolled in COURAGE?

Background: The COURAGE trial reported no significant differences in major cardiovascular outcomes when coronary angioplasty (PCI) was added to optimal medical therapy (OMT) after a median 4.6 year follow-up. Patients were enrolled from US Veteran Affairs (VA) (n=968), US non-VA (US) (n=385) and Canadian (CDN) (n=631) healthcare systems; randomization was blocked by hospital and prior bypass surgery. We examined cardiovascular outcomes by individual healthcare system (HCS) to determine whether HCS (and their associated practice cultures) was associated with the study outcomes.

Methods: Cox regression analyses after adjustment for baseline patient characteristics was used to assess the association of HCS with death and for the composite endpoint of death/myocardial infarction (MI).

Results: Baseline demographics were not significantly different among treatment groups within each HCS. Five years after randomization, the percent of pts that exercised 30-45 min at least 5 times/week was 33%, 35% and 46% (p<0.001) and LDL cholesterol was <70 mg/dl in 39%, 42% and 50% of pts (p<0.001) in the VA, US, and CDN HCS, respectively. In spite of these differences, the interaction between HCS and PCI or OMT for the endpoint death (p=0.25) or the composite endpoint of death/MI (p=0.24) were obtained after analyses for cardiovascular death and cardiovascular death/MI.

Conclusions: In COURAGE, PCI was not shown to improve survival or reduce death/MI compared to OMT across all 3 healthcare systems studied.

Routine PCI Improves Short but not Long-term Angina Status in Patients with an Occluded Infarct Artery: Results from the Outed Artery Trial (OAT)

Gerard P. Devlin, Daniel B. Mark, Gervasio A. Lamas, Antonio C. Carvalho, Vladimir Dzavik, Sandra A. Forman, Carlos R. Vozzi, Michael Ragosta, Jamie M. Rankin, Paul Caramori, George Sopko, Eduardo Balcells, Jonathan Leor, Bruce A. Barton, Judith S. Hochman, Wakefield Hospital, Hamilton, New Zealand, New York University School of Medicine, New York, New York

Background: OAT (n=2201) reported no reduction in the primary endpoint of death, re-MI or heart failure with routine (3-28 days post-MI) percutaneous coronary intervention (PCI) (n=1101) of an occluded infarct-related artery (IRA) relative to medical treatment (MED) (n=1100). Anginal symptoms and non-procedural revascularization (revasc) were major secondary endpoints.

Methods: Angina status and revasc were collected at 4 months and then annually. Rx comparisons are by intention-to-treat.

Results: During follow-up, 764 pts developed angina. Compared with MED, 6 per 100 more pts assigned to PCI were angina free at 1 year (p=002) (figure) narrowing to 3 per 100 at 5 yrs (p=0.08). Use of anti-angiinal therapy was similar in the 2 groups. At 5 yrs, revasc was more frequent in MED (22% vs. 19% for PCI, p=0.03). However, in pts with follow-up angina (n=764), revasc rates were not different between groups (17% PCI vs. 19% MED, p=0.56). Most pts with angina in follow-up either had no revasc or had it performed prior to symptom onset (PCI 83% vs. MED 81%, p=0.56). Reasons for revasc were similar in the 2 groups including ACS in 37%, stable angina in 33%, physician preference in 18%, other in 12%. Conclusions: In a large randomized clinical trial of stable post-MI pts, PCI of an occluded IRA produced a modest early benefit on an angina status that was 3 per 100 for 5 years. Follow-up revasc was slightly more common in the MED group and was not driven by more frequent ischemia, with almost one in five procedures related to physician preference alone.
Methods: Thirty patients undergoing elective CABG surgery (15 in on-pump and 15 in off-pump) were enrolled in the study. Functional and biochemical responses to aspirin were evaluated by arachidonic acid (ARA) - induced platelet aggregation and urine 11-dehydro thromboxane B2 metabolite excretion. Samples were collected before surgery (baseline; >7 days after aspirin withdrawal) and on days 1, 2 and 5 after surgery.

Results: Baseline ARA aggregability was 55%; 95% CI [52%, 58%]. On day 1, platelet aggregability decreased (22%; 95% CI [16%, 28%]; p<0.05). On day 2, despite the aspirin administration, platelet aggregability increase above the values from day 1 (52%; 95% CI [27%, 38%]; p<0.05). Only on day 5, sufficient inhibition of platelet aggregation was achieved (15%; 95% CI [10%, 20%]; p<0.05).

Preoperative urine concentration of 11-dehydro TX B2 was 96ng/mL; 95% CI [67, 122]. On day 1, there was increase in concentration (18ng/mL; 95% CI [104, 256]; p<0.05) and on day 5, the concentration remained almost similar in comparing with the preoperative values (85ng/mL; 95% CI [49, 120], n=NS). Only on day 5, significant decrease in concentration of thromboxane metabolite was achieved (62ng/mL; 95% CI [38, 88]; p<0.05).

Conclusion: Aspirin did not sufficiently inhibit platelet aggregation and thromboxane formation in the early postoperative period. Thus, antiplatelet treatment strategy should be intensified or modified in patients early after bypass surgery.
**1031**

**Stable Ischemic Syndrome; Coronary Artery Bypass Surgery**

**Tuesday, April 01, 2008, 9:00 a.m.-12:30 p.m.**

McCormick Place, South Hall

**ACC.Poster Contributions**

**Stable Ischemic Syndrome Using Dipyridamole Stress CMR in Patients With Known or Suspected Coronary Disease**

**Vicente Bouj, Juan Sanchis, Julio Nunez, Luis Mainar, Oliver Husser, Maria P. Lopez-Lorente, Vicente Ruiz, Eva Rumiz, Francisco J. Chorro, Angel Llacer, Hospital Clinico Universitario, Valencia, Spain, University of Valencia, Valencia, Spain**

**Background:** Data on the prognostic value and the therapeutic implications of the ischemic cascade on the basis of stress perfusion cardiovascular magnetic resonance) CMR is largely preliminary to date.

**Methods:** Dipyridamole stress CMR was performed in 601 patients with ischemic chest pain and known or suspected coronary artery disease. Myocardial infarction and coronary revascularization within the previous 3 months were exclusion criteria. The presence (>1 segment) of perfusion deficit (at stress first-pass perfusion imaging) and inducible wall motion abnormalities (WMA) with dipyridamole were analyzed. According to the ischemic cascade, patients were categorized in C1 (no evidence of ischemia, n=354, 59%), C2 (isolated perfusion deficit, n=181, 30%) and C3 (simultaneous perfusion deficit and inducible WMA, n=66, 11%).

**Results:** During a median follow-up of 80 weeks, 69 major adverse cardiac events (MACE), including 21 cardiac deaths, 14 nonfatal myocardial infarctions and 34 re-admissions for unstable angina with documented abnormal angiography were detected.

In non-revascularized patients, MACE were 4% in C1, 20% in C2 and 39% in C3 (p<0.001). Once adjusted for baseline characteristics, C2 (3 [1.5-5.9], p<0.001 vs. C1) and C3 (7.7 [3.4-17.3], p<0.001 vs. C1) independently increased the risk of MACE. Once adjusted for a fair propensity score (C-statistic=0.83) to undergo revascularization, CMR-related revascularization (n=102, 17%) increased the risk of MACE in C1 (4% vs. 21%, 3.0 [9.0-12.5], p=0.06) and had neutral effects in C2 (20% vs. 19%, 1.1 [0.5-2.4], p=0.7). Only in patients with severe ischemia, C3, CMR-related revascularization independently reduced the risk of MACE (39% vs. 11%, 0.2 [0.1-0.7], p=0.01).

**Conclusions:** Assessment of the ischemic cascade using dipyridamole stress CMR is useful for predicting the outcome in patients with ischemic chest pain. The presence of ischemia in stress perfusion CMR correlates to a higher risk but only patients with severe ischemia, namely simultaneous perfusion deficit and inducible WMA, benefit from revascularization in terms of event rate reduction.

**1031-41**

**Effect of Amlodipine, Atorvastatin and the Combination on Transient Myocardial Ischemia in Coronary Artery Disease from the DUALA Study**

**John Dearfield, Jan Bults, Philipp Beller, Erik Tauthou, University College of London, London, United Kingdom**

**Background:** Transient myocardial ischemia (TMI) in patients with coronary disease (CAD) is associated with poor outcome and may reflect disturbed arterial biology. We hypothesized that the pleiotropic effects of statins would decrease ischemia.

**Methods:** Randomized double blind parallel group multi country trial (2 weeks run-in and 24 weeks active therapy, titrated at Week 6) comparing 3 treatments: 1) Amlodipine (AM) 10 mg. 2) Atorvastatin (A) 10 mg 10 mg. 3) Combination (AM/A) 5/10 mg. In 311 patients (78% men, mean age 62 yrs) with stable angina (≥2 attacks/week), CAD history, ≥3 TIMI episodes and/or ≤15 min ischemia on 48 hr Holter monitoring, Efficacy variables were change in TMI by Holter monitoring, exercise ischemia and inflammatory biomarkers at Week 26.

**Results:** Background therapy included beta blockers (81%), nitroglycerin (62%) and aspirin (79%). TMI episodes decreased by >66% with >50% of patients becoming washout in the week following non-cardiac surgery (hazard ratio (HR) 27.3 [95% CI, 10.1, 74.2], p<0.001). Only in patients with severe ischemia, TMI-related revascularization independently reduced the risk of MACE (39% vs. 11%, 0.2 [0.1-0.7], p=0.01).

**Conclusions:** Assessment of the ischemic cascade using dipyridamole stress CMR is useful for predicting the outcome in patients with ischemic chest pain. The presence of ischemia in stress perfusion CMR correlates to a higher risk but only patients with severe ischemia, namely simultaneous perfusion deficit and inducible WMA, benefit from revascularization in terms of event rate reduction.


**ABSTRACTS - Myocardial Ischemia and Infarction**

**A225**

**11:00 a.m.**

**1031-43**

*Carotid Intima-Media Thickness Measurement is an Excellent Screening Tool for the Detection of Severe Coronary Artery Disease Associated with Left Ventricular Systolic Dysfunction*

Harmony R. Reynolds, David A. Stuckman, Peter J. Hynes, Nitasha Sanswat, Paul A. Tuckin, Bernardo D. Vargas, Raj M. Khandwalla, Izhak Kronzon, Barry P. Rosenzweig, NYU School of Medicine, New York, NY

**Background:** CAD is the most common cause of LV systolic dysfunction (LVSD). Pts with ischemia as the cause of LVSD may warrant revascularization. Angiography is the most accurate method of CAD diagnosis but is invasive and expensive and has some risk. Noninvasive imaging for CAD involves radiation exposure, medication, and/or contrast.

**Carotid ultrasound for measurement of intima-media thickness (CIMT) is safe, inexpensive and well correlated with CAD.**

**Aim:** To assess the accuracy of CIMT measurement for diagnosis of ischemic cardiomyopathy.

**Methods:** Pts with LVSD (EF<40%) of uncertain etiology referred for coronary angiography underwent carotid ultrasound. Pts with known CAD were excluded. Two echocardiographers blinded to CAD status determined CIMT and plaque (defined as ≥0.9 mm increase over background IMT). Significant CAD was defined as ≥50% stenosis of any major vessel. Ischemic cardiomyopathy was defined as: (a) left main ≥50%, (b) proximal LAD ≥75% or (c) ≥2 major arteries with ≥75% stenosis.

**Results:** Mean EF was 26±10% in 96 pts aged 60±12 yrs; 69% were male. Significant CAD was found in 50.0% and ischemic cardiomyopathy in 32.3%. Carotid plaque was seen in 66.7%. Mean CCA IMT was ≥0.9 mm in 44.2%. See Table for diagnostic accuracy. The combination of mean CCA IMT ≥0.9 mm and no plaque had negative predictive value 96% for ischemic cardiomyopathy.

**Conclusion:** CIMT is an excellent screening tool for excluding ischemic cardiomyopathy and should be considered as the first test to determine etiology of LVSD.

**Table 1** shows trends in serum creatinine between the two groups before and after catheterization.

<table>
<thead>
<tr>
<th>Serum Creatinine (mg/dL)</th>
<th>N=37</th>
<th>N=56</th>
<th>P value</th>
</tr>
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<tbody>
<tr>
<td>Baseline</td>
<td>1.1</td>
<td>1.2</td>
<td>0.35</td>
</tr>
<tr>
<td>48 hours after PCI</td>
<td>1.2</td>
<td>1.1</td>
<td>0.59</td>
</tr>
<tr>
<td>1 month after PCI</td>
<td>1.1</td>
<td>1.1</td>
<td>0.75</td>
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</table>

**11:00 a.m.**

**1031-45**

**Efficacy and Safety of Ranolazine in Chronic Angina: Observations from the Randomized, Double-blind, Placebo-controlled MERLIN-TIMI 36 Trial**

Sean R. Wilson, David A. Morrow, Benjamin M. Scirca, Sabina A. Murphy, Jacqueline L. Bures, Carolyn H. McCabe, Eugene Braunwald, Brigham and Women’s Hospital, Boston, MA

**Background:** Ranolazine (RAN) is a novel anti-anginal that has been shown to reduce angina frequency and improve exercise performance in selected patients (pts) with early exercise testing and those with frequent angina. RAN has previously not been studied in as large and diverse group of pts with angina.

**Methods:** We investigated the efficacy and safety of RAN compared with placebo in pts with any history of prior angina (N = 3565) followed long-term (~ 1 yr) in the MERLIN-TIMI 36 trial of pts with NSTE ACS.

**Results:** Pts with prior angina received evidence-based therapy (95% ASA, 77% statins, 89% β-blockers, avg 2.7 anti-anginals) balanced between the two groups. The 1st endpoint (CV death, MI, recurrent ischemia (RI)) occurred in 29.4% vs. 25.2% (placebo vs RAN); HR 0.86; 95% CI 0.75-0.97; p=0.017). CV death or MI did not differ between treatment groups (HR 0.97; p=0.71). However, RAN significantly reduced the risk of RI (HR 0.78; p=0.0021), worsening angina (HR 0.76; p=0.0482) and intensification of anti-anginal therapy (HR 0.78; p=0.0093) (Figure). All cause mortality and symptomatic arrhythmias did not differ between RAN vs placebo (both p>0.9).

**Conclusions:** In this largest study of RAN in pts with established CAD, RAN was effective in reducing angina and RI in a substantially broader group of pts with angina than studied previously. RAN is a valuable option as part of optimal medical therapy for pts with angina.

**11:00 a.m.**

**1031-44**

**Risk of Contrast-Induced Nephropathy in Diabetic Patients With and Without Dipstick Proteinuria Referred for Cardiac Catheterization**

Rayan A. Ghany, Erik Bernstejn, Julio Chimoris, Cesar Mendoza, Eduardo de Marchena, University of Miami Miller School of Medicine, Miami, FL, Jackson Memorial Hospital, Miami, FL

**Background:** Contrast-Induced Nephropathy (CIN) is a significant concern in diabetic patients referred for cardiac catheterization. Decreased glomerular filtration rate increases the risk of CIN. However, the risk of CIN in the presence of normal creatinine levels and proteinuria is unknown.

**Methods:** We prospectively studied 93 diabetic patients undergoing non-emergent cardiac catheterization who had normal serum creatinine values (<1.4 mg/dL). Patients were stratified into those with proteinuria (n=56) and without proteinuria (n=37). Repeat serum creatinine values were obtained on day 2-5 and day 7-10. CIN was defined as an increase in serum creatinine of at least 0.5 mg/dL, within 48 hrs.

**Results:** At baseline, patients with proteinuria were slightly leaner, more likely to receive ACE inhibitors, and tended to have lower diastolic and higher pulse pressures than those without proteinuria. Patients with proteinuria received significantly greater intravenous fluids prior to cardiac catheterization.

**None of the 37 patients without proteinuria developed CIN (95% CI for proportion = 0-9.9%), whereas 4 of 56 with proteinuria developed CIN (7.1%; 95% CI 1.9-17.3%). Table 1 shows trends in serum creatinine between the two groups before and after catheterization.**

**Conclusion:** With current patient preparation protocols, the risk of CIN in diabetic patients with normal serum creatinine referred for non-emergent cardiac catheterization is low regardless of the presence of dipstick proteinuria.

**11:00 a.m.**

**1031-46**

**Sustained Increase Of Platelet Activation Indices Following Sirolimus-Eluting Stent Implantation**

Maria Markostou, George Kochiadakis, Katerina Sfridaki, Akaieteni Giaouzaki, Dimitris Arfanakis, Emmanueloul Skalidis, Ermoni Kantidakis, Panos Vardas, Heraklion University Hospital, Heraklion, Greece, Venizelio Hospital, Heraklion, Greece

**Background:** Despite the proven superiority of sirolimus-eliciting stents (SES) compared to bare metal stents (BMS), recent data demonstrates that stent thrombosis after successful SES implantation is substantially higher. In patients treated with SES or BMS we measured serial changes in sP-selectin and soluble CD40 ligand (sCD40L) - as indices of platelet activation, von Willebrand factor (vWF) - as an index of endothelial damage and levels of factor VIII, fibrinogen and d-dimer - as indices of fibrinolytic response.

**Methods:** We evaluated 50 patients (35 male, 62±28 years with stable angina > 6 months and single vessel coronary artery disease, who underwent elective percutaneous coronary intervention (PCI). SES were implanted in 29 patients and BMS in the remainder. Blood samples were taken before PCI, 48 hours and 1 month later.
to evaluate plasma concentrations of sP-selectin, sCD40L, vWF, factor VIII, fibrinogen and d-dimer each time.

Results: Circulating levels of vWF, factor VIII, fibrinogen and d-dimer did not differ significantly between the two groups (p>NS). However, a significant increase of sCD40L and sP-selectin was detected in the SES group that was maintained until the end of the 1 month (Table 1: *p < 0.05 compared to baseline).

Conclusions: Patients with SES showed a sustained increase in platelet activation indices compared to those treated with BMS. This finding may emphasize the need for more aggressive antiplatelet therapy in patients with SES.

<table>
<thead>
<tr>
<th>Table 1</th>
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<td>SES</td>
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Vascular endothelial growth factor protein levels and gene expression in peripheral monocytes after stenting: A randomized comparative study of sirolimus- and bare metal stents

Maria Markou, George Kochiadasak, Dimitrios Panotoupos, Dimitrios Arfanakis, Emmanouil Skalidis, Nikolas Iqomugensis, Michael Hamilos, George Sourvinos, Dimitrios Spandidos, Panos Varlas, Heraklion University Hospital, Heraklion, Greece, Heraklion University, Heraklion, Greece

Background: Although previous studies have indicated that vascular endothelial growth factor (VEGF) plays an important role in the vascular healing process after stent implantation, its effect on in-stent restenosis has not been fully investigated. We assessed VEGF serum protein levels and gene expression in peripheral mononuclear cells in relation to in-stent restenosis after implantation of sirolimus-eluting stents (SES) and bare metal stents (BMS).

Methods: Forty-two patients (28 men, age 62 ± 11 years) with stable angina, who underwent elective single-vascular percutaneous coronary intervention, were randomly assigned to SES (n=21) or BMS (n=21) implantation. Follow-up coronary angiography was performed 6-8 months later. Blood samples were taken before and 1 month after stent implantation. Mononuclear cells were isolated using anti-CD14+ antibodies and mRNA was extracted at baseline and 1 month after PCI. VEGF serum levels were determined each time by LIGSA.

Results: VEGF protein levels in the BMS group showed an increasing trend (from 386 pg/ml to 458 pg/ml, p=0.083) while in the SES group they decreased significantly (from 403 pg/ml to 296 pg/ml, p=0.005). Similarly, BMS implantation induced an upregulation of VEGF mRNA levels, compared to SES where a downregulation was observed (fold induction: 1.44 ± 0.84 in BMS group versus 0.72 ± 0.35 in SES group, p=0.001). A significant correlation was found between VEGF gene expression, as measured by fold induction, and late luminal loss in both groups (BMS: r=0.98, p=0.001; SES: r=0.65, p=0.002).

Conclusion: SES implantation, in comparison with BMS, results in significantly lower VEGF protein levels and gene expression in peripheral monocytes. The latter shows a strong positive relation with in-stent late-luminal loss, suggesting that its role in the reduced in-stent restenosis seen in SES may be essential.

11:00 a.m.

Prognostic Impact of Various Platelet Function Assays and Definitions of Non-responsiveness to Clopidogrel: 600 mg on Early Outcome After Elective PCI


Background: The EXCELSIOR-study showed that patients with a residual platelet aggregation (RPA) above the median of the cohort (14% ADP 5µM) after loading with clopidogrel 600 mg carried a 6.7-fold increased risk for major adverse cardiac events within 30 days following elective coronary stent implantation (PCI). Predictors for an insufficient antiplatelet effect of clopidogrel have not been defined so far.

Methods: We analyzed prospectively in 1,987 patients receiving clopidogrel 600 mg the impact of demographics, clinical parameters and concomitant medication on residual platelet aggregation (RPA) determined by optical aggregometry (ADP 5µM) at baseline and before coronary angiography without (n=1,185) or with PCI (n=802).

Results: Differences in baseline RPA accounted for 27% of variability in RPA at angiography. Female patients (+3.0%, 95% confidence interval [CI]: 1.1-5.0%; p=0.003), elderly patients (per 10 years of age: +2.0%; 1.6-2.5%; p<0.001) and patients with a blunted response to aspirin (+20.7%; 16.0-25.3%; P<0.001) had an exaggerated RPA at baseline. Demographic and clinical parameters predicting an increased RPA at angiography are summarized in the Table. Patients treated with verapamil/diltiazem (+5.7%; 95% CI: 1.1-9.8%; P=0.007) and diabetics with sulfonyl urea drugs (+6.6%; 95% CI:1.1-10.2%; p=0.001; n=94) had an increased RPA at angiography.

Conclusion: Patients treated with clopidogrel 600 mg in patients undergoing elective coronary angiography without/with PCI is affected by demographic and clinical parameters as well as by concomitant medication.

11:00 a.m.

What Drove the Marked Improvement in Angina During the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) Trial?

John H. Lee, James H. O'Keefe, John A. Spertus, Robert A. O'Rourke, Wei Zhang, David J. Maron, Paul Kilm, William S. Weintraub, William E. Boden, Mid America Heart Institute, Kansas City, MO, University of Missouri-Kansas City, Kansas City, MO

Background: Although initial percutaneous coronary intervention (PCI) + optimal medical therapy (OMT) produced greater anginal relief than OMT, OMT was equally effective at 36 months of treatment. The purpose of this study is to identify correlates of angina-free status in both PCI+OMT and OMT patients (pts).

Methods: Analysis was conducted on 2,287 pts enrolled in the COURAGE trial correlating angina-free status by the Seattle Angina Questionnaire (SAQ) with age > 65, gender, race, previous myocardial infarction (MI), diabetes, baseline Canadian Cardiovascular Society (CCS) class, previous coronary artery bypass graft (CABG), previous PCI (>6 months prior to enrollment), history of congestive heart failure and hypertension (HTN), basal metabolic index, baseline 1A1c, systolic blood pressure (BP) and diastolic BP, use of angiotension converting enzyme (ACE) inhibitors, lipid-lowering therapies, beta-blockers and angiotensin II receptor antagonists.

Results: At baseline, a similar proportion of pts in the PCI+OMT and OMT groups were angina-free by SAQ adjusted for covariates (31% vs 29%, p=0.045). At 1 month follow-up, PCI+OMT pts were more likely to be angina-free than the OMT pts (36% vs 32%; p=0.001). A significant difference persisted for up to 12 months (63% vs 54%, p=0.006), but by 24 months no significant difference in angina-free status existed between PCI+OMT and OMT (54% vs 51%, p=0.091). Significant correlates of angina-free status included use of lipid lowering therapy (OR 1.06 95% CI 1.033-1.105; p=0.001), use of ACE inhibitors (OR 1.04 95% CI 1.034-1.077; p=0.029), and age < 65 (OR 1.315 95% CI 1.128-1.533; p=0.001). Significant correlates of less angina improvement included higher baseline CCS class (p<0.001), previous CABG (p=0.004) or previous PCI (p=0.015) and history of hypertension (p<0.011).

Conclusion: Although PCI + OMT was superior to OMT for attaining angina-free status during the first year, the two strategies were equally effective at 2 years and thereafter. Lipid lowering therapy and ACE inhibitors increased likelihood of freedom from angina, while HTN, prior PCI, CABG and higher baseline CCS class predicted lower prevalence of angina-free status at 3 years.
1031-51
Healthcare Resource Utilization in Patients With Refractory Angina

Alex R. Campbell, Daniel Satran, Richard Birkett, Ross Garberich, Daniel Hayward, Rachael E. Olson, Charline R. Bousjille, Timothy D. Henry, Minneapolis Heart Institute Foundation at Abbott Northwestern Hospital, Minneapolis, MN

Background: An increasing number of patients with chronic, extensive CAD are poor candidates for traditional revascularization and have refractory angina. The extent of healthcare resource utilization for this group of “no option” patients is unknown.

Methods: The OPTIMIST in Myocardial Ischemic Syndrome Therapy (OPTIMIST) clinic at Abbott Northwestern Hospital (Minneapolis, MN) offers traditional and investigational therapies for patients with refractory angina. A prospective clinical database with 1135 patients includes detailed baseline and yearly follow up information. Over a one year period, resource utilization information for 200 consecutive living patients was analyzed as well as data for major cardiovascular interventions over a lifetime.

Results: For 200 patients (mean age 69, 82% male), lifetime cardiovascular interventions and one year follow up resource utilization are summarized (Table). Over one year, MI occurred in only 8 patients (4%). Hospitalization for a cardiac cause occurred in 71 (36%) patients (114 admissions); mean length of hospital stay was 1.9 days. Scheduled cardiology clinic visits (mean 2.4 visits per patient) as well as ER visits (70 total visits for 45 patients (23%)) were frequent.

Conclusions: Healthcare resource utilization for patients with refractory angina— including diagnostic imaging studies and hospitalization rates—is extensive. Invasive procedures are also common in this population in spite of poor candidacy for revascularization.

1031-52
Long-Term Mortality in Patients With Refractory Angina

Timothy D. Henry, Daniel Satran, Alex R. Campbell, Randall J. Johnson, Anil K. Poulouze, James Hodges, Bradley A. Bart, Rachael E. Olson, Karen L. Harvey, Patricia A. Mitchell, Theresa L. Armst, Jay H. Traverse, Minneapolis Heart Institute Foundation at Abbott Northwestern Hospital, Minneapolis, MN

Background: The population of “no option” patients with refractory angina is increasing. Controversy exists regarding long-term mortality in this group of patients.

Methods: The OPTIMIST in Myocardial Ischemic Syndrome Therapy (OPTIMIST) clinic at Abbott Northwestern Hospital (Minneapolis, MN) offers traditional and investigational therapies for patients with refractory angina. A prospective clinical database includes detailed baseline and yearly follow up information. Over a one year period, resource utilization information for 200 consecutive living patients was analyzed as well as data for major cardiovascular interventions over a lifetime.

Results: For 200 patients (mean age 69, 82% male), lifetime cardiovascular interventions and one year follow up resource utilization are summarized (Table). Over one year, MI occurred in only 8 patients (4%). Hospitalization for a cardiac cause occurred in 71 (36%) patients (114 admissions); mean length of hospital stay was 1.9 days. Scheduled cardiology clinic visits (mean 2.4 visits per patient) as well as ER visits (70 total visits for 45 patients (23%)) were frequent.

Conclusions: Healthcare resource utilization for patients with refractory angina— including diagnostic imaging studies and hospitalization rates—is extensive. Invasive procedures are also common in this population in spite of poor candidacy for revascularization.

1031-53
Refractory Angina Is Associated With Increased Arterial Stiffness and Elevated Wave Reflection Amplitude

Matheen A. Khuddus, Wilmer W. Nichols, Scott J. Denardo, C. Richard Conti, University of Florida, Gainesville, FL

Background: Early return of reflected pressure waves from the lower body augments central systolic blood pressure and increases left ventricular (LV) afterload and myocardial oxygen demand. Such changes are due to increased arterial stiffness and pulse wave velocity and are associated with increased wasted LV energy expenditure and reduced stroke volume. The aim of this study was to determine if arterial properties and wave reflection characteristics are altered in patients with chronic stable angina resistant to anti-anginal therapy.

Methods: High-fidelity radial artery pressure waveforms were recorded non-invasively by applanation tonometry and ascending aortic pressure waveforms generated using a mathematical transfer function in 32 patients (age 65±9.0 yrs) with refractory angina taking two or more anti-anginal drugs and 32 treated hypertensive patients matched for age, sex, height, weight, mean arterial pressure and heart rate. Pulse wave analysis was used to determine arterial properties and wave reflection characteristics.

Results: Sphygmomanometric determined brachial systolic (134±19 vs 128±11 mm Hg, P<NS) and diastolic (71±9.1 vs 74±7.2 mm Hg, P<NS) pressures were similar in the two groups and within the normal range but augmentation index (Aa) (28±7.7 vs 19±7.0, P<0.001) and reflected wave amplitude (14±7.2 vs 9.4±4.2 mm Hg, P<0.001) were higher in the refractory angina group compared to the treated hypertensive group resulting in an increased aortic systolic (122±18 vs 114±10.0 mm Hg, P<0.05) and pulse (50±15 vs 40±10 mm Hg, P<0.001) pressures and elevated wasted LV pressure energy (6263±4086 vs 2910±1784 dyn·sec·cm−2, P<0.001).

Conclusion: Patients with refractory angina have increased arterial stiffness and elevated wave reflection amplitude compared to treated hypertensive patients which cause the LV to expend wasted energy in late systole resulting in an imbalance between myocardial oxygen supply and demand despite adequate drug therapy as assessed by standard cuff blood pressure measurements.

1031-54
 Accuracy of 64-Slice Computed Tomography for the Definition of the Atherosclerotic Coronary Plaque: Comparison With Coronary Artery Angiography and Intravascular Ultrasound

Ilaria D'Angeli, Giovanni Pedrazzini, Francesco Faletta, Elena Pasotti, Carlo Gaudio, Tiziano Moccetti, Stefano De Castro, Angelo Auricchio, Cardiocentro Ticino, Lugano, Switzerland

Background: 64-slice computed tomography (MSCT) seems to have the ability to quantify the degree of coronary artery stenosis and to assess dimensions and characteristics of coronary plaques. The aim of the present study was to assess the diagnostic accuracy of MSCT to identify and quantify atherothrombotic coronary plaques in comparison with catheter-based angiography (QCA) and Intravascular ultrasound (IVUS). Methods: 64-slice MSCT scan demonstrated significant CAD, 28 patients with stable angina, underwent QCA and IVUS at the time of cardiac catheterization. 44 plaques in the major coronary vessels, with stenosis degree >50%, were obtained. Coronary artery angiography and intravascular ultrasound with motorized pullback at the velocity of 0.5 mm/s were performed. Correlations of lumen cross-sectional area, external elastic membrane cross-sectional area, plaque cross-sectional area, as well as percent vessel obstruction (lumen area stenosis) for MSCT and IVUS and percent vessel obstruction and lumen cross-sectional area for MSCT, QCA and IVUS were determined by calculating the Lin coefficient. For all measurements Pearson’s r was evaluated. Bland-Altman correlation analysis was determined too.

Results: The following measurements were performed. MSCT and IVUS measurements yield equal results. QCA underestimates MSCT and IVUS plaques.

Conclusions: IVUS readings may be replaced by MSCT whereas QCA, as previously shown, underestimates coronary lesions and should no longer be considered.

Table 1. Results

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MSCT vs QCA</th>
<th>MSCT vs IVUS</th>
<th>IVUS vs QCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumen Area Stenosis (%)</td>
<td>71.5±13.8 vs 71.5±13.8</td>
<td>70.4±6.7 vs 70.4±6.7</td>
<td>59.1±13.0 vs 59.1±13.0</td>
</tr>
<tr>
<td>Lumen Cross-Sectional (mm²)</td>
<td>5.3±3.0 vs 4.8±1.7</td>
<td>4.2±1.2 vs 4.8±1.7</td>
<td>4.8±1.7 vs 4.2±1.2</td>
</tr>
<tr>
<td>External Elastic Membrane Cross-Sectional Area (mm²)</td>
<td>10.5±5.0 vs 9.0±3.6</td>
<td>11.7±3.2 vs 11.7±3.2</td>
<td>12.3±3.5 vs 12.3±3.5</td>
</tr>
<tr>
<td>Plaque Cross-Sectional Area (mm²)</td>
<td>12.2±3.5 vs 12.2±3.5</td>
<td>11.7±3.2 vs 11.7±3.2</td>
<td>12.3±3.5 vs 12.3±3.5</td>
</tr>
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</table>
**Postconditioning Protects the Human Heart After Flow Restoration in Patients With Subtotal or Significant Coronary Lesions**

Efstathiou K, Iliodromitis, Ioannis A, Paraskevaidis, Dimitrios Farmakis, Ioanna Andreadou, Aikaterini Fountoulaki, Ignatios Ikonomidis, Dimitris T, Kremastinos, Attikon University Hospital, Athens, Greece

Background: Postconditioning (postC) is protective after flow restoration in ST elevation myocardial infarction but it is not known whether it is also effective in subtotal or significant coronary lesions. We sought to determine whether postC is protective, in terms of oxidative and nitrosative stress, wall motion score (WMS) and ejection fraction (EF), in patients with acute coronary syndromes or stable angina and indication for percutaneous coronary intervention (PCI).

Methods: Fifty patients with coronary artery disease and target lesions causing stenosis of 80-100% were enrolled. All patients underwent PCI and, immediately after successful stent implantation, the balloon was inflated 6 times of 10sec each with 10sec deflation period in-between in order to mimic postC.

Results: Baseline MDA, NT and conventional echocardiographic measurements including EF and WMS did not differ between postC and control group. MDA remained stable in the postC group (1.54±0.12 vs 1.55±0.13 µM), but increased gradually from the baseline (1.31±0.06 µM) to the final measurement in controls (2.26±0.21 µM, p=0.05 as all other values). NT decreased significantly in the postC group (3.4±1.2 vs 0.72±0.2 nmol/l) and increased in controls (3.24±1.64 vs 4.4±1.1 nmol/l). Both wall motion score and EF improved significantly in the postC group, from 54±10 to 58±9 (p=0.009) and from 64±8 vs 69±10% (p=0.01), respectively, but remained unaffected in controls.

Conclusion: PostC is effective not only in total but also in subtotal or significant coronary artery lesions in coronary artery disease patients. This intervention diminishes the oxidative and nitrosative stress and improves EF and WMS early after PCI.

**Key Role of Postchallenge Hyperglycemia for the Presence and Extent of Coronary Atherosclerosis: An Angiographic Study**

Christoph H. Saedl, Heinz Dreael, Harald Souji, Stefan Aezel, Heidrun Jahnle, Robert Zweier, Peter Langr, Thomas Marte, Guenter Hofele, Werner Berzer, Thomas C. Wascher, VIVIT Institute, Feldkirch, Austria, Medical University Graz, Graz, Austria

Background: The associations between impaired glucose tolerance (IGT) and postchallenge diabetes with the presence and extent of angiographically characterized coronary atherosclerosis (CAD) are unclear.

Methods: We enrolled 1040 consecutive Caucasian patients undergoing coronary angiography for the evaluation of CAD. An oral 75g glucose tolerance test was performed in patients without previously diagnosed diabetes.

Results: From our patients, 384 had normal glucose tolerance (NGT), 190 impaired glucose tolerance (IGT), 90 isolated postchallenge diabetes (postchallenge glucose ≥7mmol/l) and 366 type 2 diabetes previously diagnosed or newly diagnosed on the basis of fasting glucose (conventional diabetes). Angiographically detectable CAD was more frequent in patients with IGT, isolated postchallenge diabetes, or conventional diabetes when compared to NGT subjects (87.9%, 96.6%, 89.1% vs. 80.7%; p = 0.020, 0.001, 0.043, respectively). The prevalence of significant coronary stenoses ≥50%, compared to NGT subjects (57.4%), was similar in IGT patients (59.5%; p = 0.628), but significantly higher in patients with isolated postchallenge diabetes (57.7%; p = 0.001) or conventional diabetes (68.3%; p = 0.002). Also the number of significant stenoses compared to NGT subjects was similar in IGT patients, but significantly higher in those with isolated postchallenge or conventional diabetes. These results were confirmed after multivariate adjustment in logistic regression analyses.

Conclusions: Abnormal glucose tolerance is strongly and independently associated with angiographically characterized CAD. In IGT, non-significant CAD is more frequent than in NGT; the prevalence and number of significant stenoses increases when postchallenge diabetes evolves.

**The Ala379Val Polymorphism of Lipoprotein-Associated Phospholipase A2 Affects the Risk for Arterial Hypertension and Modifies Platelets Activation**

Despina Kardara, Dimitris Tousoulis, Christodoulos Stefanadis, Dimitris Farmakis, Ioanna Kardara, Dimitris Tousoulis, Charalampos Vlachopoulos, Christodoulos Stefanadis, 1st Cardiology Department, Hippokration Hospital, Athens Medical School, Athens, Greece

Background: Lipoprotein-associated phospholipase A2 (LP-PLA2) activity has been identified as a risk factor for atherosclerosis. LP-PLA2 has proinflammatory properties and it hydrolyses platelet activating factor. Genetic polymorphism Ala379Val has been associated with LP-PLA2 activity, but its effect on platelets activation and redox state is obscure. We examined the impact of Ala379Val polymorphism on the risk for arterial hypertension, platelets activation and systemic redox state.

Methods: In this case-control study, 488 subjects were recruited: 235 with arterial hypertension and 253 age and gender matched controls. Ala379Val polymorphism was detected by PCR, while plasma levels of cC5a, cC3a and lipids were measured by ELISA.

Results: The genotype distribution was: Val/Val: 9 (3.8%), Ala/Val:69/29 (4.4%) and Ala/ Ala: 157/66 (8.2%) in hypertensives, and Val/Val: 9 (3.6%), Ala/Val:98/38 (37.7%) and Ala/Ala: 146/63 (45.7%) in controls. The carriage of Ala379Val was associated with a significant lower risk for arterial hypertension (OR (95%CI):0.678 [0.498-0.980], p=0.04) compared to Ala homozygotes. In the overall population, ox-LDL was significantly lower in the presence of the Val allele (62.8±7.2%) compared to Ala homozygotes (71.3±2.4%), p=0.05). Val homozygotes also had lower levels of P-selectin (20.1±4mg/l) and ICAM1 (3.5±1mg/l) compared to Ala homozygotes (38.0±1.8mg/l and 5.7±3.0mg/l respectively, p=0.05 for both).

Conclusions: The presence of the 379Val variant of LP-PLA2 is associated with lower risk for arterial hypertension and decreased oxidative stress status. Furthermore, homozygosity for this allele is associated with a lower platelet aggregation, suggesting lower platelets activation. These findings suggest that this polymorphism may be implicated in the pathogenesis of hypertension and platelets activation.
Background: The overall prognosis of patients with vasospastic angina (VA) is relatively good. However, it is not well known about the long-term prognosis and influential factors for Korean patients with VA. Methods: From August 1996 to January 2007, 256 consecutive patients with VA were enrolled (215 men, 53±9 years). Coronary spasm was confirmed during the coronary angiography in all study patients by intravenous ergonovine provocation. Major adverse cardiac events (MACEs) were defined as myocardial infarction (MI), resuscitation from cardiac arrest, or repeated hospitalization due to recurrent angina. Results: 256 patients were followed for an average of 59 months (range, 5 months to 11 years). 31 patients (12.1%) were lost to follow-up. Cardiac death, a nonfatal MI, and MACEs occurred in 6 (2.3%), 3 (1.2%), and 52 (20.3%) patients, respectively. Survival, and survival without MI at 1, 3, and 5 years was 99%, 97%, and 97%, 99%, 96%, and 95%, respectively. MACEs-free survival at 1, 3, and 5 years was 91%, 81%, and 62%, respectively. MI at the initial presentation and current smoking were significantly associated with MACEs. Multivariate analysis showed current smoking to be the only independent predictor of MACEs-free survival (odd ratio 2.16; 95% CI 1.12 - 4.23; p = 0.022). Conclusion: Despite treatment with calcium channel blockers, recurrent episodes of angina were frequently observed whereas sudden cardiac death or non-fatal MI was rare. Cessation of smoking may reduce the incidence of recurrence.

**Conclusions:**

- Long-term survival was good, with a 5-year survival rate of 99%.
- Current smoking was the only independent predictor of MACEs-free survival.
- Cessation of smoking may reduce the incidence of recurrent angina.

**ABSTRACTS - Myocardial Ischemia and Infarction**

**A229**

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Sang-Yong You, Sang-Sig Jeong, Hyuk Ko, Gangneung Asan Hospital, Gangneung, South Korea

Background: The overall prognosis of patients with vasospastic angina (VA) is relatively good. However, it is not well known about the long-term prognosis and influential factors for Korean patients with VA. Methods: From August 1996 to January 2007, 256 consecutive patients with VA were enrolled (215 men, 53±9 years). Coronary spasm was confirmed during the coronary angiography in all study patients by intravenous ergonovine provocation. Major adverse cardiac events (MACEs) were defined as myocardial infarction (MI), resuscitation from cardiac arrest, or repeated hospitalization due to recurrent angina. Results: 256 patients were followed for an average of 59 months (range, 5 months to 11 years). 31 patients (12.1%) were lost to follow-up. Cardiac death, a nonfatal MI, and MACEs occurred in 6 (2.3%), 3 (1.2%), and 52 (20.3%) patients, respectively. Survival, and survival without MI at 1, 3, and 5 years was 99%, 97%, and 97%, 99%, 96%, and 95%, respectively. MACEs-free survival at 1, 3, and 5 years was 91%, 81%, and 62%, respectively. MI at the initial presentation and current smoking were significantly associated with MACEs. Multivariate analysis showed current smoking to be the only independent predictor of MACEs-free survival (odd ratio 2.16; 95% CI 1.12 - 4.23; p = 0.022). Conclusion: Despite treatment with calcium channel blockers, recurrent episodes of angina were frequently observed whereas sudden cardiac death or non-fatal MI was rare. Cessation of smoking may reduce the incidence of recurrence.

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**Conclusions:**

- Long-term survival was good, with a 5-year survival rate of 99%.
- Current smoking was the only independent predictor of MACEs-free survival.
- Cessation of smoking may reduce the incidence of recurrent angina.
risk for CAD. All patients underwent both a CMR and SPECT. CMR included cine, adenosine-stress and rest perfusion, and delayed enhancement. SPECT included stress and rest perfusion, assessment of wall motion and ejection fraction. If both of the two stress tests were positive, patients were referred for coronary angiography. Patients were followed for myocardial infarction, revascularization, or cardiac death. Results: Thirty-seven patients were referred for coronary angiography, 13 of whom had significant CAD (>70%). The sensitivity, specificity, positive predictive value and negative predictive value for CMR are 71%, 83%, 56%, and 91% and for SPECT are 64%, 87%, 60%, and 89%, respectively. In patients who had no negative CMR and SPECT, there were no clinical events on follow up (mean 2.7 years).

Conclusions: In patients being evaluated for the presence of CAD, CMR has similar diagnostic accuracy as SPECT.

Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No CAD (n=50)</th>
<th>PCI + OMT (n=13)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Group</td>
<td>1031-66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>58.1</td>
<td>58.5</td>
<td>0.58</td>
</tr>
<tr>
<td>Males</td>
<td>41(82%)</td>
<td>11 (85%)</td>
<td>0.90</td>
</tr>
<tr>
<td>Diabetes</td>
<td>12 (24%)</td>
<td>2 (16%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Hypertension</td>
<td>38 (76%)</td>
<td>10 (77%)</td>
<td>0.56</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>32(64%)</td>
<td>8 (61%)</td>
<td>0.48</td>
</tr>
<tr>
<td>Statins</td>
<td>29 (58%)</td>
<td>6 (46%)</td>
<td>0.20</td>
</tr>
<tr>
<td>Beta Blocker</td>
<td>19 (38%)</td>
<td>9 (69%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Aspirin</td>
<td>30 (48%)</td>
<td>9 (69%)</td>
<td>0.42</td>
</tr>
<tr>
<td>C-reactive Protein</td>
<td>0.4</td>
<td>0.58</td>
<td>0.36</td>
</tr>
</tbody>
</table>

11:00 a.m.

1031-66 Clinical Outcomes in Older Patients Treated with Optimal Medical Therapy with or without Percutaneous Coronary Intervention for Stable Coronary Disease: A Pre-Specified Subset Analysis of the COURAGE Trial

William E. Boden, Steven P. Sedis, Teo Koon, Robert O’Rourke, David Maron, Pamela Hartigan, Marcin Dada, William Weintraub, Western New York VA Healthcare Network and Buffalo General Hospital/SUNY, Buffalo, NY

Background: Individuals ≥65 years comprise the fastest growing segment of the U.S. population. The impact of percutaneous coronary intervention (PCI) on clinical outcomes in older patients with stable coronary artery disease (CAD) treated with optimal medical therapy (OMT) remains ill-defined. While age dichotomized at 65 years was one of 8 prespecified covariates that did not show a difference between PCI and OMT for the primary endpoint of death or MI during a median 4.6 year follow-up, other important cardiovascular (CV) outcomes that could vary by treatment in older vs. younger patients have not been previously reported.

Methods: We compared baseline characteristics and long-term CV outcomes of patients whose age was <65 years vs. ≥65 years enrolled in the COURAGE trial.

Results: Of the 2,287 patients randomized to OMT or PCI, 1,381 patients (60%) were <65 years (mean age: 56 ± 6 years) and 904 patients (40%) were ≥65 years (mean age: 72 ± 5 years). Rates of death, MI, stroke, and ACS stratified by age and PCI status are shown (Table).

C.V. Outcomes

<table>
<thead>
<tr>
<th>Death</th>
<th>Age</th>
<th>PCI + OMT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65</td>
<td>65.1(6%)</td>
<td>31(19%)</td>
<td>0.13</td>
</tr>
<tr>
<td>≥65</td>
<td>57 (12%)</td>
<td>34 (12%)</td>
<td>0.92</td>
</tr>
<tr>
<td>MI</td>
<td>&lt;65</td>
<td>83 (12%)</td>
<td>76 (11%)</td>
</tr>
<tr>
<td></td>
<td>≥65</td>
<td>60 (13%)</td>
<td>52 (12%)</td>
</tr>
<tr>
<td>Death or MI</td>
<td>&lt;65</td>
<td>159 (16%)</td>
<td>159 (16%)</td>
</tr>
<tr>
<td></td>
<td>≥65</td>
<td>104 (23%)</td>
<td>93 (21%)</td>
</tr>
<tr>
<td>Death, MI, stroke</td>
<td>&lt;65</td>
<td>144 (16%)</td>
<td>114 (16%)</td>
</tr>
<tr>
<td></td>
<td>≥65</td>
<td>109 (24%)</td>
<td>89 (22%)</td>
</tr>
<tr>
<td>ACS</td>
<td>&lt;65</td>
<td>97 (13%)</td>
<td>95 (12%)</td>
</tr>
<tr>
<td></td>
<td>≥65</td>
<td>90 (13%)</td>
<td>52 (12%)</td>
</tr>
<tr>
<td>Death, MI, stroke, ACS</td>
<td>&lt;65</td>
<td>172 (25%)</td>
<td>175 (25%)</td>
</tr>
<tr>
<td></td>
<td>≥65</td>
<td>141 (21%)</td>
<td>130 (29%)</td>
</tr>
</tbody>
</table>

Conclusions: Patients ≥65 years had more deaths than younger patients, but not more nonfatal MIs. The addition of PCI to OMT did not reduce CV outcomes. In older stable CAD patients, it is unlikely to be cost-effective as well. These data support adherence to published ACC/AHA treatment guidelines advocating OMT as the preferred initial strategy, regardless of age.

11:00 a.m.

1031-67 Circulating Progenitor Cells and Erythropoietin Levels in Patients Undergoing Enhanced External Counterpulsation

BARRY A. BOILSON, Thomas J. Kiernan, Linda J. Tesmer, Adriana Harbuzanu, Laurel S. Kleppe, Robert D. Simari, Gregory W. Barsness, Mayo Clinic, Rochester, MN

Background: The mechanism underlying the benefits of Enhanced External Counterpulsation (EECP) is not clear. We hypothesized that this could be associated with an increase in circulating bone-marrow derived progenitor cells (CPCs) and increased erythropoietin (Epo) levels, as studies have demonstrated that Epo is a potent mobilizer of bone marrow cells to the peripheral circulation, partly accounting for its pro-angiogenic properties.

Methods: Nine patients scheduled to receive EECP treatment were enrolled. Blood (5ml) was drawn on day 1, day 17, day 35 (final session) and one month post completion of therapy. Buffy coat was extracted and FACS enumeration of CD34+ and/or CD133+CPCs was performed using ISHAGE criteria. Epo levels were measured at baseline and at day 35.

Results: Flow cytometric analysis revealed an increase in CPC counts over the course of treatment, which was statistically significant for CD133+ and CD34+, CD133+CPCs (p<0.05) (see figure). Epo levels also increased significantly with EECP therapy (12±2 MlIU/ml at baseline to 22±3 MlIU/ml at day 35, p<0.05).

Conclusions: This study shows that CD133+ and CD34, CD133+CPCs are significantly increased in response to EECP therapy, and this is matched by a significant increase in circulating Epo. This may reflect increased release of progenitor cells from the bone marrow, likely through hormonal activation. Homing of these cells to the coronary vasculature may effect improvements in vascular function and clinical symptomatic improvement.

Figure: One-way ANOVA analysis of progenitor cell counts over time

11:00 a.m.

1031-68 Serial Analysis of Neointimal Coverage Following Sirolimus-eluting Stent Implantation Using Optical Coherence Tomography: Comparison with Bare-metal Stent

Tatsueo Ig, Mitsuyoshi Terashima, Yoshihiro Takeda, Jean-François Sermuly, Osamu Katoh, Tetsuo Matsubara, Takahiko Suzuki, Toyohashi Heart Center, Toyohashi, Japan

Background: Late stent thrombosis (LST) in sirolimus-eluting stents (SES) after discontinuation of antipilelet therapy develops a serious complication. Previous pathologic studies have shown the relationship between LST and delayed arterial healing following SES implantation. However, the time course of arterial healing is unknown in the clinical setting. Optical coherence tomography (OCT) is a novel imaging technique with high resolution and is expected to visualize microscopic vascular response to coronary intervention. The aim of this study was to investigate healing process following SES implantation in comparison with bare metal stent (BMS) using OCT.

Methods: We evaluated 8 SES in 6 patients and 5 BMS in 5 patients. Serial OCT images of implanted stent segment were analyzed at intervals of 1mm. Eight SES including 1270 struts and 6 BMS including 787 struts were evaluated in each stent at 2-month and 8-month chronologically. Every observed strut was classified into either covered or uncovered by OCT findings. The frequency of uncovered struts in each stent were calculated.

Results: At 2-month, frequency of uncovered struts was significantly higher in SES than in BMS (18.0 ± 13.6% vs 12.2 ± 17%, p<0.02). Although uncovered struts gradually decreased with time, even 8 months after implantation of SES, these sites were not completely covered, whereas BMS were almost completely covered (6.4 ± 5.1 vs 6.5 ± 0.9%, p=0.03).

Conclusions: The window of thrombotic risk for SES extends far beyond that for BMS.
Enhanced External Counterpulsation Improves One Year Mortality in Angina Patients With End Stage Coronary Disease

William E. Lawson, John CK Hui, Elizabeth D. Kenna, Mark A. Silver, Osem Sonan, Sheryl F. Kelsey, Gregory Barness, Andrew Michaels, SUNY Stony Brook, Stony Brook, NY, University of Pittsburgh, Pittsburgh, PA

Background: Enhanced External Counterpulsation (EECP) improves angina class and ischemia, exercise tolerance and function, QOL in refractory angina patients (pts) with end stage coronary disease, but its effect on mortality and what factors predict survival in this group of pts is unknown.

Methods: The IEPR is a prospective registry of 8,000 EECP treated pts. About 14% of pts do not complete (<30 hours) EECP therapy (1.7% for medical reasons); providing a comparator group for Landmark analysis when early events (within 60 days of starting therapy) are censored. Demographics, comorbidities, baseline characteristics were recorded and (1 year) outcomes, including mortality, were compared using Kaplan-Meir survival analysis and a Cox proportional hazards regression model from centers providing 1-year follow up on a sufficient number of pts. Survival analysis included a landmarking method to detect subendocardial ischemia. We sought to determine the relationship between CRT and CMR abnormalities in a selected population of women.

Results: The mean age of women was 54 ± 9.3 years, 19% were non-white, 48% were dyslipidemic, 34% hypertensive, 46% had history of smoking. An abnormal CRT was shown in prior research. Coronary reactivity testing (CRT) is useful in this diagnosis as the possibility of invasive catheterization. MagnetoCardioGraphy (MCG) is a no risk technology developed for the rapid, non-invasive evaluation and detection of ventricular function and perfusion abnormalities by CMR. This observation suggests CMR may be a useful tool to detect subendocardial ischemia. We sought to determine the relationship between CRT and CMR abnormalities in a selected population of women.

Conclusions: Women with clinical evidence of ischemia and open coronary arteries by angiogram underwent both a CRT and CMR. Four markers of microvascular dysfunction measured during CRT included intra-coronary artery adenosine coronary flow reserve (CFR) (non-endothelial microvascular function), changes in coronary blood flow (CBF) and coronary artery diameter with intra-coronary acetylcholine (endothelial macrovascular function), and vasodilatation following intra-coronary nitroglycerine injection (non-endothelial macrovascular function). CMR was assessed for perfusion abnormality using a 17 segment visual scoring. We performed uni- and multivariate linear regression analysis with CMR perfusion abnormality and CRT variables. The mean age was 54 ± 9.3 years, 19% were non-white, 48% were dyslipidemic, 34% hypertensive, 46% had a history of smoking. None were current smokers and there were no diabetics. Univariate analyses demonstrated that CFR and CBF predicted CMR perfusion abnormality (coefficient = -7.43, p=0.045 and coefficient = 5.3, p=0.048, respectively). There was no statistical associated trend found with either acetylcholine or nitroglycerine (p>0.19, p=0.58, respectively). By multivariate analysis the association between CBF and CFR with CMR abnormality became nonsignificant; however both continued to show trends toward predicting CMR perfusion abnormality (p=0.05, 0.07, respectively). In women with clinical evidence of ischemia and open coronary arteries, there is a relationship between abnormalities in CBF, CFR and the percent of stress perfusion abnormalities by CMR. This observation suggests CMR may be a useful tool in evaluation of suspected abnormal CBF and study in a larger group including normal controls is needed.

Cardiocardiography

Indranil Rag: Amelia Young, David Gallegos, Linn Defensor, Robert J. Siegel, Kirsten Tolstrup, Cedars Sinai Medical Center, Los Angeles, CA

Background: Early diagnosis of coronary artery disease (CAD) is complicated by the poor sensitivity of standard tests (ECG and troponin) and the contraindication for stress testing in unstable angina patients. Current used diagnostic tests carry risks that involve stress provocation, injection of medication, use of nuclear tracer, contrast, or radiation, as well as the possibility of invasive catheterization. MagnetoCardioGraphy (MCG) is a no risk technology developed for the rapid, non-invasive evaluation and detection of ventricular repolarization abnormalities at rest.

Methods: 111 patients with stable angina, asymptomatic chronic ischemic heart disease or acute chest pain and 29 normal controls were studied with unsubinned 9 channel MCG in a non-invasive clinical setting. Scan time was 5 to 6 minutes. The MCG data were then analyzed utilizing an automated MCG analysis program and results were available immediately. All patients were angina free at the time of scanning.

Results: The patient mean age was 59 ± 13 years and 68% were men. Most had normal ECGs and normal troponin I (88%). A diagnosis of CAD was established in 38% of patients after non-invasive and invasive testing. A normal MCG was seen in all controls. MCG detected CAD with high degree of accuracy (p<0.0001) and high diagnostic value: sensitivity 88%, specificity 80%, positive (PPV) and negative predictive value (NPV) of...
Defibrillation Threshold Decreases With Repeated Episodes of Long Duration Fibrillation

Derek J. Dossell, Jose Osorio, Gregory P. Walcott, Raymond E. Ideker, University of Alabama at Birmingham, Birmingham, AL

Background: Many patients with sudden cardiac arrest persist in ventricular fibrillation (VF) for several minutes before defibrillation, and refibrillation is common. However, most defibrillation studies have examined only short duration VF (SDVF). The aim of this study was to determine if the defibrillation threshold (DFT) is different after long duration VF (LDVF) compared to SDVF.

Methods: In 9 swine, during 5 alternating episodes of electrically induced SDVF (10 s) and LDVF (150 s), external biphasic shocks of increasing strength were delivered until VF was terminated. The shock that terminated VF was used as an approximation of the DFT. Between episodes of VF, the animals were allowed 5 or 30 min after SDVF or LDVF, respectively, to achieve hemodynamic and metabolic stability. During a 6th VF episode (n=6), shocks at the DFT for the 5th LDVF episode were delivered every 15 s until VF was terminated.

Results: While the SDVF DFT did not change, the LDVF DFT decreased significantly after successive VF episodes (see figure). A repeated measures test showed that treatment group (SDVF vs. LDVF) was a significant factor in DFT level. In the 6th LDVF episode, VF was terminated with 32±10 J after 137±41 s.

Conclusions: The DFT of LDVF, but not SDVF, decreases markedly after successive episodes. This decline may occur after 120-150 s of VF. Further studies into the mechanism of this reduction in LDVF DFT may lead to more effective defibrillation strategies for clinically relevant scenarios of LDVF.

Clinical Relevance of Hemolysis During Circulatory Support With Percutaneously Implantable Axial Flow Pumps

Markus Ferrari, Markus Schlösser, Ruediger Pfeifer, Gerald S. Werner, Hans R. Figulla, Clinic of Internal Medicine 1, Friedrich-Schiller-University, Jena, Germany, Clinic of Internal Medicine 1, Darmstadt, Germany

Background & Objectives: Percutaneously implantable axial flow pumps (pAFP) provide continuous circulatory support independently of cardiac rhythm. They are ideal devices for immediate term circulatory support in cardiogenic shock. However, extend of use was limited due to hemolysis so far. We therefore evaluated the hemolysis rate during long term use of pAFP.

Methods: We included 14 patients who had circulatory support with pAFP (Impella recover 5.0 or Impella ACP 6.0). Repetitive blood samples (free hemoglobin, fHb; ULN < 3.1 μmol/l) were taken every 4 hours during pAFP support, and every 8 hours after removal of the device for additional 3 days. Results: The pAFP was implanted in 8 patients due to severe cardiogenic shock (4 pts. were on IABP before), for high risk coronary angioplasty (5 pts.), and weaning from emergency cardio-pulmonary bypass (1 pt.). The mean age was 70 +/- 7.3 years, all were on IABP before, for high risk coronary angioplasty (5 pts.), and weaning from emergency cardio-pulmonary bypass (1 pt.). The mean age was 70 +/- 7.3 years, all were on IABP before, for high risk coronary angioplasty (5 pts.), and weaning from emergency cardio-pulmonary bypass (1 pt.). The mean age was 70 +/- 7.3 years, all were on IABP before, for high risk coronary angioplasty (5 pts.), and weaning from emergency cardio-pulmonary bypass (1 pt.). The mean age was 70 +/- 7.3 years, all were on IABP before, for high risk coronary angioplasty (5 pts.), and weaning from emergency cardio-pulmonary bypass (1 pt.). The mean age was 70 +/- 7.3 years, all were on IABP before, for high risk coronary angioplasty (5 pts.), and weaning from emergency cardio-pulmonary bypass (1 pt.). The mean age was 70 +/- 7.3 years, all were on IABP before, for high risk coronary angioplasty (5 pts.), and weaning from emergency cardio-pulmonary bypass (1 pt.). The mean age was 70 +/- 7.3 years, all were on IABP before, for high risk coronary angioplasty (5 pts.), and weaning from emergency cardio-

Resuscitation with Intravenous Infusion of Liposome-Encapsulated Hemoglobin (Artificial Oxygen Carrier Named TRM645) from Lethal Hemorrhagic Shock

Borpeel Takase, Satoshi Shono, Manabu Kinosita, Yoshio Nogam, Yoshitaka Ogata, Hidemi Hattori, Masayuki Ishihara, National Defense Medical College, Tokorozawa, Japan, Terumo R&D Center, Ashigarakami-gun, Japan

Background: Liposome-encapsulated hemoglobin (TRM645), which is similar to natural red blood cells (RBC) except smaller size (250 nm), can serve as blood substitutes of oxygen-carrying capacity comparable to RBC. Intravenous blood infusion (iO2), which is alternative to peripheral i.v. infusion, is expected as an important field treatment in military and civilian emergency because intramedullary blood vessels in the bone marrow do not collapse in shock.

Methods: Study 1: We performed graded blood exchange experiment up to 75% blood loss in mice (52±7g, 8 mice). Eight mice were gradually exchanged with 5% Albumin (Alb group) through superior vena cava while 8 mice exchanged with TRM645 (TRM645 group) through the right carotid artery. We euthanized mice when body weight loss was approximately equal. Study 2: We performed central i.v. iO2 experiment up to 75% blood loss in mice (52±7g, 8 mice). Eight mice were gradually exchanged with 5% Albumin (Alb group) through superior vena cava while 8 mice exchanged with TRM645 (TRM645 group) through the right carotid artery. We euthanized mice when body weight loss was approximately equal.
CS was defined as a patient having: 1. A shock index >1 or Systolic Blood Pressure (SBP) orders or a “mixed” distributive and CS picture were also excluded.

Figure 1: The survival rate after IABP

Figure 2: The change of survival rate after IABP

Conclusion: The incidence of cardiogenic shock in the community appears to be higher than previously reported. This may be explained by our use of more sensitive shock criteria. The in-hospital mortality was lower than expected, possibly due to recent improvements in our therapeutic approach.

11:00 a.m.

1031-90
Clinical Profiles of Patients Undergoing Coronary Artery Bypass Surgery or Percutaneous Coronary Intervention in California: A Comparative Analysis of Over 60,000 Patients

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Background: The clinical characteristics and peri-procedural outcomes among patients undergoing coronary artery bypass surgery (CABG) or percutaneous coronary intervention (PCI) have not been well defined.

Methods: Using the California hospital discharge data, after excluding patients with emergent or salvage acuity, the perioperative risk profiles of all patients who had either PCI or CABG in 2004 were compared. Differences in peri-procedural myocardial infarction (MI), and re-admission for CABG and death were also determined.

Results: 61,641 patients had PCI (42,232, 68.5%) or CABG (19,409, 31.5%). Compared to PCI, CABG patients were more likely non-white and had more hypertension, diabetes, peripheral arterial disease, cerebrovascular disease, heart failure, dysrhythmia, chronic obstructive pulmonary disease, obesity, hepatic failure and anemia (all p<0.001). However, CABG patients were less likely to: be female, have an urgent procedure, or have a history of prior CABG/coronary surgery/PCI (all p<0.001). On peri-procedural outcomes, CABG patients had lower odds of procedure-related MI (OR: 0.57, 95%CI: 0.53-0.78), but higher peri-procedural mortality (OR: 2.55, 95%CI: 2.25-2.88).

Conclusions: The clinical characteristics of patients undergoing CABG and PCI differed significantly. CABG had higher peri-procedural mortality but less peri-procedural MI and need for a follow-up CABG.
Predicted Impact of Nesiritide on Dialysis and All-Cause Hospital Mortality in Patients Undergoing Cardiac Surgery by Demonstrated Improvement in Post-Operative Glomerular Filtration Rate

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Background: The Nesiritide Administered Peri-anesthesia in Patients Undergoing Cardiac Surgery (NAPA) trial showed that nesiritide preserved renal function in cardiac surgery patients. Due to the small sample size, efficacy estimates on dialysis and mortality were inconclusive.

Method: We built a decision tree model to predict the impact of nesiritide on dialysis and all-cause hospital mortality based on the post-operative glomerular filtration rate change (ΔGFR) in the NAPA trial. The probabilities for dialysis and hospital mortality were obtained from a meta-analytic review of the literature. Analyses were performed in three scenarios: 1. Full probabilistic analysis, repeatedly sampled probabilities for all variables from distributions based on 95% confidence intervals (CI). II. Best-case nesiritide analysis, used the 95% CI boundary values of ΔGFR favoring nesiritide. III. Best-case placebo analysis, used the 95% CI boundary values of ΔGFR favoring placebo. 1000 consecutive Monte Carlo simulations for cohorts of 1000 hypothetical patients were performed for each scenario. Incremental dialysis rate (IDR) and incremental hospital mortality rate (IMR) for nesiritide versus placebo were calculated for total NAPA sample and two subgroups stratified by presence of pre-operative renal dysfunction, respectively.

Results: For the total sample, the model indicated significantly lower dialysis and mortality rates in nesiritide group (P < 0.05) in all three scenarios (ΔGFR: -2.90%, -5.10%, -0.50%). The improvement was more pronounced in the stratum with pre-operative renal dysfunction (P < 0.05) (ΔGFR: -4.60%, -7.90%, -1.20%; IMR: -3.40%, -6.10%, -0.88%). In the stratum without pre-operative renal dysfunction, the protective effect of nesiritide was not significant in scenario II (ΔGFR: -1.90%, -4.00%, 0.25%; IMR: -1.30%, -3.00%, 0.20%). Conclusion: If demonstrated preservation of GFR can be extrapolated, nesiritide may reduce dialysis and all-cause hospital mortality rates; however, this effect does not exhibit robust superiority over placebo in patients without pre-operative renal dysfunction.

Emergent Coronary Bypass Surgery Following Percutaneous Coronary Intervention: Incidence, Predictors and Outcomes


Background: Technical advances have allowed percutaneous coronary intervention (PCI) to be performed with increasing safety. PCI is more commonly being performed at sites without surgical back-up. This study aimed to identify predictors of emergent coronary artery bypass graft (CABG) surgery since stent approval.

Methods: The study population consisted of 9164 unsellected patients who underwent PCI since August 1994. Of this group 117 patients required CABG within 24 hours of PCI. Comparisons were made between CABG and no-CABG groups and logistic regression analysis was then performed to identify predictors of urgent CABG.

Results: The incidence of emergent CABG was 1.3%. Patients in the CABG group were younger (61.8±13.6 vs. 64.2±12.1, p=0.04), had more diseased vessels (2.3±0.7 vs. 2.0±0.9 p<0.001), more prior PCI (44.4% vs.30.7% p<0.001), greater Type C lesions (49.7% vs. 28.0% p<0.001) and more restenotic lesions (18.7% vs.10.1% p=0.001). Independent predictors of emergent CABG are listed. See table. Patients requiring emergent CABG had significantly worse in-hospital outcomes (cardiac death: 7.7% vs. 0.6% p<0.001, Q-wave MI: 4.4% vs. 0.4% p<0.001, neurological events: 10.3% vs.11.1% p=0.001, renal insufficiency 19.6% vs.5.0% p<0.001).

Conclusions: Emergent CABG following PCI is infrequent but is associated with significantly worse outcomes. Patients with multiple predictors of emergent CABG may identify those better treated at sites with surgical back-up.

Magnetically Targeted Cell Delivery Improves 30-day Endothelialization of Synthetic Vascular Grafts

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Background: Synthetic vascular grafts often exhibit incomplete endothelialization and this has precluded their use in smaller vessels. Improvement of healing could lead to smaller caliber conduits for coronary applications. Superparamagnetic iron labeled autologous endothelial cells were coated on magnetized polyurethane grafts and implanted in pig carotids. We evaluated healing at 30 days. Methods: 5g omental fat was cultured for 7d to obtain microvascular endothelial cells. Superparamagnetic iron labeled autologous endothelial cells were coated on magnetized polyurethane grafts and implanted in pig carotids. We evaluated healing at 30 days. Results: Magnetically and non-magnetic grafts had circular necrotic rim (~1 mm thick). H&E staining showed excellent endothelialization, with well organized neointima.
in magnetic segments (A). Non-magnetic controls showed markedly disorganized neointima, along with patchy endothelialization (B). Prussian blue stain showed a faint ring of residual iron adjacent the inner graft surface.

Conclusions: Endothelial cell delivery to a magnetic graft resulted in significantly improved healing. The superior endothelialization and neointimal organization may allow for the creation of smaller synthetic conduits for coronary and peripheral applications.

11:00 a.m.

1031-88 Long Term Clinical Outcomes of the Symmetry Aortic Connector Anastomotic Device in Coronary Artery Bypass Surgery

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Background: The St. Jude Medical Symmetry Bypass System Aortic Connector device is a sutureless device that facilitates anastomosis of bypass grafts to the aorta during coronary bypass surgery (CABG) without the need for cross-clamping. Short and medium term clinical outcomes data suggest a higher graft occlusion rate in those who received this device. Data are lacking for the long-term clinical outcomes of this device.

Methods: To assess the long-term clinical outcomes of the Connector device, we performed a retrospective matched case-control analysis at our institution for patients who underwent implantation of at least one Connector device during their CABG between November 2001 and December 2002. We included 95 Connector patients and 120 matched controls who underwent CABG using a traditional anastomotic technique.

Results: After a mean follow-up of 4.6 ± 1.6 years the primary composite endpoint of death, non-fatal MI and revascularization was significantly more frequent in the Connector group (OR 2.18, 95% CI = 1.23 - 3.85, p<0.009). This was largely driven by a higher frequency of MI in the Connector group. No significant differences were observed for the individual secondary endpoints of total mortality, non-fatal MI, ACS, stroke and CHF hospitalization.

Conclusions: In the most extensive follow-up data to date, significantly higher rates of major adverse cardiovascular events were observed in patients receiving the Symmetry aortic connector device during CABG. This was largely driven by higher rates of non-fatal MI in the Connector group, which is consistent with the previously proposed mechanism of premature saphenous vein graft thrombosis and neointimal hyperplasia of the Connector device. We therefore recommend increased surveillance for patients who underwent CABG with this device.