ACC.POSTER CONTRIBUTIONS

1003

Myocardial Ischemia--Basic

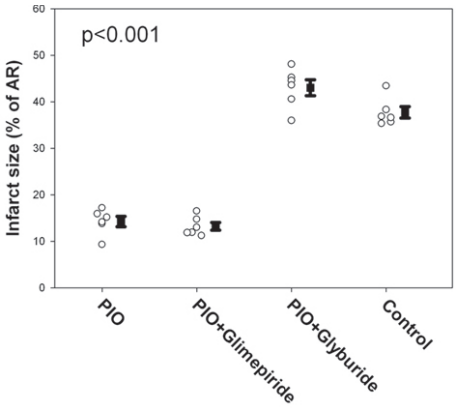
Sunday, March 30, 2008, 9:00 a.m.-12:30 p.m.
McCormick Place, South Hall

11:00 a.m.

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

Yumei Ye, Yu Lin, Saraswathy 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 4h 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.

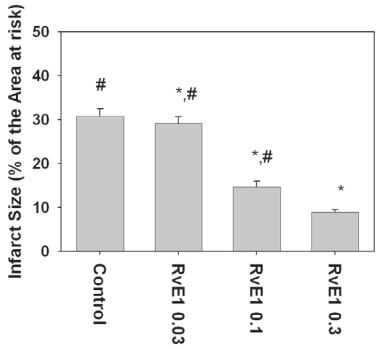


11:00 a.m.

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

Yochai Birnbaum, Yumei Ye, Yu Lin, Saraswathy Manickavasagam, Regino J. Perez-Polo, Per Gjorstrup, University Of Texas Medical Branch, Galveston, TX, Resolvyx 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 confirmed multiple actions in the control of inflammation including both anti-inflammatory properties and activation of survival pathways. We asked whether RvE1, administered before reperfusion, can limit myocardial infarct size (IS). **Methods:** Rats were anesthetized with ketamine and xylazine and underwent 30 min of coronary artery occlusion and 4h of reperfusion. Just before reperfusion rats received i.v. RvE1 (0.03 mg/kg, 0.1 mg/kg or 0.3 mg/kg) or vehicle alone (control). Area at risk (AR) was assessed by blue dye and IS by TTC. **Results:** RvE1 did not affect heart rate or mean blood pressure. Body weight, left ventricular weight and the size of AR were comparable among groups. RvE1 dose-dependently limited IS (Figure. * p<0.05 vs. control; # p<0.05 vs. RvE1 0.3). **Conclusions:** RvE1 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. Salloum, 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 (I/R) 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 I/R in female mice.

Methods: Adult female mice were pretreated (ip, 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 (39.9±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). Furhtermore, survival rate was lower 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 I/R in women with coronary artery disease.

*P<0.05 vs. Control			
Group	LVEDD (mm)	LVESD (mm)	FS (%)
Control	3.1 ± 0.1	1.6 ± 0.1	46.7 ± 1.4
Saline	3.5 ± 0.1*	2.4 ± 0.2*	30.4 ± 4.1*
SIL	3.0 ± 0.1	1.4 ± 0.1	52.2 ± 2.0
VAR	2.9 ± 0.3	1.4 ± 0.2	52.7 ± 5.1

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 Tsubokawa, Kunimasa Yagi, Atsushi Nohara, Chiaki Nakanishi, Hatsue Ueda, Noboru Fujino, Masaaki Kawashiri, Hidekazu Ino, 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 anti-oxidative 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 MSCHO-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 MSCHO-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 (5×106 ±0.4 ×106 cells/rat) or MSCHO-1was injected around 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, MSCHO-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 MSCHO-1 attenuated left ventricular remodeling and improved function (% FS: 32.1% (MSCHO-1 group) V.S. 20.4% (control group), infracted size:

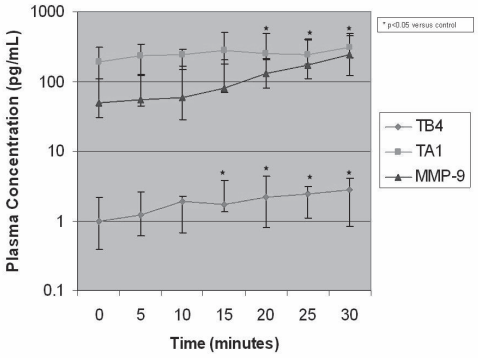
21.1%(MSCHO-1 group) V.S. 36.9%(control group), p<0.05). Capillary density was markedly increased in the MSCHO-1 group.
Conclusion: These results demonstrate transplantation of MSC with transient overexpression of HO-1 could enhance the reduction of myocardial injury after acute ischemia, probably through suppression of the allogenic 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. Shah, Nirat 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 mechanisms 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. Strande, Jidong Su, Xiangping Fu, Anna Hsu, Garrett J. Gross, John E. Baker, Medical College of Wisconsin, Milwaukee, WI

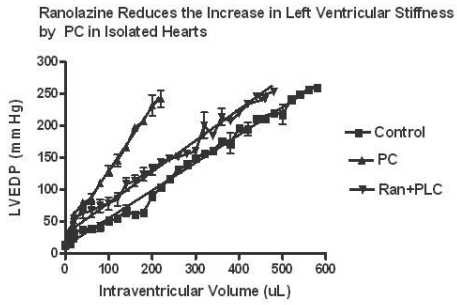
Background: Harnessing endogenous cardioprotectants is a novel therapeutic strategy to combat ischemia/reperfusion (I/R) injury. Thrombin causes whereas exogenous adenosine prevents I/R injury. We hypothesized that blocking thrombin activation with a Protease-Activated Receptor 4 (PAR4) antagonist would 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 P4pal10 in an in vivo and in vitro rat model of myocardial I/R injury. P4pal10 (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. P4pal10 also significantly decreased IS by 21% and 19% respectively when given after the onset of ischemia or at reperfusion. Tc-Y-NH2 (1-10 μM) treatment immediately before ischemia decreased IS by 51% in the in vitro model and increased recovery in ventricular function by 26% following I/R 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 (5-HD) and sarcolemmal KATP channels (HMR 1098) abolished P4pal10-induced cardioprotection in vivo.
Conclusion: Thrombin receptor blockade by PAR4 inhibition provides protection against injury from myocardial I/R 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.

11:00 a.m.

1003-47 Ranolazine Attenuates Palmitoyl-L-Carnitine Induced Ventricular Diastolic Dysfunction

Yuzhi Wu, Luiz Belardinelli, John Shryock, CV Therapeutic, Palo Alto, CA

Background: Palmitoyl-L-carnitine (PC), an ischemic metabolite, alters Na+ channel function and causes cellular Na+ and Ca2+ overload. Ranolazine (Ran) is anti-anginal drug and a selective blocker of late sodium current. This study was to determine if Ran attenuates PC-induced diastolic dysfunction (increased wall stiffness, reduced vascular conductance and ischemia).
Methods: Guinea pig isolated hearts perfused at constant flow (Langendorff method) were used to study left ventricular end-diastolic pressure (LVEDP), coronary perfusion pressure (CPP), and cardiac lactate and adenosine release. Hearts were treated with 4 uM PC for 30 min followed by 30 min treatment with Ran or vehicle. To measure wall stiffness, hearts were exposed to no drug (control), PC, or PC + 10uM Ran for 30min; the incremental increase of LVEDP caused by an increase of intraventricular volume was measured.
Results: PC increased LVEDP, wall stiffness (see Figure), CPP, and lactate and adenosine release. Ran (10 μM) significantly reduced the PC-induced increase in LVEDP by -61 ± 5 % (n=6, p<0.001) and reduced wall stiffness (Figure). Ran (10 μM) attenuated the PC-induced increase of CPP by -27 ± 3% (n=6-7, p<0.05). Ran (10 μM) reduced the PC-induced increase of lactate and adenosine release by (-50 ± 7 and -75 ± 4 %), respectively (n=6, p≤ 0.05 for both).
Conclusion: Ran attenuated PC-induced ventricular diastolic dysfunction, as indicated by reduction of wall stiffness (positive lusitropic effect), ischemic metabolites, and CPP



11:00 a.m.

1003-48 Killer Immunoglobulin-like Receptor Genotype and the Risk of Acute Coronary Syndromes

Phillip A. Horwitz, Trudy L. Burns, John A. Spertus, Lan Xiao, Thomas M. Morgan, Paul W. Naumann, Jonathan W. Heusel, University of Iowa, Iowa City, IA, Mid America Heart Institute and University of Missouri–Kansas City, Kansas City, MO

Background: Chronic inflammation is a known risk factor for acute coronary syndromes (ACS). Killer immunoglobulin-like receptors (KIR) regulate both tolerance and activation of natural killer (NK) and T cells. KIR genes are encoded in a cluster of polymorphic genes and exist as either activating or inhibitory receptors with opposing effects on immune cell activation. KIR genotypes have been associated with a variety of human diseases characterized by chronic inflammation. Our objective was to investigate the association between KIR genotype and risk of ACS.
Methods: We conducted a case-control study on 192 Caucasian subjects with ACS and 192 controls. Case subjects were prospectively enrolled after admission for ACS. Controls were randomly selected from a cohort of outpatients without prior manifestations of coronary artery disease undergoing blood draws for routine clinical testing. KIR genotypes were determined by PCR-based amplification of 15 distinct KIR genes. KIR genotype frequencies, clinical and demographic variables were compared between cases and controls using chi-square and Student's t tests. Logistic regression models were used for multivariable analyses after adjusting for known cardiac risk factors.
Results: Mean age was 63±12 and 61±13 years for cases and controls, respectively (p=0.17). 68% of cases and 56% of controls were male (p=0.01). Prevalence of the inhibitory KIR genes 3DL1(95.3 vs. 89.1%; p=0.02) and 2DL3 (93.8 vs. 88.0; p=0.05) were higher and the activating KIR 2DS3 lower (19.8 vs. 31.3%; p=0.01) in case vs. control subjects. Prevalence of the inactive variant of the activating KIR 2DS4n was also higher in cases (83.9 vs. 73.4%; p=0.01). In multivariable analysis, the adjusted odds of activating KIR 2DS3 were significantly lower in ACS cases relative to controls (OR 0.42; 95%CI 0.22-0.82). Other significant covariates associated with case status were male sex, less education, smoking, no alcohol use, and a family history of premature atherosclerosis.
Conclusions: KIR gene frequencies differ in ACS patients compared to controls, suggesting that KIR gene products may influence T- and NK- cell activation, vascular inflammation and the risk of ACS development.

11:00 a.m.

1003-49 Endothelin-1 receptor blockade and left ventricular unloading immediately prior to reperfusion result in equivalent myocardial salvage compared to reperfusion alone in a rabbit myocardial infarction model

Sophie Tamareille, James Amirian, Patricia Felli, Fenghua Li, William Barry, Richard Smalling, The University of Texas at Houston Medical School, Houston, TX, The University of Utah Health Science Center, Salt Lake City, UT

Background: Previous work has shown that during acute ischemia/reperfusion (I/R), left ventricular (LV) unloading reduces endothelin-1 (ET-1) release and is cardioprotective. We have also found that ET-1 release is associated with calcium overload related cell death. We tested the hypothesis that ET-1 released during acute myocardial infarction might mediate I/R injury by stimulating an increase in intracellular calcium concentration ([Ca2+]i) and triggers the apoptotic cascade.
Methods: 24 anesthetized rabbits were subjected to 1 hour of left circumflex coronary artery occlusion followed by 3 hours of reperfusion. Unloading was initiated 15 min prior to reperfusion and maintained during the entire period of reperfusion (unloaded group, n=6). A control group (n=6) was subjected to reperfusion alone. 12 animals were treated with ET-1 receptor antagonist BQ123 with or without unloading. In parallel, isolated rabbit cardiomyocytes were subjected to simulated I/R with or without ET-1 or BQ123 and intracellular Ca2+ was assessed with flow cytometry.
Results: Just prior to reperfusion, LV unloading significantly decreased LV end-diastolic pressure. LV support significantly reduced ET-1 release from the heart at 2 hours of reperfusion (21.37±2.83 pg/mL vs 54.34±11.34 pg/mL, P=0.03). Infarct size, expressed as % of zone at risk, was significantly reduced in the unloaded group (3.39±1.35%) and in the BQ123 treated groups with or without unloading (4.61±1.09 and 5.06±3.81 respectively) compared to controls (17.50±4.52%). LV unloading caused a significant reduction in the % of apoptotic cells (2.75±0.38% vs 5.84±1.97%, P=0.003) associated with a significant increase in the anti-apoptotic Bcl-2 protein expression in the ischemic region. In isolated ventricular myocytes subjected to simulated I/R, BQ123 significantly reduced both ET-1-induced [Ca2+]i increase and cell death.
Conclusions: Our results suggest that the molecular basis of reperfusion injury involves endothelin-1 release which stimulates calcium overload and apoptosis. Intravenous ET-1 receptor blockade prior to reperfusion should be evaluated as an adjunct to reperfusion therapy in STEMI patients.

11:00 a.m.

1003-50 Human Umbilical Cord Stem Cells Decrease Myocardial Cytokines, Inflammatory Cells, and Infarct Size

Robert J. Henning, Ujwala Eadula, Masood Shariff, Felipe Alvarado, Mark Vasko, Vincent DeLostia, JAMES A.HALEY MEDICAL CENTER/UNIVERSITY OF SOUTH FLORIDA, TAMPA, FLORIDA

We investigated whether human umbilical cord blood stem cells (**HUCBC)** can decrease cytokines, inflammatory cells and infarct (**MI**) size. We ligated the left coronary artery in rats and injected $4X10^6$ HUCBC in Isolyte or Isolyte alone into each MI. We measured cytokine proteins in HUCBC (N=15) and Isolyte (N=15) treated LVs at 2, 6, 12, 24, and 72 hrs after MI. We counted LV CD3, CD4, CD8 T cells and CD11b macrophages by flow cytometry at 24 and 72 hrs after MI treatment with HUCBC (24 hrs N=17; 72 hrs N=19) or Isolyte (24 hrs N=17; 72 hrs N=19). MI size was determined by tetrazolium stain. **RESULTS:** In Isolyte treated rats, LV cytokines increased above controls from 2 to 72 hrs after MI : TNFα increased from 6.7$\pm$0.8% to 52.3$\pm$4.6%, monocyte chemoattractant protein (**MCP**) from 9.5$\pm$1.1% to 39.8$\pm$2.0%, fractalkine from 11$\pm$1.5% to 28.1$\pm$1.3%, monocyte inflammatory protein (**MIP**) from 10.3$\pm$1.6% to 23.9.0$\pm$1.5%, interleukin (**IL**)-1β from 6.1$\pm$0.04% to 19.0$\pm$1.2%, ciliary factor (**CNTF**) from 12.1$\pm$0.02% to 21.9$\pm$1.1%, and interferon-γ (**INF-γ)** from 8.7$\pm$0.3% to 26.0$\pm$1.7% (all p<0.001). In HUCBC treated MIs, TNFα, MCP-1, fractalkine, MIP, IL-1 β, CNTF, and INF-γ did not significantly change. The percentage of CD3, CD4 and CD11b in 50,000 myocytes was less in HUCBC than in Isolyte LVs at 24 hrs (p<0.01) and the decreases in CD3 and CD4 persisted at 72 hrs (p<0.01) (**Table**). MI sizes averaged 10$\pm$1% in HUCBC treated LVs in contrast to Isolyte LVs that averaged 28$\pm$1% (p<0.01). **CONCLUSION**: HUCBC decrease MI cytokines, inflammatory cells and infarct size.

CELL COUNT % BY FLOW CYTOMETRY: HUCBC vs. ISOLYTE					
TIME	TREATMENT	CD3	CD4	CD8	CD11B
24 Hrs Post MI	ISOLYTE	11.50±1.61	7.50±1.52	2.47±0.50	2.39±0.27
	HUCBC	5.64±1.02	2.94±0.70	1.60±0.33	1.67±0.24
	SHAM	4.51±1.12	3.00±0.90	1.44±0.34	0.67±0.12
72 Hrs Post MI	ISOLYTE	8.01±1.18	5.07±0.80	2.57±0.28	2.40±0.47
	HUCBC	4.12±0.53	2.32±0.39	2.19±0.28	1.80±0.26
	SHAM	4.11±1.08	2.76±0.84	1.39±0.28	0.67±0.09

11:00 a.m.

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

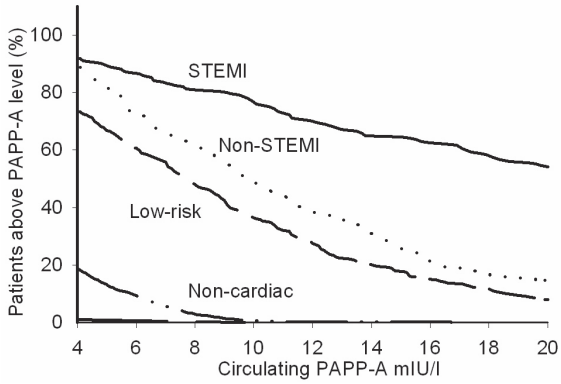
Background: Recruitment of bone marrow-derived c-kit cells has been associated with tissue angiogenesis and repair after myocardial infarction. The purpose of this study was to test the hypothesis that injection of an acellular extracellular matrix emulsion in ischemic myocardium enhances angiogenesis 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 immunohistological 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 trichome 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 vWF-positive vessles (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 syndrome. 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 mIU/l.
Results: Considering the peak PAPP-A value from each patient, 91% of patients with myocardial infarction, 74% of patients with low-risk acute coronary syndrome, 19 % of patients with non-cardiac disease and 1% of healthy volunteers had detectable PAPP-A, p<0.01 for all comparisons. In the figure the percentage of patients with PAPP-A above different cut-off levels are shown.
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.



11:00 a.m.

1003-53 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 a postconditioning regimen of 4 cycles of 20 seconds of reperfusion/20 seconds of reocclusion 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 11 in young control ($p = 0.004$); 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 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 adult rats, postconditioning still markedly lowered ventricular arrhythmias in old rats. Unlike some studies that suggest that the benefits of preconditioning are lost in elderly subjects, postconditioning robustly reduced ischemia/reperfusion induced ventricular tachycardia in the senescent heart.

11:00 a.m.

1003-54 Effect of Beta-blockade on Regional Function and Myocardial Cytokine Levels in Chronic Ischemic Cardiomyopathy: An Experimental Evaluation

Dai-Trang Le, Marco Pascotto, Ibrahim Sari, Thanjavur Bragadeesh, Antonio Micari, Helmy Siragy, 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 coronary arteries in 29 chronically instrumented dogs. Microcatheters 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-6, and IL-1β levels were measured before and at 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	28.7 ± 5.2*	31.0 ± 5.8†	32.0 ± 5.3†‡
TNF-α (pg/mL)				
Placebo	59.8 ± 36.5	80.6 ± 44.5	70.1 ± 38.9	52.0 ± 28.4
Metoprolol	43.3 ± 21.9	57.5 ± 3.5	47.0 ± 20.5	43.1 ± 24.3
Carvedilol	60.3 ± 35.2	47.6 ± 23.4*	46.1 ± 33.1	50.4 ± 8.8
IL-6 (pg/mL)				
Placebo	0.48 ± 0.30	0.67 ± 0.25	0.59 ± 0.25	0.59 ± 0.27
Metoprolol	0.33 ± 0.16	0.39 ± 0.17†	0.37 ± 0.18*	0.28 ± 0.19†
Carvedilol	0.34 ± 0.12	0.39 ± 0.18†	0.42 ± 0.15	0.42 ± 0.24
IL1-β (pg/mL)				
Placebo	60.0 ± 13.0	61.3 ± 15.8	51.6 ± 15.7	60.9 ± 6.0
Metoprolol	50.1 ± 15.0	54.1 ± 11.4	51.0 ± 14.7	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; †p<0.01 vs. Placebo; ‡ 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-1β levels. In comparison, plasma cytokine levels did not change between the groups. Conclusion: We have shown that in a multivessel chronic ischemia model, improvement of LV function was associated with suppression of myocardial and not circulating pro-inflammatory cytokines. 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.

1003-55 Therapeutic Benefits of Umbilical Cord Blood-derived Mesenchymal Stem Cells in Ischemic Cardiac Injury

Yong Sook Kim, Youngkeun Ahn, Moon Hwa Hong, Hye Jeong Park, Jin Sook Kwon, Hyun Ju Lee, Chang Hun Song, Kye Hun Kim, Young Joon Hong, Ju Han Kim, Hyung Wook Park, Myung Ho Jeong, Jeong Gwan Cho, Jong Chun Park, Chonnam National University Hospital, Gwangju, South Korea, Chosun University Hospital, Gwangju, South Korea

Background: We designed this study to demonstrate the therapeutic potential of umbilical cord blood (UCB)-mesenchymal stem cells (MSCs) cellular properties.
Methods: MSCs were isolated from UCB and characterized. Cell migration was assayed by wound healing assay, and angiogeneic potential of MSC was evaluated by in vitro tube formation. The expressions of Ang-1, VEGF isoforms, ie VEGF121, VEGF165, and VEGF189, CARP, and STAT-3 were determined by RT-PCR or Western blot analysis. For in vivo study, myocardial infarction was induced by ligation of left anterior descending coronary artery for 30 min followed by release in rats, and MSCs were injected around the infarcted area. Before and 2 weeks after surgery, the echocardiograph and histologic analysis were performed.
Results: The mRNA and protein expression level of CARP in UCB-MSCs were higher than those of BM-MSCs. UCB-MSCs were transfected with CARP siRNA for 72 hours to reduce the CARP protein level to 30% of basal level. In wound healing assay, it was delayed in CARP siRNA transfected UCB-MSCs compared with that of control UCB-MSCs. Cell invasion after CARP siRNA transfection were significantly delayed to 1.4-fold compared with control UCB-MSCs ($P<0.05$). Endothelial growth medium (EGM) was used to trigger the angiogeneic events. Tube formation was triggered by EGM, whereas attenuated by AG490, an inhibitor of STAT3. EGM increased the expression level of Ang-1, VEGF121, VEGF165, and phosphorylation of STAT3. AG490 blocked the tube formation, while restored by H2O2 (0.2 mM). From these data, CARP could be a responsible factor for the cell behavior such as migration and invasion, and STAT3 could be responsible for tube formation of UCB-MSCs. In animal study, Masson's trichrome staining showed fibrosis was decreased in UCB-MSC-treated infarcted myocardium compared with control one. In echocardiograph findings, FS was 43.1%, and EF was 79.3% in UCB-MSC injected rats (control FS; 17.2%, and control EF; 40.6%).
Conclusions: Our results demonstrated that UCB-MSCs could contribute to therapeutic application to cardiovascular diseases thanks to their mobility and angiogenetic potentials.

11:00 a.m.

1003-56 Lnk 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, Hiromi 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 myoangiogenesis 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$^-$/GFP$^+$ BM cells isolated from Lnk$^{-/-}$/GFP mice or wild type (WT)/GFP mice were used for BM transplantation (BMT) into irradiated Lnk$^{-/-}$ mice or WT mice. Four weeks after BMT, MI was induced by ligating LAD of each mouse. Echocardiography and a micro-tip catheter examination 4 weeks after MI revealed significant preservation of LV function in Lnk$^{-/-}$ mice undergoing BMT from Lnk$^{-/-}$ mice (KO->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->KO, 39.5±1.7%, $P<0.05$, (2) Regional wall motion score: WT->WT, 26.0±0.4; WT->KO, 20.3±0.7; KO->WT, 20.3±0.6; KO->KO, 18.4±0.4, $P<0.05$, (3) +dP/dt: WT->WT, 6508±604; WT->KO, 8783±444; KO->WT, 10015±414; KO->KO, 11279±358 mmHg/sec, $P<0.05$]. Necropsy examination disclosed significant augmentation of capillary density in KO->KO mice than WT->WT or WT->KO mice, while in KO->WT or WT->KO mice than WT->WT mice (WT->WT, 651±176; WT->KO, 941±176; KO->WT, 1036±73; KO->KO, 1123±177 /mm^2, $P<0.05$) and inhibition of LV fibrosis area in KO->KO mice than all other groups, while in WT->KO or KO->WT mice than WT->WT mice (WT->WT, 20.1±6.2; WT->KO, 9.5±5.0; KO->WT, 9.1±3.7; KO->KO, 5.4±2.9%, $P<0.05$). All parameters in WT->KO mice were similar as those in KO->WT 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.

11:00 a.m.

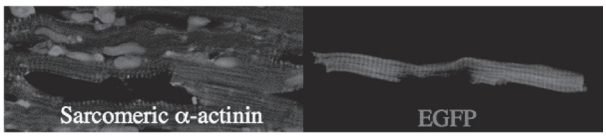
1003-57 Human Amniotic Membrane-derived Mesenchymal Stem Cell Acquired Immune Tolerance by HLA-G Expression and Differentiated into Cardiomyocyte in vivo

Hiroko Tsuji, Yukinori Ikegami, Shunichiro Miyoshi, Naoko Hida, Nobuhiro Nishiyama, Ikuko Togashi, Hikaru Nakamizo, Hironori Asada, Taro Uyama, Mamoru Tanaka, Kaoru Segawa, Junko Inoue, Kazuhiro Minegishi, Hitoshi Ishimoto, Satoshi Ogawa, Yasunori Yoshimura, Akihiro 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 (HAMC) had a potential of "working" cardiomyogenic transdifferentiation in vitro (68%). In the present study, we aim to show the induction of immune tolerance by transplanted HAMC and survival of transdifferentiated cardiomyocyte from HAMC in vivo.

Methods & Results: Flowcytometric surface marker analysis revealed that HAMC 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 HAMCs (approximately 200,000) were transplanted into the border zone of infarcted heart of wistar rat (xerograft), and immunohistochemical analysis was performed to determine the survival of EGFP-positive transdifferentiated cardiomocytes. Six weeks after the transplantation, many rod-like and EGFP-positive transdifferentiated cardiomocytes with clear striation of sarcomeric a-actinin (Fig) and cardiac troponin-I (>2,000) were survived. Enzyme-linked immunoassay of sera revealed that 4 of 24 rats transplanted with HAMCs were positive for soluble HLA-G.

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



11:00 a.m.

1003-58 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 efferent vagus 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 result:** C57/BL 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 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: 75.00±8.89 vs 76.10±10.53, P=NS). Similarly, unilateral vagotomy had no effect on ejection fraction (EF) 3 days after AMI (50.00±22.00 vs 54.00±19.84, P=NS). However, 21 days after AMI, there was a significant increase in left ventricular dilation and decreased EF in the vagotomy group when compared to the sham vagotomy group (41.00±14.99 vs 56.00±21.21, P<0.05). There was a significant increase in cellular infiltrate in the infarct zone of those animals that underwent vagotomy when compared to sham (40±23 vs. 21±6 leukocytes per high-power field, P<0.05). Mason's trichrome staining showed that the infarct zone had a greater area of collagen in the vagotomized animals compared to sham (55.63%±18.95 vs 33.72%±10.98, P<0.05). **Conclusion:** The unilateral vagotomy significantly increases the myocardial inflammatory response following AMI leading to increased 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.

11:00 a.m.

1003-59 Predictors of Sudden Cardiac Death Change With Time After Myocardial Infarction: Results From the VALIANT Trial

Jonathan P. Piccini, Karen S. Pieper, Scott D. Solomon, Sana Al-Khatib, Frans Van de Werf, Marc A. Pfeffer, John JV McMurray, Robert M. 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 VALsartan 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 (SCD 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, initial CrCl, and clinical HF are more robust risk stratifiers.

Table 1. Predictors of SCD vary with time after MI

Variable*	Initial Hospitalization (149 events)		Discharge to 30 days (182 events)		30 days to 180 days (365 events)		180 days to 3 years (693 events)	
	Chi-square	HR (95% CI)	Chi-square	HR (95% CI)	Chi-square	HR (95% CI)	Chi-square	HR (95% CI)
Measures made only once at enrollment								
CrCl	26.1	0.82 (0.76-0.89)	13.5	0.89 (0.84-0.95)			22.8	0.89 (0.84-094)
Current smoking	4.7	1.49 (1.04-2.13)			16.1	1.66 (1.30-2.12)		
Diabetes					15.7	1.57 (1.26-2.00)	15.3	1.43 (1.20-1.72)
Prior MI			13.2	1.74 (1.30-2.35)	7.0	1.36 (1.08-1.72)	26.9	1.64 (1.36-1.98)
Quant. imaging evidence of LV dysfunction					7.8	1.37 (0.10-1.71)	4.6	1.20 (1.02-1.43)
Measures made at the beginning of each time interval								
Heart rate	21.5	1.30 (1.16-1.45)	17.5	1.24 (1.12-1.38)	8.7	1.13 (1.04-1.22)	8.5	1.11 (1.03-1.19)
Systolic BP	14.9	0.80 (0.72-0.90)	3.9	0.93 (0.86-1.00)				
Worsening NYHA class			26.7	2.08 (1.32-3.27)	7.0	1.42 (1.10-1.84)		
Rehospitalization for HF			13.2	2.24 (1.45-3.47)	16.3	1.91 (1.40-2.61)	21.3	1.65 (1.33-2.04)

*Continuous variables (CrCl, HR, SBP) are in units of ten.

11:00 a.m.

1003-60 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 then 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 (29±2% of the left ventricle in ranolazine group and 26±2 in the vehicle group, p = ns). Ranolazine reduced infarct size (46±4 % of risk zone versus 60±5% vehicle, P <0.03). However, RMBF was similar in both groups in the risk zone during ischemia (0.14±0.08 ml/min/g ranolazine and 0.14±0.06 vehicle, p=ns) and at 3 hours reperfusion (0.29±0.06 ranolazine and 0.32±0.03 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.

11:00 a.m.

1003-61 Myocardial Hibernation in the Absence of Augmented Glucose Metabolism in Diabetic Hearts

Joaquin B. Gonzalez, Sharat Koul, 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 dysfunction 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 elevated prior to and during 6th 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±9%, respectively), as were those just prior to 6th CS (-28±9% and -17±4%, 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: Diabetic myocardium 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.

11:00 a.m.

1003-62 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 without adversely affecting re-endothelialization, and hence may limit late stent thrombosis. The trial stainless steel stent was coated with 400 mcg pimecrolimus and an outer layer of parylene C (UnicoatTM) to control drug release (Avantec Vascular Corp., Sunnyvale, CA). Porcine studies (12 weeks) with bare metal, polymer only, different doses of drug with polymer showed low injury and inflammatory scores, mature endothelialized intima, no granulomas, thrombosis, or aneurysm. Historical controls with the same metal stent are from the IMPACT trial.
Methods: This prospective registry enrolled 15 patients with 3-3.5 mm diameter de novo lesions <14mm length.
Results: By 6 months, there was ischemia driven target vessel revascularization in 7 of 13 patients (54%).

	Pimecrolimus n=15	Bare metal n=50	P value
BASELINE			
Lesion length, mm	6.22±1.93	11.80±3.95	<0.05
Ref diameter, mm	2.86±0.55	2.72±0.47	
POST-PROCEDURE			
In-stent min lumen diam, mm	2.76±0.43	2.56±0.40	
In-lesion diam stenosis, %	20.4±15.4	19.5±14.0	
6 MONTH			
In-stent late loss, mm	1.44±0.89	0.85±0.55	<0.05
In-lesion restenosis, %	61	27	<0.01

Conclusions:Preclinical porcine studies with this pimecrolimus DES showed good luminal patency with low injury and inflammation scores; however the porcine studies did not predict the increase in late loss and restenosis observed in this first-in-man study, that was greater than historical bare metal controls. This emphasizes the difference between species and argues for caution in first-in-human trials and justifies a small initial cohort

11:00 a.m.

1003-63 Functional Improvement After Bone Marrow-Derived Mononuclear Versus Nonmodified Mesenchymal Stem Cell Therapy in Chronic Myocardial Infarction

Myrielle Mathieu, Bachar El Oumeiri, Philippe Thoma, Thierry Metens, Karim Touihri, Ielham Hadad, Lynn Ray, Naïma Mazouz, Naïma Mazouz, Aurore de lavareille, Philippe Willemsen, Robert Naeije, Guy Heyndrickx, Jozef Bartunek, Kathleen MC Entee, Free university of Brussels, Brussels, Belgium, OLV, Aalst, Belgium

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 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 ($227.10^6 \pm 32.10^6$ cells, n = 8) or culture expanded nonmodified-MSC ($232.10^6 \pm 40.10^6$ 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 9 weeks and 1.5 ± 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 ± 0.08 at baseline to 1.7 ± 01 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<0.05). This was associated with a reduction in the MRI infarct size (from 13 ± 0.67 % at baseline to 10 ± 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 MSC 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 vascularity after healed MI.

11:00 a.m.

1003-64 Novel Pharmacological Compounds as Triggers of Preconditioning In Vivo

Ioanna Andreadou, Theano Fotopoulou, Maria Koufaki, Andrew Tsotinis, Anastasia Zoga, Anastasia Pyriochou, Dimitrios Farmakis, Efstathios K. Iliodromitis, Dimitrios T. Kremastinos, Attikon University Hospital, Athens, Greece

Background: Potential triggers of preconditioning currently in clinical use include adenosine and its analogues and KATP channel openers, such as nicorandil. We assessed the effect of new compounds with aromatic heterocycles, such as indole, quinoline and purine and the pharmacophoric nitroxy ester group. The indole and quinoline derivatives possess structural features of nitrate containing KATP channel openers.
Methods: Male rabbits were randomly divided into 4 groups and subjected to 30 min of ischemia and 3 h of reperfusion with the following prior interventions Controls, no intervention; group A, administration of indole analogue; group B, administration of quinoline analogue; group C, administration of the N6,N9-substituted adenine analogue, C6. Compounds were administered in a total dose of 4 mg, 40 min and 1 min before sustained ischemia. Myocardial infarct size was determined with TTC staining and fluorescent microspheres. Blood samples were drawn at different time points for malondialdehyde (MDA) determination as a lipid peroxidation index and for cGMP. In order to test whether combined treatment of compounds A and C with the mito KATP blocker 5-hydroxydecanoic acid (5-HD) alters the infarct size, 2 additional groups were assessed in the first series of experiments.
Results: Reduction of the infarct size was observed in all treated groups (20.5±5.2%, 22.4±4.7%, 19.8±3.1% vs 47.4±2.6% in control, p<0.05). Combined indole and 5-HD treatment abolished infarct size reduction while combined adenine analogue and 5-HD did not. All tested compounds reduce the circulating MDA level at the 20th min of reperfusion (p<0.05). MDA was significantly elevated at the 20th min of ischemia in groups A and B compared to baseline. cGMP circulating levels were significantly elevated in groups A and B at the 20th min of ischemia compared to controls.
Conclusion: The administration of the new compounds reduced infract size and triggered preconditioning in vivo. The indole and quinoline analogues accomplish it via c-GMP, mitoKATP channel opening and free radical production, while the adenine analogue acts independently of the mitoKATP channels opening.

11:00 a.m.

1003-65 Myelosuppressives Improve Cardiac Dysfunction After Myocardial Infarction by Activating Cell Survival Signaling, Mobilizing CD34 Positive Cells and Attenuating Fibrosis and Apoptosis

Hiroaki Ushikoshi, Yu Misao, Takamasa Ohno, Yiwen Li, Ngin Cin Khai, Genzou Takemura, Takako Fujiwara, Hisayoshi Fujiwara, 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:** (1) *In*

vitro: 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 vivo*: An MI model was created by permanent coronary occlusion. On the next day after MI, 5FU (100 mg/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 inhibited cardiac fibroblast proliferation in a dose-dependent manner *in vitro*. (2) 5FU and Cy increased peripheral CD34+ cells (5FU: 30.5 ± 5.5 /μl, Cy: 21.8 ± 4.6 /μl *vs.* C: 11.2 ± 6.1 /μl, $p < 0.05$). Myelosuppressives 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 (by LVEF; 5FU: 42.9 ± 6.4%, Cy: 38.8 ± 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 area (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 the MI area of both groups (5FU: 1.8 ± 1.0 %, Cy: 0.9 ± 0.8 % *vs.* C: 4.4 ± 1.1 %, $p < 0.01$). Finally, immunoblotting revealed upregulated SDF-1/CXCR4 axis, ANP, Bcl2 and activated Akt, indicating enhanced survival signaling in treated hearts. **Conclusions:** Upregulation 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.

11:00 a.m.

1003-66 Impaired Glucose Tolerance Is Associated With Endothelial Damage Following Acute Myocardial Infarction

Shahirose S. Jessani, Vellore J. Karthikeyan, Teri Millane, Gregory YH Lip, University department of medicine, City hospital, Birmingham, United Kingdom, Department of medicine, Basildon, 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 testing 3-5 days after admission. We established existing endothelial cell damage by measuring vWF levels in the fasting state, and investigated the effect on the endothelium of a 75 g glucose load. 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 change in vWF levels in response to oral glucose tolerance test correlated with the change in plasma glucose levels (Spearman, $r = 0.302$, $p< 0.001$).

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.

Table vWF by glycaemic status post acute myocardial infarction

vWF i.u/dl mean (SD)	Normal glucose tolerance (n = 52)	Impaired glucose tolerance (n= 48)	Diabetes mellitus (n = 25)
Age (years)	57.4 (12.4)	61.0 (12.9)	57.9 (11.9)
Male, n (%)	43 (82.7)	43 (89.5)	21 (84)
Fasting vWF	118.2 (20.3)	134.27 (27.4)*	134.1 (17.2)*
2-h post glucose challenge	125.4 (19.4)[a]	145.9 (29.4)*[a b]	145.4 (17.7)*[a b]

Between group analyses by ANOVA with Tukey post hoc test.
Pre and post glucose challenge vWF analysis by paired t- test.
* Significantly higher ($p < 0.001$) compared to NGT;
[a] Significantly higher vWF at 2-hour post glucose challenge ($p < 0.0001$).
[b] Significantly higher vWF compared to NGT ($p < 0.01$).

11:00 a.m.

1003-67 Fibroblast Growth Factors Promote 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 Lim, Korea University Medical College, Seoul, South Korea

Background: Bone-marrow mesenchymal stem cells (BMMSCs) have the capacity for self-renewal, differentiation into a variety of cell types including cardiac and endothelial lineages, and thus represent an attractive source for myocardial regeneration. Despite this promise, little is known about the mechanisms underlying the proliferation of BMMSCs. The purpose of this study is to identify the factors and signaling pathways involved in the proliferation of Sca-1$^+$ BMMSCs. **Methods:** Sca-1$^+$ BMMSCs were purified by magnetic-activated cell sorting (MACS) system from bone marrow of ICR mice. The effect of cytokines, growth factors, and signal pathways involved in the proliferation of Sca-1$^+$ BMMSCs was analyzed by BrdU incorporation assay and Western blotting. **Results:** Flow cytometry analysis revealed that Sca-1$^+$ BMMSCs were enriched to > 90% after sorting four rounds with the MACS system. Among the cytokines and growth factors examined in this study, fibroblast growth factor 2 (FGF-2) and FGF-4 significantly stimulated the proliferation of Sca-1$^+$ BMMSCs (Control, 1±0.05 vs. FGF-2, 4.34±0.22 vs. FGF-4, 3.62±0.26, $P < 0.05$), as determined by BrdU incorporation. PI3K/Akt, ERK1/2 and JAK/STAT3 pathways were investigated after stimulation with FGF-2 or FGF-4. No changes were observed in total ERK1/2 and Akt; however, the pERK1/2 and pAkt levels were up-regulated within 15 min for the FGF-2- or FGF-4-treated Sca-1$^+$ BMMSCs. Moreover, the pERK1/2 and pAkt up-regulation induced by FGFs was completely abolished by the pretreatment with the MEK1/2 inhibitor U0126 and the PI3K/Akt inhibitor, LY294002. However, no change in pJAK2 or total JAk2 levels was observed in Sca-1$^+$ BMMSCs induced by FGFs. As a consequence of PI3K/Akt and ERK1/2 activation, the up-regulation of c-Jun, the downstream target of ERK1/2 in Sca-1$^+$ BMMSCs after stimulation with FGF-2- or FGF-4 was observed after 12 or 24 h. Moreover, the activation of c-Jun was significantly reduced by U0126 in FGF-2 or FGF-4-treated Sca-1$^+$ BMMSCs. **Conclusions:** Taken together, the data suggest that FGF-2 and FGF-4 promote the proliferation of Sca-1$^+$ BMMSCs through the activation of the ERK1/2 and PI3K/Akt signaling pathways.

11:00 a.m.

1003-68 Is Sarco(endo)plasmic Reticulum Ca2+-ATPase (SERCA) Inhibition Detrimental or Beneficial for Postischemic Myocardial Function and Injury? Evidence From SERCA2a-deficient Mice

M.A. Hassan Talukder, Li Zuo, Anuradha Kalyanasundaram, Velayutham Murugesan, Muthu Periasamy, Jay L. Zweier, The Ohio State University, Columbus, OH

Intracellular Ca^{2+} overload with reduced activity of SERCA2a is one of the important mediators of ischemia/reperfusion (I/R) injury. While upregulation of SERCA function is well documented to improve postischemic cardiac function, there are also reports where pharmacological inhibition of SERCA improved postischemic myocardial function. Therefore, to address this issue, I/R studies were performed in isolated hearts from heterozygous SERCA-knockout (HT) and wild-type (WT) mice. Both myocardial stunning (20-min I) and infarction (30-min I) models were investigated for 60-min R. Rhod-2 spectrofluorometry was used to measure cytosolic Ca^{2+} fluorescence (CaF), and EPR spin trapping to measure free radicals during R. Table shows that with R following 20-min I, there was no significant difference in the postischemic contractile function between 2 strains. However, following 30-min I, postischemic contractile function was significantly lower in HT hearts with larger myocardial infarction. Compared to WT, basal systolic CaF was significantly lower and diastolic CaF was significantly higher in HT hearts. After 30-min I, diastolic CaF was markedly elevated in HT hearts. Postischemic coronary free radicals were similar in both strains. Thus, these findings provide direct evidence that functional SERCA2a level plays a crucial role in postischemic Ca^{2+} overload, myocardial contractile function and salvage. SERCA2a inhibition does not improve rather it worsens postischemic myocardial performance.

Parameters at baseline and with global ischemia and reperfusion					
Protocols	Parameters / Models	Stunning WT (n)	Stunning HT (n)	Infarction WT (n)	Infarction HT (n)
Baseline (PI)	LVDP (mmHg)	114±9 (5)	89±8 (5)	84±11 (6)	76±5 (6)
	LVEDP (mmHg)	3.1±0.6 (5)	5±0.8 (5)	3.3±0.8 (6)	3.1±0.7 (5)
	D-CaF (RU)	ND	ND	367±28 (5)	646±17 (5)**
	Peak systolic CaF(~fold increase from D-CaF)	ND	ND	~1.7-fold (5)	~1.4-fold (5)*
Global Ischemia	D-CaF (RU)	ND	ND	1432±60 (5)	1783±12 (5)***
Reperfusion (60-min)	LVEDP (mmHg)	16±4 (5)	33±6 (5)*	18±2 (6)	47±10 (6)*
	LVDP (%PI)	93±7 (5)	80±3 (5)	68±4 (6)	37±6 (6)**
Morphometry	Infarct size (% LV)	ND	ND	13±1.5 (5)	24±3.5 (5)**
LVDP, left ventricular developed pressure; LVEDP, left ventricular end diastolic pressure; D-CaF (RU), diastolic Ca^{2+} fluorescence in relative units	PI, pre-ischemia; n, number of experiments	ND, not determined	*P<0.05 vs. WT	**P<0.01 vs. WT	***P<0.001 vs. WT

11:00 a.m.

1003-69 Ranolazine Prevents Ischemia-Induced ST Segment Changes and Left Ventricular Mechanical Dysfunction in Rabbits

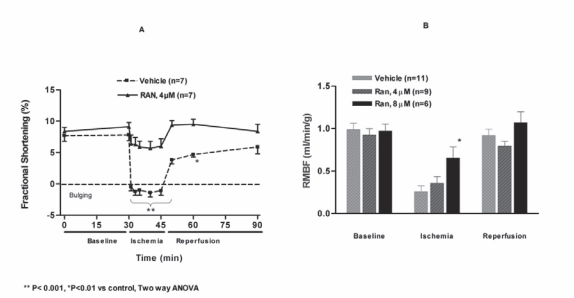
Wei-Qun Wang, Chelsea Robertson, Paige Ivey, Arvinder K. Dhalla, Luiz Belardinelli, CV Therapeutics, Inc, Palo Alto, CA

Background: Ranolazine (Ran) is an anti-anginal drug that improves Na+ and Ca++ homeostasis during ischemia in vitro. This study was undertaken to determine whether Ran prevents left ventricular dysfunction induced by ischemia in vivo.

Methods: In anesthetized female rabbits (n=62) regional myocardial ischemia (15 min) was caused by ligation of the left anterior descending coronary artery and followed by 45 min of reperfusion. Epicardial ECG (epi-ECG), fractional shortening (FS, measured by piezoelectric crystals), and regional myocardial blood flow (RMBF, measured by color microspheres) were examined. Ran was given 30 min prior to ischemia.

Results: Ran (1, 4 and 8 μM) dose-dependently prevented the ischemia-induced ST elevation (2.3 ± 0.8, 0.8 ± 0.6 and 0.4± 1.0 mV, $p<0.05$ for Ran 8 μM vs control 4.1± 1.1mV). The end-diastolic (EDL) and end-systolic segment length (ESL) of the ischemic region were significantly prolonged (2.1 ± 0.2 and 3.3 ± 0.3 mm, respectively), and FS of the ischemic region was significantly impaired with either akinesis (4/7) or systolic bulging (3/7) occurring during ischemia. Ran (4μM) significantly prevented a) the prolongation

of EDL (-0.1 ± 0.2 mm) and ESL (0.3 ± 0.3 mm), b) the reduction in FS (Figure A), and c) myocardial akinesis (0/7) and systolic bulging (0/7). RMBF 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.



11:00 a.m.

1003-70 **A Novel EBV Encoded Protein Is Associated With ICAM Expression in Patients With Acute Myocardial Infarction**

Glen E. Cooke, Amanda Lesinski, Mackenzie Taylor, James Green, Christopher Jones, Min Chen, W. James Waldman, Marshall V. Williams, Jr., Deborah A. Knight, Philip F. Binkley, Ronald Glaser, The Ohio State University, Columbus, OH

Background:We have identified a novel early Ebstein Barr Virus (EBV) protein (dUTPase) produced during virus replication. We have further shown that this protein can induce the upregulation of several pro-inflammatory cytokines including TNFalpha and IL-6, two cytokines that have been shown to be related to cardiovascular disease. We have also shown that depression/stress can reactivate latent EBV.
Methods:To determine whether this protein, and thus EBV, may play a role in coronary atherosclerosis, we measured cytokines by ELISA and antibody titres to EBV dUTPase in 297 consecutive patients undergoing percutaneous coronary intervention for stable angina, unstable angina, or acute myocardial infarction.
Results:Acute myocardial infarction was associated with the highest measures of IL-6 (ANOVA p = 0.05; 4.6 + 2.6pg/mL in patients with acute myocardial infarction vs 3.2 + 2.3pg/mL in stable angina). Similarly, Intracellular Adhesion Molecule 1 (ICAM1) was significantly higher in patients with acute MI (ANOVA p < 0.05; 304 + 116pg/mL in AMI versus 265 + 86pg/mL in stable angina). However, the highest values of ICAM1 were found in patients having an acute MI and who were antibody positive for dUTPase (ANOVA p = 0.008; 369 + 183pg/mL in AMI and positive for dUTPase versus 249 + 70 pg/mL in stable angina and negative for dUTPase antibody).
Conclusions:These data indicate that: 1. pro-inflammatory cytokines are expressed to the greatest degree in acute myocardial infarction as compared to stable ischema; 2. EBV acting through early viral proteins may play a role in the stimulation of the pro-inflammatory mechanisms that precipitate AMI.

11:00 a.m.

1003-71 **Do Selected Markers of Inflammatory Response During the Acute Phase of ST-Segment Elevation Myocardial Infarction Relate to Outcome?**

Pierre Theroux, Paul W. Armstrong, David J. Moliterno, Franz-Josef Neumann, Amanda L. Stebbins, Kenneth W. Mahaffey, Judith S. Hochman, Christian W. Hamm, Christopher B. Granger, APEX AMI Investigators, Montreal Heart Institute, Montreal, QC, Canada, Duke Clinical Research Institute, Durham, NC

Background: Inflammation portends accelerated progression in chronic cardiovascular disease. During acute STEMI, inflammation may be causative and/or consequential. We evaluated this in a case-control APEX-AMI substudy where pexelizumab was given to STEMI undergoing primary PCI < 6 hrs of symptoms.
Methods: Comprehensive biomarkers were evaluated in 201 patients (cases) with death, shock or heart failure < 90 days and 584 controls matched for age, sex, and site of MI. Blood was obtained early after symptoms (median 2.7 hrs) before study drug and PCI. The 12 biomarkers in at least 800 pts (C-reactive protein (CRP), NT pro-BNP, Il-6, Il-4, Il-10, IL-12, IL-1β, TNFα, interferon gamma (IFNγ), IL-1 receptor antagonist (ra), MBL, and interferon-inducible protein (IP-10)) were entered into multivariable models and related to outcomes.
Results: Biomarkers were all elevated and univariable and multivariable associations with the 90 day composite of death, shock and heart failure are below. Higher levels of pro-inflammatory cytokine (IL-6), T cell-focused chemokine IP-10, anti-inflammatory cytokine IL-1ra and NTpro-BNP all independently predicted adverse outcome in all models tested.

Biomarker	Univariable relationship		Multivariable model	
	Hazard ratio	P value	Hazard ratio (95% CI)	P value
IL-6	2.64 (per 10 ng/ml)	<0.0001	2.14 (1.39, 3.30)	0.0005
IP-10	0.8 (per 200 Units)	0.0031	0.76 (0.66-0.89)	0.0006
NT proBNP	1.28 (per 100 g/ml)	<0.0001	1.27 (1.11, 1.47)	0.0007
IL-1ra	1.58 (per 200 units)	<0.0001	1.19 (0.99-1.42)	0.05
IL-12	1.00 (per 5 ng/ml)	NS	--	NS
IL-10	1.16 (per 10 ng/ml)	<0.0005	--	NS
CRP	1.31 (per 5 ng/ml)	<0.0001	--	NS
IFNγ	1.04 (per 5 ng/ml)	0.04	--	NS

Conclusions: The acute phase of STEMI is associated with a marked systemic inflammatory response detectable in selected markers within a few hours of symptoms. This reaction is strongly associated with an adverse outcome, complementing the predictive value of CRP in multivariable models.

11:00 a.m.

1003-72 **Induction of HO-1 Reduces the Metabolic and Nitro/ Oxidative Effects of Ischemia-Reperfusion in Diabetic Rat Hearts**

Danilo Neglia, Cecilia Vecoli, Daniela Giannessi, Maristella Maltinti, Virginia Ottaviano, Simona Baldi, Michela Novelli, Pellegrino Masiello, Aldo Paolicchi, Renata Barsacchi, Nader G. Abraham, Antonio L'Abbate, CNR Institute of Clinical Physiology, Pisa, Italy

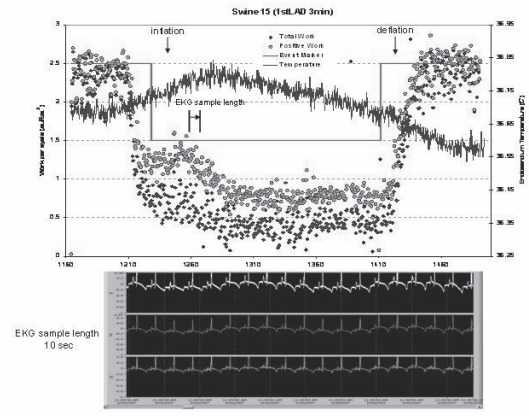
Background. Ischemia/reperfusion damage could be exacerbated in diabetic hearts by myocardial overexpression of inducible nitric oxide synthase (iNOS) resulting in increased interaction of NO with superoxide (O2-) and production of peroxynitrite (ONOO-). In this study we tested the hypothesis that cobalt protoporphyrin (CoPP), inducer of heme oxygenase-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 cmH2O) followed by 30 min at low perfusion pressure (20 cm H2O) 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 malonildialdehyde (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<0.0001 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.

11:00 a.m.

1003-73 **Regional Myocardial Temperature During Coronary Occlusion in the Wwine: Comparison With Electrocardiographic Changes**

Amany Ahmed, Muhammad S. Munir, Igor V. Stupin, Jill Robertson, Koovapudi J. Shankar, Sreedevi Gondi, Ibrahim Aboshady, Marlos R. Fernandes, Christiano O. Cardoso, Fred Baimbridge, Ed Sobash, Alan M. Brewer, S. Ward Casscells, Texas Heart Institute, Houston, TX

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.
Results:



12 occlusions (total 14) were associated with an initial rise (ascending phase) in T; with a mean ΔT of 0.04±0.03ºC in the SE, and a mean ΔT of 0.07±0.04ºC in the MM. When the peak T rise in MM was compared to the SE (p = 0.006). With ongoing occlusion, a drop (descending phase) in T occurred, resulting in a mean ΔT of -0.11±0.07ºC in the SE, and a mean ΔT of -0.14±0.11ºC in the MM. Onsets of ΔT following CO were observed instantaneously, and preceded ischemic EKG changes by mean of 35±29s.

Conclusions: The myocardium exhibited a detectable temperature response to ischemia in the SE and the MM, prior to surface EKG changes. There was transmural heterogeneity during the ascending phase of this response, with a higher peak in the MM. Temperature monitoring may become a complement to EKG analysis for improved detection of ischemia; either intra-operatively or via pacemaker leads.

11:00 a.m.

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

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

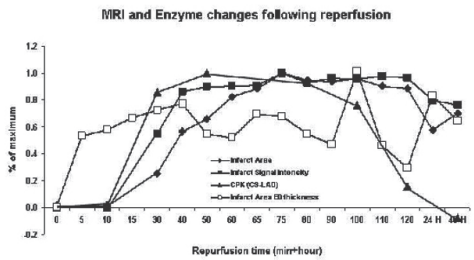
Background: Uncoupling of mitochondrial oxidative phosphorylation by endogenous uncoupling proteins (UCP) has emerged as a cardioprotective mechanism by preventing cardiac cell death under metabolic or oxidative stress. However, it is not clear whether lack of myocyte UCP3 is associated with increased 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 (30.8+/-6.6% vs. 12.4+/-1.2%, p=0.009). Accordingly, there were significant differences in the infarct area to area 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 in cardiomyocytes prevents myocardial damage during oxidative stress. The regulation of mitochondrial UCP3 by pharmacological or genetic means may be a new potential therapeutic target for effective myopreservation 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, Jiarui 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 inotropy. During ischemia, myocardial signal intensity showed no increase. 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.

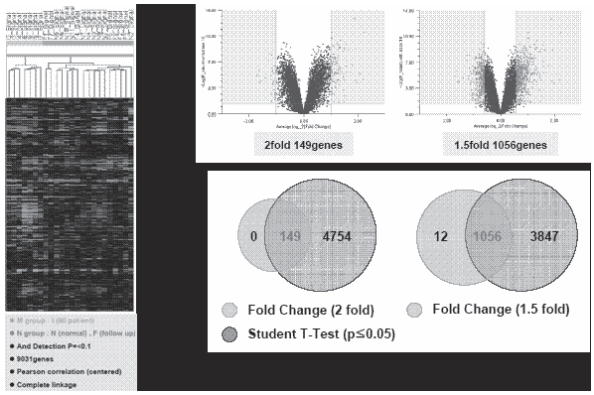


11:00 a.m.

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 molecular markers which allow diagnosing AMI in early times.
Methods:To define testing group for early AMI detection, peripheral bloods from patients presented with 2 hours of pain onset were included as AMI. To assess and identify characteristic molecular profiling of AMI, total RNA of peripheral blood was subjected to human whole genome expression array (Human-6 V2, Illumina, USA) in 10 patients at 2.0±0.5h after onset of AMI and compared with healthy subjects or 2 weeks follow-up samples from the same patients.
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 S 100 calcium binding protein P, MMP 9, 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 Cataliotti, 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. Genome-wide microarray analysis was performed on kidney cortex (KC) and medulla (KM) (Affymetrix GeneChip® Rat Genome 230 2.0). **Results**: EF decreased after MI (S:62.8±2.3, MI:42.8±6.5 %, p<0.01) and LVEDd increased (p<0.005) PRA and aldosterone activation 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 RM (KC S:1.1±0.2, MI:3.5±0.6 %, p<0.001 and KM S:1±0.2, MI:18.8±6 %, p<0.005). Microarray analysis revealed that 303 genes significantly changed in KM and 407 genes in the KC after MI (1.5 fold, P<0.05). Gene dysregulation was related to cell proliferation, metabolic processes and cell communication (Z value>2). **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.

1003-78 **Paracrine Cytoprotective Effects of Inner Chorion-Derived Human Mesenchymal Stem Cells**

Kazuhiko Harada, Noritoshi Nagaya, Shunsuke Ohnishi, Shin Ishikane, Michihiro Fujiwara, Tomoaki Ikeda, Department of Biochemistry, National cardiovascular center research institute, Suita, Japan, Department of regenerative medicine and Tissue engineering, National cardiovascular center research, 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 outer chorion and basic fibroblast 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.

1003-79 **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 with regard to the mechanisms of myocardial regeneration still exist. This study is to develop the reporter-vector systems for monitoring of 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 using the genomic DNA isolated from C57BL/6 mice and cloned into pDsRed vector. A 844-bp fragment of Flk1 and a 1,061-bp fragment of Tie2 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 differentiation of BMMSCs and P19 embryonic stem cells along the cardiomyogenic or endothelial lineage was specifically monitored by the appearance of cardiac- or endothelial-specific promoter-driven EGFP or DsRed as determined by immunocytochemistry. Furthermore, dual-reporter systems for simultaneous tracking of DsRed driven by the cardiac-specific promoters and EGFP driven by the endothelial-cell-specific promoters were constructed, and their specificity in monitoring of cardiac and endothelial differentiation was confirmed in BMMSCs and P19 embryonic stem cells. **Conclusions:** These results showed that 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.

11:00 a.m.

1003-80 **The Cardioprotective Role of Osteopontin-1 in the Pathogenesis of Murine Ischemic Cardiomyopathy**

Georg D. Duerr, Martin Zoerlein, Daniela Dewald, Bettina Mesenholl, Prisca Schneider, Alexander Ghanem, Susan Rittling, Armin Welz, Oliver Dewald, University Clinical Center Bonn, Bonn, Germany

Background: Repetitive brief ischemia and reperfusion (I/R) is associated with ventricular dysfunction in development of ischemic cardiomyopathy. We investigated the role of matricellular protein and macrophage maturation marker osteopontin-1 (OPN) in our closed-chest murine model of repetitive I/R.
Methods: Daily 15 minutes LAD occlusion followed by reperfusion was performed for 3, 5 and 7 consecutive days (d) in C57/Bl6 wildtype (WT) and OPN KO mice (n=8/group). Hearts were examined echocardiographically and processed for histological and mRNA studies.
Results: OPN mRNA expression was induced 15 fold in Taqman RT-PCR after 3d I/R in WT mice followed by a transient chemokine induction and macrophage infiltration. This led to extensive interstitial fibrosis with global and regional left ventricular dysfunction and without myocardial infarction after 7d I/R. In contrast, OPN KO mice showed microinfarctions in the ischemic region after 3d I/R followed by a scar formation. Total collagen area was comparable between the strains. The microinfarctions in OPN KO mice showed dense collagen deposition and a strong macrophage infiltration after 5d I/R (27.9±12.7 cells/field, F4/80). The non-infarcted ischemic area in OPN KO mice showed only loose interstitial collagen deposition and lower macrophage density (7.0±1.6/field) when compared to WT mice (33.3±8.2/field; $p<0.05$). Anterior wall thickening was significantly lower in OPN KO hearts (32.1±6.1% vs. WT 51.8±5.6%; $p<0.05$), but fractional shortening was comparable between the strains. mRNA induction of CCL2 and CCL4 was significantly decreased in OPN KO hearts and accompanied by up to 5 fold lower induction of glutathione peroxidase 1, heme oxygenase 1 and zinc-storage proteins metalothionein 1 & 2.
Conclusions: The cardioprotective mechanism of OPN seems to involve a cascade where sufficient induction of free radical scavenger enzymes, metallothionein and chemokines is leading to macrophage infiltration and subsequent interstitial fibrosis without myocardial infarction. OPN may therefore prevent cardiomyocyte loss through modulation of inflammatory response and interstitial remodelling in murine ischemic cardiomyopathy.

11:00 a.m.

1003-83 **Myocardial perfusion changes in the first week after STEMI strongly influence left ventricular size and function at 6 months follow-up: results from the Acute Myocardial Infarction Contrast Imaging (AMICI) multicenter trial**

Stefania Funaro, Emanuela Berardi, Emanuele Canali, Mariapina Madonna, Antonella Mattatelli, Alessandra Labbadia, Antonio Scarà, Leda Galiuto, Luciano Agati, Department of Cardiology, La Sapienza University, Rome, Italy, Department of Cardiology, Catholic University Sacred Heart, Campobasso, Italy

Background: Clinical significance of microvascular damage (MD) changes after reperfusion is still under discussion. At this aim we studied the correlation between MD changes in the first week after STEMI and LV functional outcome at 6 month F/U.
Methods: 110 STEMI patients were enrolled in the AMICI multicenter trial. MD was assessed using myocardial contrast echocardiography on day 1 after reperfusion (T1) and at pre-discharge (T2). The following echo parameters were calculated at T1,T2 and at 6 months F/U: contrast defect length (CDL%), wall motion abnormalities (WMA%), ejection fraction (EF%) and end diastolic volume (EDV).
Results: During the first week after STEMI, CDL% reduced (Group 1) in 31% of patients (from 29±14 to 14±15), didn't change (group 2) in 21% (from 28±13 to 28±13) and increased (Group 3) in 13% (from 28±8 to 36±7). Microvascular perfusion was normal (Group 4) at T1 and T2 in 35% of patients. At T1, there weren't statistical differences in MD extent between Groups 1, 2 and 3 (CDL% 29±14, 28±13, 28±8, respectively, ns). At T1, WMA% and EF%, were less compromised in group 4 than in the remaining groups (WMA%: 48±18, 45±15, 54±11, 21±17 respectively, $p<0.05$ and EF%: 44±9, 42±6, 42±7, 53±7 respectively $p<0.05$) while EDV was similar in the 4 groups (110±30, 109±9, 118±26, 100±25 respectively). At F/U, patients with normal perfusion had the best outcome with a significant reduction in WMA% and EDV (- 30 % and -7 % respectively) and a significant improvement in EF (+ 8 %). Among patients with microvascular damage at T1 only those with CDL% reduction showed WMA% and EDV reduction (-33 % and - 3 % respectively) and EF% improvement (+ 9 %). In patients with stable MD, no changes in WMA or EF might be detected at F/U. Finally a significant EDV increase (+ 22 %) was detected in patients with increased MD after STEMI.
Conclusions: Patients with normal microvascular perfusion after STEMI had smaller infarct size and better systolic function with significant reduction in EDV at F/U. Similar results were observed in patients showing MD reduction in the first week after STEMI. The persistence or worsening of MD was strongly connected to a bigger infarct size with a more depressed EF% and a significant EDV increase at F/U.

11:00 a.m.

1003-84 **Reverse Remodeling During Healing After Reperfused Myocardial Infarction Through Matrix and Cytokine Modulation With Vasopeptidase Inhibition**

Arivazhagan Palaniyappan, Vijayan Menon, Halliday Idikio, Richard R. Uwiera, Bodh I. Jugdutt, University of Alberta, Edmonton, AB, Canada

Background: Angiotensin II and matrix metalloproteinases (MMPs) and tissue inhibitors of MMPs (TIMPs) modulate cardiac remodeling and nitric oxide synthases (NOSs) modulate function. We hypothesized that decreased effects of angiotensin II induced by dual inhibition of neutral endopeptidase and the angiotensin-converting enzyme with the vasopeptidase inhibitor omapatrilat or the the angiotensin type 1 receptor blocker candesartan improves MMP-9/TIMP-3 balance and decreases iNOS, reverses left ventricular (LV) remodeling and limits dysfunction during healing after reperfused myocardial infarction (RMI).
Methods: We randomized Sprague-Dawley rats 24 hours after RMI (1 hour of left anterior descending coronary occlusion followed by reperfusion) to 3 weeks of oral placebo, omapatrilat (10 mg/kg), or candesartan (30 mg/kg). A sham group had no occlusion. We measured LV function and remodeling (2D-echocardiography/Doppler), MMP activity (zymography), and MMP, TIMP and NOS proteins (Western blots) in the ischemic and non-ischemic zones, and infarct size at 3 weeks.
Results: Compared to sham, RMI in placebo induced ST-segment elevation, infarction (25% LV; 60% risk), LV dysfunction (decreased ejection fraction and diastolic function) and remodeling (increased LV diastolic and systolic volumes; infarct expansion and thinning). Compared to placebo, both omapatrilat and candesartan limited LV dysfunction and remodeling with improved ($P<0.001$) LV ejection fraction, volumes and diastolic dysfunction, and less ($P<0.001$) infarct expansion and thinning. Compared to the non-

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 RMI.

11:00 a.m.

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, 2x106/kg hUSSCs labeled by 111Indium (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 under intracardiac Echo guidance. Animals were terminated after 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 infracted, border, and rim of adjacent normal tissue, in addition to remote LV, LA, RV, RA, mitral and aortic valves, were also cut 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 6±6% for Endo, 15±16% and 3±2% for Epi group (P>0.05) respectively. Epicaridal 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 in 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.

11:00 a.m.

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 (2382 ± 234/mm2 vs. 1389 ± 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. Inflammatory cell infiltration started ~60-90 min after reperfusion and was limited by treatment with KAI-9803 (246 ± 17/mm2 vs. 399 ± 34/mm2 inflammatory 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.

11:00 a.m.

1003-88 **Decreased levels of inflammatory cytokines and circulating endothelial progenitor cells after implantation of paclitaxel-eluting stents**

Wojciech Wojakowski, Andrzej Ochala, Beata Ksiazek, Maciej Kazmierski, Andrzej Pyrlik, Joanna Ciosek, Iwona Mroz, Marek Krol, Katarzyna Maslankiewicz, Barbara Korzeniowska, Rafal Wyderka, Michal Tendera, Medical University of Silesia, Katowice, Poland

Background: Increased levels of inflammatory markers are predictors of adverse cardiac events and restenosis in patients undergoing PCI. Paclitaxel-eluting stents (PES) significantly lower the risk of restenosis. Paclitaxel can modulate the activity of immune cells leading to altered levels in systemic inflammatory markers and transcription of inflammation- and apoptosis related genes. We hypothesized that in patients with stable CAD undergoing the elective PCI, implantation of PES leads to suppression of procedure-associated increase of inflammatory cytokines, circulating progenitor cells and inflammatory genes in circulating MNC in comparison to bare metal stents (BMS). **Aim:** to assess the influence of paclitaxel-elutins stents on procedure-related increase of hematopoietic cytokines, circulating $CXCR4^+$ and $CD34^+CD133^+VEGFR2^+$ progenitor cells and expression of inflammatory genes in comparison to BMS in patients undergoing elective PCI. **Methods:** 28 patients undergoing elective one-vessel PTCA with implantation of PES and 26 with BMS were enrolled. Blood samples were drawn at before PTCA, 24 hours and 4 weeks after PTCA. **Results:** PTCA with BMS lead to increased levels of MCP-1, IL-10, sCD40L and hsCRP after 24, however there was no increase in patients treated with PES [MCP-1 (510±112 vs. 362±71 pg/mL, p<0.05); IL-10 (4.4±2.1 vs. 3.1±1.3 pg/mL, p<0.05); sCD40L (4.97±2.4 vs. 3.2±1.5 pg/mL, p<0.03); hsCRP (3.4±1.1 vs. 2.8±0.9 pg/mL, p<0.05). Number of circulating CD34+CD133+VEGFR2+ EPC (1.7±1.0 cells/μL) increased 24 hours after PTCA in patients with BMS (3.9±1.6 cells/μL), but not with PES (2.0±0.9 cells/μL). No changes in levels of chemoattractants SCF, G-CSF, VEGF and SDF-1 were found after 24 hours and 4 weeks. No differences in levels of cytokines and EPC were found after 4 weeks between PES and BMS. Microarrays were used for the evaluation of transcriptional activity of inflammatory genes in circulating MNC. **Conclusion:** Implantation of paclitaxel-eluting stents has anti-inflammatory effect on PTCA-related increase of cytokine levels and may have unfavorable effect by suppression of the mobilization of progenitor cells.

ACC.POSTER CONTRIBUTIONS

1010

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

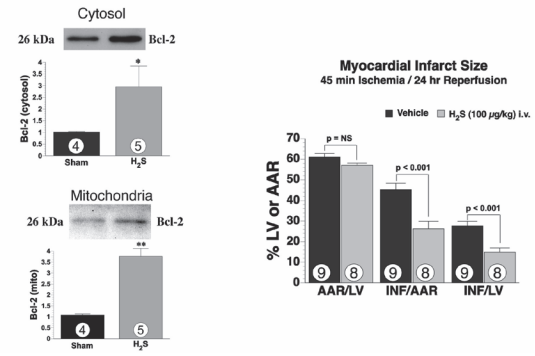
Sunday, March 30, 2008, 1:00 p.m.-4:30 p.m.
McCormick Place, South Hall

3:00 p.m.

1010-41 Hydrogen Sulfide (H2S) Preconditions the Myocardium Against Myocardial Ischemia-Reperfusion Injury via Up-regulation of Anti-Apoptotic Signaling

Susheel Gundewar, Saurabh Jha, Sang Yong Ji, Arun Ramachandran, Denise J. Nunez, Iris Toedt-Pingel, Sandeep Patel, John W. Calvert, John W. Elrod, David J. Lefer, Albert Einstein College of Medicine, Bronx, NY

Background: Hydrogen sulfide (H_2S) is an important endogenously produced gaseous signaling molecule with a diverse physiological profile. Moreover, the emergence of H_2S as a potent cardioprotective mediator, either through its exogenous administration or through the up-regulation of its endogenous production, necessitates the elucidation of its cytoprotective mechanisms. Therefore, we evaluated several potential mechanisms of H_2S mediated myocardial preconditioning. **Methods:** H_2S donor (100 μg/kg), or vehicle was administered (i.v.) to mice. Hearts were excised 24 hr after H_2S administration and left ventricular tissue was processed for a glutathione assay or for Western blot analysis. In a separate group, mice were treated with H_2S and then 24 hr later subjected to transient myocardial ischemia for a period of 45 min followed by reperfusion for 24 hr, at which time the hearts were excised and evaluated for infarct size using 2,3,5-triphenyltetrazolium chloride (TTC) staining. **Results:** H_2S increased the protein expression of the anti-apoptogen, Bcl-2, in both the cytosolic and mitochondrial cellular compartments. However, H_2S did not increase the protein levels or activation of eNOS, MnSOD or glutathione. Mice treated with H_2S donor did 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 H_2S mediated cardioprotection.



3:00 p.m.

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 AAR (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 reperfusion. A similar protocol in 3 pigs injected with H11K was performed in the presence of N (G)-nitro-L-arginine methyl ester (L-NAME), a NO synthase inhibitor. Additional 4 pigs injected with H11K were used for determination of gene expression, as well as, cell survival pathway.
Results: H11K-injected myocardium showed a 4-fold increase in H11K protein expression compared to control ($p<0.01$). Although the AAR was similar between groups, infarct size, expressed as a fraction of AAR, was reduced significantly ($p<0.05$) in the H11K-injected group (32±5%) compared to the LacZ group (50±5%). H11K-injected myocardium showed a significant ($p<0.05$) 2- to 4-fold increase in the expression of the inducible isoform of NO synthase and cyclooxygenase-2, both mediators of the 2nd window of ischemic preconditioning. Pigs with injected H11K virus, but pretreated with L-NAME, no longer demonstrated the cardiac protection, i.e. infarct size was 67±11%, similar to that observed in pigs injected with LacZ and pretreated with L-NAME (72%).
Conclusion: Pre-emptive conditioning of the swine heart by H11K activates cell survival mechanisms that recapitulate the mechanisms of delayed preconditioning, and markedly decreases infarct size following lethal ischemia in a NO-dependent mechanism, which places H11K as a potential tool for the treatment of ischemic heart disease.

3:00 p.m.

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

Mariann Gyongyosi, Jeronimo Blanco, Terez Marian, Lajos Tron, Ors Petnehazy, Zsolt Petrasi, Rayyan Hemetsberger, Imre Pavo jr, Dara Kraitchman, Johann Wojta, Kurt Huber, Dietmar Glogar, Medical University of Vienna, Vienna, Austria, The Johns Hopkins University, School of Medicine, Baltimore, MD

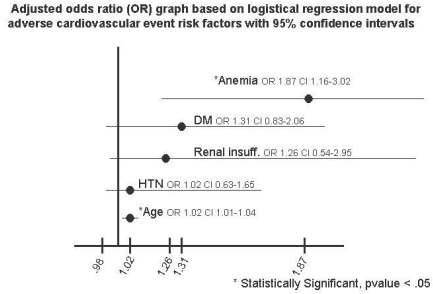
Background: Reporter gene imaging offers the ability to non-invasively serially track stem cell fate. To-date most studies have been performed in small animals. Methods: Myocardial infarction (MI) was created by percutaneous balloon occlusion of the LAD in farm pigs. Bone marrow (BM) was harvested and mesenchymal stem cells (MSCs) were selected and modified for transgene expression of the trifusion protein (lentiviral vector expressing renilla luciferase, red fluorescent protein and herpes simplex truncated thymidine kinase (LV-RL-RFP-tTK) as positron emission tomography (PET) reporter gene. In vitro assays of [18F]-FHBG uptakes of the LV-RL-RFP-tTK 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-tTK 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-tTK 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-tTK 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 (EDV: 80.0+/-6.2 vs. 88.0+/-7.7 ml, infarct size: 29.5+/-5.2 vs. 30.2+/-4.1%, EF: 43.7+/-5.9vs 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.

3:00 p.m.

1010-44 Anemia as a Predictor of Myocardial Infarction, Need for Coronary Revascularization, and In-Hospital Mortality in Women Presenting With Chest Pain

Miret Habashy-Ibrahim, Bruce Bernstein, W. David Hager, Rodrigo M. Lago, Anita M. Kelsey, Saint Francis Hospital and Medical Center, Hartford, CT, University of Connecticut Health Center, Farmington, CT

Background: Cardiovascular (CV) disease is the leading cause of death in women. Studies have shown that lower levels of hemoglobin (Hgb) may be a risk factor for adverse CV outcomes in women. The clinical impact of anemia (Hgb < 12g/dL) in women undergoing catherization for chest pain has not been evaluated. We examined the association between Hgb and CV disease outcomes and in-hospital death from any cause in this population.
Methods: We conducted a retrospective study of 428 women undergoing cardiac catheterization for chest pain between 2005 and 2006 and evaluated the risk of myocardial infarction (MI), revascularization (percutaneous coronary intervention or coronary artery bypass surgery), and death. Logistic regression analysis adjusted for age, type 2 diabetes, chronic kidney disease and hypertension was performed to identify predictors of adverse CV outcomes.
Results: The overall incidence of anemia was 33% (139 out of 428). Only Age (OR 1.02, 95% CI 1.01-1.04) and anemia (OR 1.87, 95% CI 1.16-3.02) were found to be independent predictors of adverse CV outcomes and death. In this population, anemia was a stronger predictor of MI, revascularization, or death than age, type 2 diabetes, chronic kidney disease or hypertension . Conclusion: Women with anemia undergoing angiography for chest pain have an increased likelihood of adverse CV outcomes compared to non-anemic women. This result corroborates previous findings and may indicate the need for more aggressive risk stratification of anemic women.



3:00 p.m.

1010-45 Human adipose tissue-derived stem cell preserved heart function in athymic nude rats following permanent ischemia

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

Backgroud: 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 lipoaspiration. 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, separately, when ASC CM was added to MM ($p<0.01$). Intramyocardial injection of ASCs into periinfarct zone of athymic nude rat 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 fraction of 56.56±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±17.29µl and 139.15±20.96µl, respectively) than saline group (390.76±29.80µl 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±5.75% (VS control 25.97±5.56%, $p<0.05$). 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.

3:00 p.m.

1010-46 Nonuniform Struts Distribution as the New Potential Mechanism of Stent Thrombosis After Drug-Eluting Stent Implantation

Maksymilian P. Opolski, Radoslaw M. Pracon, Gary S. Mintz, Teruo Okabe, Jerzy Pregowski, Sung Yun Lee, Eva van der Waal, Probal Roy, Kimberly A. Smith, Rebecca Torguson, Zhenyi Xue, Lowell F. Satler, Kenneth M. Kent, Augusto D. Pichard, Ron Waksman, Neil J. Weissman, Washington Hospital Center, Washington, DC

Background: Relation of nonuniform struts distribution to stent thrombosis (ST) has not been reported previously. The aim of the study was to compare stent struts distribution in the setting of ST and control patients.
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 maximum interstrut angle (60.8 ± 8.3 vs 55.7 ± 4.8, $p=0.014$), smaller minimum stent area (4.6 ± 1.1 vs 5.6 ± 1.7mm2, $p = 0.0489$) and smaller mean lumen area (5.6 ± 1.3 vs 6.8 ± 1.8mm2, $p=0.041$). SDI was significantly higher in the ST group (7.9 ± 1.8 vs 6.8 ± 0.9, $p=0.010$). Maximum interstrut angle tended to be larger in late ST group (>30 days) than in patients with subacute ST (<30 days), (66.1 ± 10.8 vs 57.8 ± 5.0, $p=0.071$).
Conclusion: In conclusion, nonuniform struts distribution which may represent partial stent fracture at the time of DES implantation suggests a new potential mechanism of ST in drug-eluting stents.

COMPARISON OF ST AND CONTROL GROUP			
	ST	CONTROL	p
NO OF STRUTS	8,44±0,55	8,67±0,57	0,201
MAX INTERSTRUT ANGLE	60,77±8,28	55,73±4,81	**0,014**
SDI	7,87±1,83	6,76±0,90	**0,010**
MEAN LUMEN AREA	5,59±1,32	6,71±1,78	**0,041**
STENT AREA	5,75±1,38	6,81±1,78	0,054
MIN STENT AREA	4,62±1,12	5,61±1,65	**0,049**
PLAQUE AREA	7,74±2,88	7,48±2,92	0,787
MEAN VESSEL AREA	13,33±3,78	14,20±4,40	0,528

3:00 p.m.

1010-47 Role of Oxygen and ROS in Bone Marrow Derived Progenitor Cells Accumulation in Infarcted Hearts: Implications for Ventricular Aneurysm Formation

Nicanor I. Moldovan, Mirela I. Anghelina, Omer I. Butt, Tiangshen Wang, Jay L. Zweier, Ohio State University, Columbus, OH

Background. We tested the hypothesis that bone marrow progenitor cells (BMPC) contribute to a repairing process spontaneously taking place in the infarcted hearts. We also studied the pattern of their distribution in regions prone to ventricular aneurysms, compared to that of oxygen and reactive oxygen species (ROS). **Methods.** We performed coronary ligation for 7 days (n=6), or sham-operation (n=6) in C57/B6 mice transplanted with bone marrow from LacZ-expressing (Rosa) donors. We also measured pO_2 at the core of the infarcts by implanting EPR O_2-sensitive (LiPc) probes. We assessed the formation of ROS by fluorescent staining with CM-DCF-DA (for H_2O_2) and hydroethidine (for superoxide). We determined the pattern of BMPC engraftment by whole-organ incubation with X-gal, followed by sectioning and immunostaining. **Results.** In the border zone, we found an abundance of $LacZ^+$ cells co-expressing, in a mosaic pattern, the progenitors markers c-Kit, Oct3/4 or ABC-G2. Cardiomyocyte markers troponin I and connexin 43 were found in proliferating cell clusters, and in small cardiomyoblasts functionally integrated with mature $LacZ^-$ cardiomyocytes. At the core of the infarct, we also found a lack of organized microvessels, yet an abundance of extravascular erythrocytes percolating a loosely-organized tissue, in pockets corresponding to excessive ventricular thinning and/or aneurysms. These erythrocytes apparently mediated oxygen diffusion, as directly demonstrated by recovery of local oxygenation to a pre-infaction level (~20 mm Hg), after the third day of ischemia. Remarkably, a similar spatial distribution was found for ROS, as detected by the fluorescent probes. **Conclusions.** At one week post-infarction, we found substantial BMPC engraftment showing cardiogenic differentiation, in a pattern inversely correlated to that of extravascular erythrocytes and ROS in aneurysm-prone areas. These data suggest that ventricular rupture is likely to occur in regions where BMPC cannot perform their maintenance and/or repairing activity, due to the damaging effects of ROS occurring from passive 'reperfusion' of myocardium by percolated erythrocytes.

3:00 p.m.

1010-48 Role of Antiretroviral Therapy and HIV Infection in Atherosclerosis

Priscilla Y. Hsue, Peter W. Hunt, Jeffrey N. Martin, Amanda Schnell, S. Craig Kalapus, Steven G. Deeks, University of California, San Francisco, San Francisco, CA, San Francisco General Hospital, San Francisco, CA

Background: HIV patients are at higher risk for atherosclerosis. In order to define the pathogenesis of HIV-associated atherosclerosis, we studied carotid intima-media thickness (IMT) in a unique group of HIV-infected patients able to fully control HIV replication in the absence of therapy ("HIV controllers"). These patients were compared to treated patients both with and without detectable viral loads, and to controls.
Methods: We measured carotid IMT by high resolution ultrasound in 363 HIV patients and 92 controls. HIV patients were stratified based on treatment and viral load. We adjusted for traditional risk factors and HIV characteristics. The primary outcome was mean maximal IMT of 12 pre-selected segments.
Results: The median age was 47 years (IQR: 41-53); 84% were male. The median IMT was higher in each of the four HIV infected sub-groups compared to controls (see table); these differences remained significant after controlling for traditional risk factors. Increasing duration of protease inhibitor use was associated higher carotid IMT (Spearman's rho: 0.21, $p<0.001$).
Conclusions: After adjustment for traditional risk factors, both HIV infection and duration of exposure to protease inhibitors were independently associated with higher levels of subclinical atherosclerosis. The treatment-independent effect of HIV infection on IMT appeared to be due to factors other than HIV replication or advanced immunodeficiency, as evidenced by high IMT in our HIV controllers.

Median IMT in HIV Groups and Controls		
	Median IMT (mm)	P value (for each HIV subgroup compared to controls)
Uninfected (n=92)	0.72	
HIV+, ART-, VL<75 (n=24)	0.89	<0.001
HIV+, ART-, VL>75 (n=91)	0.82	<0.001
HIV+, ART+, VL<75 (n=180)	0.96	<0.001
HIV+, ART+, VL>75 (n=68)	0.90	<0.001

3:00 p.m.

1010-49 Increased Monocytic Expression of Urokinase Receptor in Acute Coronary Syndrome

Wei Chen, Wen Ling Zhu, Shu Yang Zhang, Lian Feng Chen, Xuan Wang, Tai Bo Chen, Zhen Yu Liu, Hong Zhi Xie, Quan Fang, Peking Union Medical College Hospital,Chinese Academy of Medical Sciences, Beijing, People's Republic of China

Background:Studies have suggested that urokinase receptor (uPAR) is highly expressed in atheromatous plaques and plays a crucial role in inflammation by modulating cell migration and matrix degradation. We hypothesized that uPAR is also increased in the circulating monocytes of patients with acute coronary syndrome (ACS) compared to patients with chronic stable angina (CSA) and may be a marker of clinical instability.
Methods:Consecutive angina patients were prospectively assessed including 157 ACS (58 ST elevation myocardial infarction, 26 non-ST elevation myocardial infarction, 73 unstable angina) and 43 CSA. The percentage of uPAR positive monocytes and the mean

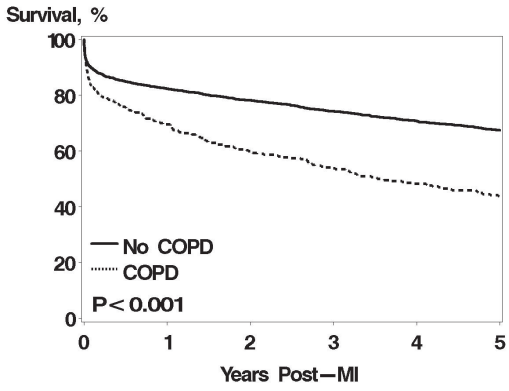
fluorescence intensity index (MFI Index) of uPAR were measured by flow cytometer.
Results:The percentage of uPAR positive monocytes was significantly higher in patients with ACS (49.03±31.73)% than in patients with CSA (12.15±14.02) %, p<0.001. Within ACS subgroups, monocytic uPAR expression peaked at 59.13% in ST elevation myocardial infarction, and was elevated to 57.24% and 39.06% in non-ST elevation myocardial infarction and unstable angina, respectively. uPAR MFI Index was increased from 1.99 of CSA to 4.48 of ACS,p<0.01. Age, body mass index, high sensitive C reactive protein and plasma cholesterol concentrations did not correlate with uPAR positive percentage and MFI Index.
Conclusions: Increased uPAR in circulating monocytes was documented in patients with ACS. These findings suggest a potential role of increased uPAR as a marker of monocyte activity and atheromatous vulnerability.

3:00 p.m.

1010-50 Myocardial Infarction and Chronic Obstructive Pulmonary Disease in the Community

Francesca Bursi, Robert Vassallo, Susan Weston, Jill Killian, Veronique Roger, Mayo Clinic, Rochester, MN

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: 3259 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% 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 (44%, 95% CI 39%-49%) compared to those without COPD (68%, 95% CI 66%-69%), p<0.01 (figure). After adjusting 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).
Conclusions: 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.



3:00 p.m.

1010-51 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. Pearte, Vankelpuran S. Srinivas, 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, 2201 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 akinesis / dyskinesis of the infarct zone. Severe inducible ischemia was an exclusion criterion for OAT. We compared outcomes based on performance and results of stress testing.
Results: 598 (27%) pts (297 PCI, 301 MED) underwent stress testing. Radionuclide imaging or stress echocardiography was performed in 40%. Pts who had stress testing were younger with higher ejection fractions, and had lower rates of death (7.8% vs. 13.2%), Class IV CHF (2.4% vs. 5.5%), and the primary endpoint (13.9% vs. 18.9%) than pts without stress testing (all p<0.01). Mild-moderate ischemia was observed in 40% of pts with stress testing, and was not related to outcomes.

5-year event rate	Inducible Ischemia (N=240)	No Inducible Ischemia (N=358)	P value Ischemia vs. No Ischemia	P value Interaction with PCI vs. MED
Death, MI or Class IV CHF	14.8%	13.1%	0.67	0.93
Death	6.8%	8.5%	0.48	0.28
Nonfatal MI	8.1%	5.9%	0.47	0.84
Class IV CHF	1.8%	2.7%	0.48	0.47

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.

3:00 p.m.

1010-52 Plasma Adiponectin and Resistin Levels as Predictors of Mortality in Patients with Acute Myocardial Infarction

Sang Hak Lee, Jung-Sun Kim, Eui Young Choi, Sungha Park, Seok-Min Kang, Donghoon Choi, Jong-Won Ha, Yangsoo Jang, Namsik Chung, Yonsei Cardiovascular Center, Seoul, South Korea

Background: Adiponectin and resistin are adipocyte-derived cytokine and related to insulin resistance, inflammation and development of vascular disease. Prior reports showed that they are correlated to cardiovascular event in healthy or low-risk population. However, their prognostic importance in acute myocardial infarction (MI) is unclear. The purpose of this study was to determine the predictive value of adiponectin and resistin in patients with acute MI.
Methods: Adiponectin and resistin were measured in 397 consecutive patients (age: 62 ± 12 years, male: 72%) with acute MI who were enrolled in Infarction Prognosis Study. The patients were then followed up prospectively for the occurrence of all-cause mortality. Potential determinants of mortality were identified by univariate and multivariate analyses with Cox regression model.
Results: Twenty-eight patients (7.1%) died during the follow up (12 ± 7 months). The survival rates for patients with the lower, middle, and upper tertile of plasma adiponectin level were 98, 94, and 87% (p=0.002 by log rank test), while those of plasma each tertile of resistin level were 94, 98, and 87% (p=0.002 by log rank test). Age, history of hypertension, mode of treatment, left ventricular systolic dysfunction, fasting plasma glucose level, plasma adiponectin and resistin levels were significantly associated with mortality in univariate analyses. Multivariate regression analyses identified three independent variables that were predictive of mortality: hypertension (OR=2.75, CI: 1.08-6.95, p=0.03), adiponectin (OR=7.40, CI: 1.69-32.3, p=0.01), resistin (OR=2.45, CI: 0.95-6.34, p=0.02).
Conclusions: In patients with acute MI, plasma adiponectin and resistin levels are predictive of mortality, independent of other risk factors. In particular, high adiponectin level showed positive correlation to mortality in this population.

3:00 p.m.

1010-53 Adaptive Remodeling of Culprit Artery Following Sirolimus Eluting Stent Implantation in Acute Myocardial Infarction: Its Effect on Late Stent Malapposition

Mitsunori Harada, Soichiro Kumagai, Shinji Mokuno, Atsushi Tanaka, Shinji Kamiya, Takayuki Saito, Yuji Yamanaka, Toshihiro Obayashi, 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:** We investigated preinterventional IVUS images of 40 consecutive patients with AMI who underwent IVUS-guided SES implantation (stent to artery ratio>1.1). 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 / mean 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 to 9.5±2.4mm², p=NS). Both 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.

3:00 p.m.

1010-54 Comparison of Clopidogrel Responsiveness between Chronic Renal Failure Patients and Normal Renal Function Subjects Using VerifyNowTM 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, 67±9 years) and 37 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 groups using VerifyNowTM P2Y12 Assay.
RESULTS: There were no significant PRU difference between each three groups (239±87 PRU in group 1, 307±86PRU in group 2, 302±95 PRU 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=0.003) and 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 plavix 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.

3:00 p.m.

1010-55 Timing of Coronary Artery Bypass Grafting Following Non-ST-Elevation Acute Coronary Syndrome and Mortality

Marc W. Deyell, 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 NSTACS and short and long-term mortality. Methods: The cohort consisted of all patients who underwent isolated CABG within 60 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 (APPROACH) 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 (48.6%) 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.

3:00 p.m.

1010-56 High Sensitivity C-Reactive Protein is an Independed Predictor of Coronary Events in Emergency Department Patients With Chest Pain

Michael P. Chrissoheris, Hanna B. Slim, Joyce Oen-Hsiao, Costin Ionescu, Amir F. Mohani, Ronan Ali, Amenuve Bekui, Thomas J. Donohue, Andre Ghantous, Hospital of Saint Raphael, New Haven, CT

Background: High sensitivity C-reactive protein (hs-CRP) is a marker of coronary events in patients presenting with acute coronary syndromes. It is not known if hs-CRP can predict subsequent coronary events in low risk patients with chest pain presenting to the Emergency Department (ED).
Methods: 296 Consecutive patients presenting to the ED with chest pain and admitted for observation were enrolled. In addition to standard clinical evaluation, a single measurment of hs-CRP level was performed. Patients with hsCRP≥10mg/l ("non-cardiac" range) were excluded. Primary end-point was the combined events of myocardial infarction, revascularization and cardiovascular death during index admission and out to 30-days post discharge.
Results: Sixty one patients reached the primary endpoint

Variables	No Event (N=235)	Event (=61)	p-value
Age (mean yrs)	60	66	0.0004
Gender (%male)	48.3	68.8	0.005
Smoking (current or past, %)	56.03	77.59	0.0008
Hypertension (%)	72.2	86.8	0.018
Statin use	42.8	60.6	0.013
Known CAD (%)	34.18	62.3	0.00001
hsCRP <1mg/l	75 (26.8%)	12 (19.6%)	0.038
hsCRP 1-3mg/l	75 (31.9%)	16 (26.2%)	
hsCRP >3 <10mg/l	85 (36.1%)	33 (54.1%)	
TIMI score	1.6	2.8	0.00001

Multiple logistic regression showed that an hs-CRP level in the highest tertile was an independed predictor for the development of the primary end-point, with an odds ratio of 2.7 (1.1-6.6 p=0.023).
Conclusions: Among presumed low risk patients presenting to an ED with chest pain, a single measurment of hs-CRP independedly predicted the presence of unstable coronary disease.

3:00 p.m.

1010-57 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

Yoritaka Otsuka, Nobuaki Kokubu, Takuya Taniguchi, Nobuhito Yagi, Yoichiro Kasahara, Yu Kataoka, Mitsuru Abe, Yuji Yasuga, Atsushi Kawamura, Hiroyuki Yokoyama, Yoichi Goto, Hiroshi Nonogi, Hitonobu Tomoike, National Cardiovascular Center, Suita, Japan

Background: The longevity of the Japanese women is world' 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.

3:00 p.m.

1010-58 Revascularization but not early invasive management is associated with a good prognosis in patients with non-ST-segment elevation acute coronary syndrome

Alexander Hirsch, Fons Windhausen, Jan G.P. Tijssen, Anthonius J.M. Oude Ophuis, P. Marc van der Zee, Jan Hein Cornel, Freek W.A. Verheugt, Robbert J. de Winter, on behalf of the ICTUS investigators, Academic Medical Center, Amsterdam, The Netherlands

Background In several observational studies revascularization was associated with a substantial reduction in mortality in patients with non-ST-elevation acute coronary syndrome (NSTE ACS). These results have strengthened the belief that routine early angiography and revascularization leads to a reduction in mortality.
Objective To investigate the association between actual in-hospital revascularization and long-term outcome in patients with NSTE ACS included in the ICTUS trial and to compare these results to the outcomes of randomized treatment strategies.
Methods In the ICTUS trial 1200 patients with NSTE ACS and an elevated troponin T were randomized to an early invasive or selective invasive strategy. For this analysis the outcome measures were death from hospital discharge until 4-year follow-up and death or spontaneous myocardial infarction (MI) until 3 years among patients who were revascularized during hospital admission compared to non-revascularized patients.
Results Among the 1189 patients discharged alive, 58% patients underwent revascularization during initial hospitalization. Mortality after 4 years was 4.8% in revascularized patients and 10.0% in non-revascularized patients. The cumulative event rates for death or MI at 3 years were 7.7% and 15.1% respectively. In multivariate Cox regression analyses, in-hospital revascularization was independently associated with a reduction in 4-year mortality and 3-year event rate of death or MI (HR 0.60; 95% CI 0.37-0.96 and 0.45; 0.31-0.66). However, when intention-to-treat analysis was performed, no differences in event rates were observed between the early invasive and selective invasive strategy; 7.0% vs. 6.9% for death at 4 years (HR 1.10; 0.70-1.74) and 12.6% vs. 8.9% for death or MI at 3 years (HR 1.27; 0.88-1.85).

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.

1010-59 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 Cudilo, 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 treating 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 < vs. >6 (p = 0.939) or <12 vs. >12 (p = 0.986) 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.

1010-60 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 Cudilo, Phyllis Sanderson, Neil S. Freund, James M. Galloway, University of Arizona, Tucson, AZ

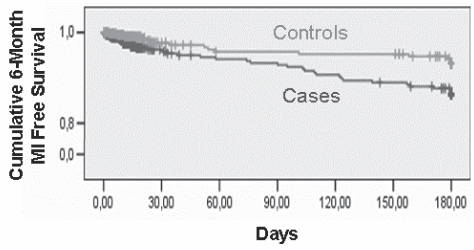
Background: National database studies have reported a significant but minor delay in presentation of Native American (NA) patients with acute myocardial infarction (AMI). The Native American Cardiology Program (NACP) experience is a strong clinical impression of a markedly greater delay in rural NA patients.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

1010-61 Reduced Benefit of Delayed Coronary Artery Bypass Graft Surgery in Acute Coronary Syndromes

Jorge M.S Ferreira, Carlos Aguiar, Ana Almeida, Jose Santos, Luis Santos, On Behalf of Investigators of Portuguese Registryof ACS, Hospital Santa Cruz, Carnaxide, 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 coronariography 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 unselected 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 prospectivelly 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 (3.9% 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.

1010-62 Impact of the Degree of Platelet Function on Thrombin Generation Profiles in Patients with Type 2 Diabetes Mellitus

Dominick J. Angiolillo, Bhaloo Desai, Yoshie Suzuki, Liudmila Rozum, Ronald Charlton, Steven B. Shoemaker, 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 reactivity is associated with thrombotic risk. Activated platelets not only lead to 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 thombin 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.

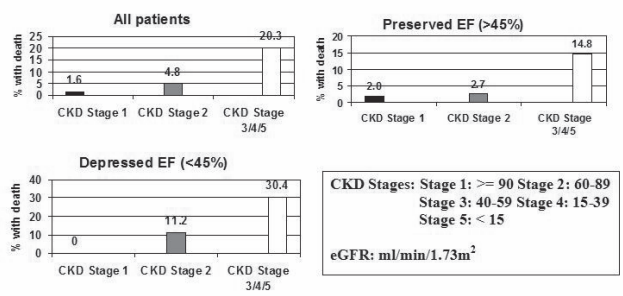
3:00 p.m.

1010-63 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

Rudyney Azevedo, José Marconi de Souza, Marcos D. Ferreira, Aurelia Mussi, Edson Stefanini, 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 (±13.1) years, admitted to the CCU of a University Hospital from January 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

used to calculate the estimated glomerular filtration rate.Patients were classified into CKD stages based on eGFR (tab). Multivariable stepwise Cox analysis was performed.
Results Of 613 patients, 68 (11.0%) had in-hospital death during index MI. Of these, 32 (47.0%) had preserved EF and 36 (52.9%) had depressed EF. CKD was associated with older age, female gender, diabetes, hypertension, and history of CHF. Prevalence of death was higher with increasing CKD Stage (tab). In a logistic regression model eGFR was independently correlated with in-hospital death.
Conclusions The renal impairment in a real world situation is a significant early independent risk factor for death among patients whom had a myocardial infarction with or without left ventricular systolic dysfunction.



3:00 p.m.

1010-64 **The Impact of Inflammatory Status on the Release of sCD40L in Coronary Atherosclerosis: Evidence for a Critical Role of the Underlying Disease State**

Dimitris Tousoulis, Charalambos Antoniades, Aggeliki Nikolopoulou, Katerina Koniari, Carmen Vasiliadou, Nikolas Koumallos, Kiriakoula Marinou, Gerasimos Siasos, Gerasimos Siasos, Costas Tsioufis, Christodoulos Stefanadis, 1st Cardiology Department, Hippokration Hospital, Athens Medical School, Athens, Greece

Background: The soluble form of CD40-ligand is released from activated platelets during the acute phase of myocardial infarction (AMI). Although sCD40L is considered to be part of the physiological immune response, the mechanisms regulating its release in different disease states remain unknown.
Methods: This study enrolled 596 subjects: 201 pts with stable coronary artery disease (CAD), 109 pts with AMI (recruited by their admission to the hospital) and 286 healthy controls. Circulating sCD40L, interleukin 6 (IL-6), vascular cells adhesion molecules (sVCAM-1) and intercellular adhesion molecules (sICAM-1) were measured
Results: Patients with AMI had significantly higher levels of sCD40L (18.8±1.2 ng/ml) and IL-6 (9.1±0.5pg/ml) compared to CAD (7.0±0.5 ng/ml and 5.0±0.4pg/ml $p<0.01$ for both) or controls (4.6±0.2ng/ml and 2.1±2.3pg/ml $p<0.01$ for both vs CAD or AMI). Similarly, SICAM-1 and sVCAM-1 levels were higher in CAD (316±8 and 753±39 ng/ml) and AMI (360±18 and 806±52 ng/ml) compared to controls (287±6.5 and 631±270 ng/ml, $p<0.05$ for both vs CAD and AMI). IL-6 was the only independent predictor of sCD40L in healthy individuals (β(SE):0.491(0.096), p=0.0001). However, in CAD or AMI, only diabetes mellitus (β(SE):2.689(1.082), p=0.044 and β(SE):10.406(3.215), p=0.002 respectively) and smoking (β(SE):3.470(1.111), p=0.002 and β(SE):9.694(2.478), p=0.0001 respectively) (but not IL-6), were independently associated with sCD40L.
Conclusions: IL-6 is an independent predictor of sCD40L levels in healthy individuals. However, diabetes mellitus and smoking (but not IL-6 or adhesion molecules) are the only independent predictors of sCD40L levels in CAD and AMI patients. These findings suggest that the complex interaction between proinflammatory cytokines and sCD40L release is largely dependent on the underlying disease state.

3:00 p.m.

1010-65 **Sex-Based Differences in Mortality Following Acute Coronary Syndromes**

Jeffrey S. Berger, Dianne Gallup, Matthew Roe, Paul W. Armstrong, R John Simes, Harvey D. White, Frans Van de Werf, Eric J. Topol, Christopher B. Granger, Robert A. Harington, Robert M. Califf, Richard C. Becker, Pamela S. Douglas, Duke Clinical Research Institute, Durham, NC

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 38,048 (28%) were women. There were 102,004 (26% women) with ST-segment elevation myocardial infarction [STEMI], 14,466 (29% women) with non-STEMI [NSTEMI], and 19,777 (40% women) with unstable angina [UA]). After multivariable adjustment with previously validated STEMI and NSTEMI/UA mortality models, we compared 30-day mortality of women versus men (C-index=0.81).
Results: The overall mortality at 30 days was 9.6% among women and 5.3% among men ($P<0.01$). After multivariable adjustment women still had significantly increased risk of death (OR 1.26, 95% CI 1.20-1.33). Importantly a significant interaction existed between sex and type of ACS ($P<0.001$). A clear gradient existed such that in STEMI patients, 30-day mortality was significantly higher in women compared to men (12.3% vs 5.3%; adjusted OR 1.36, 95% CI 1.28-1.43), yet in patients with NSTEMI, no significant difference in mortality was found (6.4% vs 4.3%; adjusted OR 0.89, 95% CI 0.74-1.07). By contrast, in unstable angina, women had a significantly lower 30-day mortality rate than men (2.4% vs 2.8%; adjusted OR 0.64, 95% CI 0.51-0.80).
Conclusions: Sex-based differences in 30-day mortality rates exist in ACS but have a striking variation depending on which syndrome is present. Whereas STEMI conferred an increased risk in women, no significant difference was noted in NSTEMI, and UA actually conferred a lower risk of death. Appreciating these differences and understanding their pathophysiology may lead to both better management and improved overall prognosis.

3:00 p.m.

1010-66 **Comparison of Infarct Size and Cardiac Function in Patients With and Without Diabetes Mellitus After Primary Percutaneous Coronary Intervention for Acute Myocardial Infarction**

Stanley Chia, O. Christopher Raffel, Faisal Merchant, Fred Senatore, Ik-Kyung Jang, EVOLVE Investigators, Massachusetts General Hospital, Boston, MA

Background: Patients with diabetes mellitus have worse clinical outcomes compared to non-diabetics after primary percutaneous coronary intervention (PCI) for acute ST-elevation myocardial infarction (STEMI). Whether the poor prognosis is directly related to differences in infarct size and cardiac function is unknown. We investigated the impact of diabetes mellitus on infarct size and left ventricular ejection fraction (LVEF) after primary PCI.
Methods: We evaluated 387 patients (69 diabetic: 318 non-diabetic) from the EVOLVE (EValuation Of MCC-135 for Left VEntricular Salvage in Acute Myocardial Infarction) study, a randomized double blind, placebo-controlled trial comparing the efficacy of intracellular calcium modulator as an adjunct to primary PCI in patients with first STEMI. Infarct size and left ventricular ejection fraction (LVEF) were assessed after 5 and 30 days using single-photon emission computed tomography.
Results: Diabetic patients (11 type I; 58 type II) were more often female (33 vs 20%), hypertensive (65 vs 44%), dyslipidemic (49 vs 32%) and had higher BMI (30 vs 28 kg/m2; all $P<0.05$) compared to non-diabetics. There were no differences between those with or without diabetes with regard to distribution of infarct-related artery, post-procedural Thrombolysis In Myocardial Infarction (TIMI) flow grades 3 (83 vs 86%) or corrected TIMI frame counts. Compared to non-diabetics, patients with diabetes had significantly larger infarct size when assessed 5 days post-PCI (median: 10 vs 6%, P=0.004). At 30 days, LVEF was also worse in diabetic patients (50 vs 53%, $P<0.05$). In a subgroup of patients who had Tc-99m sestamibi injected prior to reperfusion (10 diabetic: 82 non-diabetic), the estimated myocardial salvage post-PCI did not differ between the two groups.
Conclusion: Although diabetic patients have similar high rates of TIMI flow grade 3 after primary PCI compared to non-diabetics, they were more likely to have larger infarct size as well as reduced LVEF. The differences in myocardial infarct size and cardiac function despite successful primary PCI in diabetic patients may contribute to worse long-term outcomes.

3:00 p.m.

1010-67 **Predictors of Benefit Using an Early Invasive Strategy in the Management of Unstable Angina/Non ST-Elevation Myocardial Infarction**

Jayanta Das, George A. Diamond, Shervin Eshaghian, Sameer Amin, Prediman K. Shah, Sanjay Kaul, Cedars Sinai Medical Center, Los Angeles, CA

Background: The 2007 AHA/ACC treatment guidelines recommend early invasive (EI) management of unstable angina (UA)/non-ST-elevation myocardial infarction (NSTEMI), in patients with high-risk features.
Objective: To identify key correlates of clinical benefit associated with EI strategy.
Methods: Regression analyses were performed to assess association of 5 variables (see table) with outcomes in 8 trials - TIMI IIIB, MATE, FRISC II, TACTICS-TIMI 18, VINO, RITA 3, and ICTUS (N=9,640). Analyses with and without VANQWISH were performed given its outlier status. Strength of the association was determined by r2 (the square of the correlation coefficient) and statistical significance adjudged at $P<0.05$.
Results: A statistically significant association between treatment benefit and baseline mortality in the control arm was seen. A modest, but nonsignificant, association was observed regarding difference in between-group revascularization rate. Time to angiography, frequency of cardiac biomarker elevation, and ST segment depression exhibited no effect on treatment benefit. Similar trends, albeit weaker associations, were observed with inclusion of VANQWISH.
Conclusions: The strongest predictors of benefit with early invasive strategy were control group mortality and difference in revascularization rate. Treatment decisions should be based on a global assessment of patient risk (as afforded by TIMI, PURSUIT or GRACE risk scores) rather than a single biomarker determination or admission ECG.

	8 trials (- VANQWISH)		9 trials (+ VANQWISH)	
Variable	**r^2**	**P value**	**r^2**	**P value**
Mortality in control group	0.83	0.002	0.23	0.19
Difference in revascularization	0.31	0.150	0.39	0.06
Time to angiography	0.04	0.610	0.06	0.53
Biomarker elevation (troponin)	0.02	0.768	0.06	0.55
ST segment depression	0.07	0.570	0.07	0.52

3:00 p.m.

1010-68 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

Raffaele Bugiardini, 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 6-month period in 11 adjacent hospitals 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 (55.2% vs 77.0%, p <0.001), statins (71.1% vs 92.8%, p <0.001) and ACE-inhibitors (58.8% 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: 0.31-0.55); statins: OR 0.43 (95% CI 0.33- 0.58); ACE-inhibitor: OR 0.46 (95% CI 0.35-0.60)].
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. Simplistically, aggressive medical treatment must be applied more consistently to patients identifiable by the active clinical decision not to investigate with cardiac catheterization.

3:00 p.m.

1010-69 Genetic Polymorphisms and the Cardiovascular Risk of Cyclooxygenase-2 Inhibitors

Christine St.Germaine, James Hanley, Peter Bogaty, Luce 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 interest identified by literature review. Strictly adjudicated phenotypes and a detailed drug history, including exposure to COX-2 inhibitors, were available for all patients. We identified 115 exposed patients who reported treatment with rofecoxib (n=43), celecoxib (n=49), or another NSAID (n=23) within 10 days prior to hospital admission and selected 345 unexposed subjects matched for age, sex and hospital center. P-values were not adjusted for multiple testing.
Results We observed statistically significant gene-drug interactions between NSAID exposure and 16 SNPs. Furthermore, when 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 (COR=3.6; 95% confidence interval [CI], 1.6 - 6.7.9; P=0.001) as well as two SNPs in the cyclooxygenase-1 (COX-1) gene (COR=6.9; 95% CI, 1.4 - 35.7; P=0.02 and COR=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=0.002).
Conclusions Genetic polymorphisms within the COX-1, CRP and Klotho genes are candidates for gene-drug interactions influencing the cardiovascular outcomes of users of NSAIDs and COX-2 inhibitors. These findings suggest that genetic susceptibility may contribute to coronary instability in some users of this class of drugs.

3:00 p.m.

1010-70 Short-Term Prognostic Implications of Electrocardiographic Versus Echocardiographic Left Ventricular Hypertrophy in Patients With a First Non-ST-Elevation Acute Myocardial Infarction

Jose A. Barrabes, Jaume Figueras, Josefa Cortadellas, Rosa M. Lidon, Sonia Ibars, Hospital Universitari Vall d'Hebron, Barcelona, Spain

Background: Left ventricular hypertrophy (LVH) has adverse prognostic implications in patients with acute myocardial infarction (AMI), yet its definition varies. In 453 consecutive patients with a first non-ST elevation AMI, we assessed the value of three different criteria for LVH on the admission ECG in predicting in-hospital complications and, in 296 of them, the prognostic information added by echocardiographic LVH.
Methods: LVH was defined as Sokolow-Lyon voltage ≥3.5 mV, a Cornell voltage of 2.8 mV, a Cornell product >244 μV·s, or as an LV mass index (g/m2, corrected ASE formula) >150 in men or >120 in women.
Results: The percentage of patients having LVH was 5% by Sokolow-Lyon, 5% by Cornell voltage and 6% by Cornell product, 10% met either of these criteria and 24% had echocardiographic LVH. Taking echocardiography as a reference, sensitivity for detection of LVH increased from 13 to 26% by combining the ECG criteria. There was a poor agreement (kappa <0.2) between these criteria or between electrocardiographic and echocardiographic LVH. Rates or complications were as follows: death, 6%, reinfarction, 4%, angina, 16%, and severe heart failure, 12%. LVH tended to be related to in-hospital death (11 vs. 5% in patients meeting or not the Cornell product criterion, respectively, P=NS), was not associated with recurrent ischemic events (18 vs. 18%, P=NS) and was closely related to heart failure occurrence (36 vs. 10%, P<0.001), with the strongest association found for the Cornell product criterion. This association persisted after adjusting for the baseline clinical predictors (odds ratio 3.4, 95% CI 1.4-8.4) and the prediction was not further improved by considering echocardiographic LVH. Compared to the remaining patients, those with LVH had a similar CK-MB peak (109±25 vs. 133±8 ng/ml, P=NS) and similar prevalence of multivessel disease (45 vs. 40%, P=NS).
Conclusions: The adverse short-term implications of LVH in patients with non-ST elevation AMI are related to a higher risk of heart failure but not to more ischemic events. Agreement between ECG and echocardiographic LVH is poor, but the latter does not seem to have an incremental value over electrocardiographic LVH in predicting complications.

3:00 p.m.

1010-71 Does an Early Invasive Strategy in NSTEMI Management Result in Long-Term Benefit?

Jayanta Das, George A. Diamond, Shervin Eshaghian, Sameer Amin, Prediman K. Shah, Sanjay Kaul, Cedars Sinai Medical Center, Los Angeles, CA

Background: Two prior meta-analyses have yielded a significant advantage for early invasive (EI) compared to selective invasive (SI) management for acute coronary syndromes (ACS), at a mean follow-up of 17 to 24 months.
Objective: To determine whether the benefits of EI strategy are sustained beyond 2 years.
Methods: We examined 9 studies with short-term (6-21m) and 3 studies with long-term (3-5y) follow-up. A random-effects meta-analysis was used to derive risk ratios (RR) for death, nonfatal MI (NF MI) and composite of death or MI. Posterior probabilities (Pr) that relative risk difference in outcomes is greater than a threshold value for clinical importance (d>5%, 10%, 15%, 20%) were derived from Bayesian analysis using an uninformative prior (mean =0, SD = 10) and empirical evidence. Heterogeneity was assessed using Cochran's Q (P<0.1) and I2 (>50%).
Results: At 6-21m, EI strategy was associated with significant benefit in nonfatal MI but not in other outcomes. The Pr of benefit in nonfatal MI ranged from 97% (d>5%) to 44% (d>20%). At 3-5 years, no significant advantage was seen in any outcome with EI strategy, and the Pr of benefit in nonfatal MI ranged from 26% (d>5%) to 14% (d>20%). Significant heterogeneity was observed in outcomes at both time points.
Conclusions: Evidentiary support for EI strategy for ACS is modest at short-term and does not appear to be sustained long-term. Given the increased cost and the attendant complications, more data are warranted to elucidate optimal indications for EI strategy for ACS.

Endpoint (# of studies)	Sample Size	Risk Ratio (95% CI)	P value	Hetero P value*	I^2 Statistic	Pr d>5%	Pr d>10%	Pr d>15%	Pr d>20%
Follow-up (6-21m)									
Death (N=9)	10,560	0.94 (0.71-1.24)	0.67	0.05	49%	53%	38%	24%	13%
NF MI (N=8)	9,360	0.81 (0.7-0.94)	0.01	0.63	0%	97%	90%	72%	44%
Death or MI (N=8)	9,360	0.86 (0.7-1.05)	0.14	0.01	61%	84%	67%	45%	24%
Follow-up (3-5 years)									
Death (N=3)	5,444	0.92 (0.75-1.12)	0.38	0.24	30%	63%	41%	20%	7%
NF MI (N=2)	3,010	1.2 (0.59-2.44)	0.62	<0.01	88%	26%	22%	17%	14%
Death or MI (N=3)	5,205	0.99 (0.69-1.42)	0.96	<0.01	90%	42%	32%	22%	14%

3:00 p.m.

1010-72 Relationship between Longitudinal Morphology of Ruptured Plaques and TIMI Flow Grade in Acute Coronary Syndrome: A Three-Dimensional Intravascular Ultrasound Imaging Study

Atsushi Tanaka, Toshio Imanishi, Shigeho Takarada, Satoshi Ueno, Takashi Tanimoto, Hideyuki Ikejima, Nobuo Nakamura, Kumiko Hirata, Yu Arita, Hironori Kitabata, Akio Kuroi, Manabu Kashiwagi, Hideo Kataiwa, Hiroto Tusjioka, Takashi Kubo, Keishi Okouchi, Kazushi Takemoto, Masato Mizukoshi, Takashi Akasaka, Wakayama Medical University, Wakayama, Japan

Background: Plaque rupture plays a key role in the onset of acute coronary syndrome (ACS). However, there have been few in vivo studies that have addressed the longitudinal morphology of plaque rupture. In this study, we investigated the relationship between longitudinal morphology reconstructed from pre-intervention intravascular ultrasound (IVUS) images and TIMI flow grade at initial angiograms in the acute phase of ACS.
Methods: Our patient population comprised 72 ACS patients in whom we obtained successful reconstructed longitudinal images. Based on the site of the maximum aperture of rupture in the longitudinally reconstructed IVUS images, patients were divided into three groups: Plaques with rupture in the proximal shoulder (proximal-type; n=28), mid

portion (mid-type; n=18), or distal shoulder (distal-type; n=26) of the plaque, respectively.
Results: There were no differences in terms of coronary risk factors or the angiographic findings. The proximal-type group more frequently showed TIMI 0 on initial angiogram (proximal-type 86%, mid-type 50%, and distal-type 31%, p=0.002). A multivariable logistic regression model revealed that the presence of a proximal-type rupture correlated with presentation of ST elevation MI (p=0.019, odds ratio 8.12, 95 % CI 1.404- 49.996).
Conclusions:Longitudinal morphological features in a ruptured plaque may affect the formation of obstructive thrombus in ACS. Our results suggest that longitudinal morphology may be an important determinant of coronary artery occlusion.

3:00 p.m.

1010-73 **Impact of Baseline Thrombolysis in Myocardial Infarction Grade on Mortality in Non-ST-Segment Elevation Myocardial Infarction Patients Treated With Early Invasive Strategy**

Young B. Song, Joo-Yong Hahn, Sang Yeub Lee, Bong Gun Song, Soo Jin Cho, Jin-Ho Choi, Seung-Hyuk Choi, Hyeon-Cheol Gwon, Sang Hoon Lee, Division of Cardiology, Cardiac and Vascular Center, Samsung Medical Center, Seoul, South Korea

Background: Baseline vessel patency is known to be associated with outcomes after primary percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction (STEMI). However, the prevalence of coronary occlusion and impact of baseline Thrombolysis In Myocardial Infarction (TIMI) grade on mortality in non-ST-segment elevation myocardial infarction (NSTEMI) is not well known.
Methods: From October 2005 to May 2007, 8,565 patients completed registration in the Korean Acute Myocardial Infarction Registry. NSTEMI was present in 3,372 patients (39.4%) and STMEI in 5,074 patients (59.2%). We evaluated an impact of baseline TIMI grade on 1-month mortality in 1,168 NSTEMI patients treated with early invasive strategy.
Results: In NSTEMI patients treated with early invasive strategy, baseline TIMI grade was as follows: grade 0 in 355 patients (30.4%); grade 1 in 153 (13.1%); grade 2 in 177 (15.2%); and grade 3 in 483 (41.4%). Baseline characteristics were not significantly different between patients with baseline TIMI grade 0 to 1 flow (group I) and those with baseline TIMI grade 2 to 3 flow (group II) except age (60 in group I versus 64 in group II, p = 0.001). Patients in group I were significantly more likely to have a left circumflex (LCx) artery culprit lesion and less likely to have left anterior descending (LAD) artery involvement compared with group II (LCx: 34.5% versus 23.0% and LAD: 34.3% versus 48.2%, p <0.001). Total mortality at 1-month was 3.3%. Patients in group I demonstrated a higher 1-month mortality than those in group II (4.7% versus 2.1%, p = 0.01). In multivariate analysis, baseline TIMI grade 0 to 1 flow was an independent predictor of 1-month mortality (OR 2.87, 95% CI 1.33 to 6.18, p = 0.006) with age (OR per 10 years 1.76, 95% CI 1.18 to 2.62, p = 0.006) and Killip class (OR 5.82, 95% CI 2.71 to 12.47, p < 0.001).
Conclusions: In NSTEMI patients treated with early invasive strategy, baseline TIMI grade is an independent predictor of 1-month mortality.

3:00 p.m.

1010-74 **Alcohol Intake and Risk of Incident Atrial Fibrillation in Women: A Prospective Cohort Study**

David Conen, Usha B. Tedrow, Julie E. Buring, Christine M. Albert, Brigham and Women's Hospital, Boston, MA

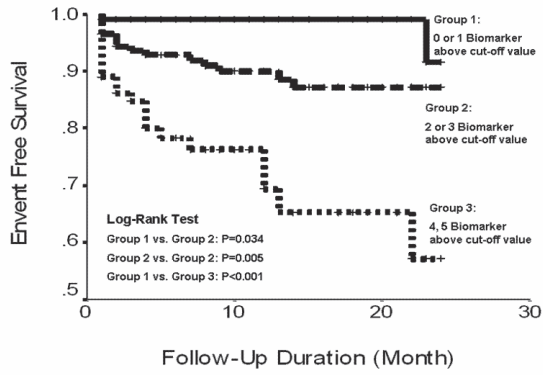
Background: Recent studies suggest that high levels of alcohol intake increase the risk of incident atrial fibrillation in men, but the relationship between more moderate levels of alcohol intake and atrial fibrillation is less clear, especially among women.
Methods: We assessed the relationship between alcohol intake and incident atrial fibrillation in a prospective cohort of 38934 women, who were free of cardiovascular disease and atrial fibrillation at study entry and who provided complete information on baseline alcohol consumption. Women were then classified into 1 of 4 categories of alcohol consumption: Non-drinkers, <1 drink per day, 1-<2 drinks per day and at least 2 drinks per day. Multivariable Cox proportional hazards models were constructed to evaluate the independent relationship between categories of alcohol intake and the risk of incident atrial fibrillation.
Results: Mean ± SD age and body mass index were 55 ± 7 years and 26 ± 5 kg/m2, respectively. During a median follow-up of 12.3 years, 1250 new cases of incident atrial fibrillation were reported. Age-adjusted incidence rates across the 4 categories of alcohol intake were 2.9, 2.6, 2.1 and 3.6 events per 1000 person-years of follow-up. Compared to non-drinking women (referent), the age-adjusted hazard ratios (95% confidence interval) for women drinking <1 drink/day, 1-<2 drinks/day and at least 2 drinks per day were 0.93 (0.83-1.04), 0.70 (0.54-0.91) and 1.28 (1.00-1.64). After adjustment for age, body mass index, systolic blood pressure, history of hypertension, smoking, diabetes, hypercholesterolemia and race, the corresponding risk estimates were 1.0 (referent), 0.97 (0.86-1.10), 0.77 (0.59-1.00) and 1.36 (1.05-1.77).
Conclusions: This prospective study provides evidence of a nonlinear relationship between alcohol consumption and risk of incident atrial fibrillation in women. While women drinking at least 2 drinks of alcohol per day have an increased risk of incident atrial fibrillation, the risk of atrial fibrillation might be reduced in women consuming moderate amounts of alcohol.

3:00 p.m.

1010-75 **Incremental Prognostic Value of Combining Inflammatory, Cardiorenal and Metabolic Biomarkers in Acute Myocardial Infarction: Data from Infarction Prognosis Study (IPS) Registry**

Jung-Sun Kim, Jong-Won Ha, Jaedeok Kim, Byung Ho Lee, Sung Ai Kim, Chansoo Kim, Sungha Park, Eui-Young Choi, Sang-Hak Lee, Sung Min Kang, Donghoon Choi, Yangsoo Jang, Namsik Chung, Division of Cardiology, Yonsei University, Seoul, South Korea

Background: Inflammatory (hsCRP and fibrinogen), cardiorenal (NT-proBNP and BUN) and metabolic biomarkers (FBS) have been known as predictors of MACE, respectively. Therefore, we sought to evaluate the incremental prognostic value of inflammatory, cardiorenal and metabolic biomarker in AMI. Methods: Three hundred thirty-five consecutive patients with AMI (242 men, 163 STEMI, mean age 63 ± 12) were prospectively enrolled in Infarction Prognosis Study (IPS) registry. Subjects were divided into 3 groups based on number of biomarkers were above each cut-off values (hsCRP: 10 mg/L, fibrinogen: 400 mg/dl, BUN: 20 mg/dl, NT-porBNP: 500 pg/ml, FBS: 110 mg/dl)(Group 1: < 2, Group 2: 2-4, Group 3: ≥ 4). Mean follow-up duration were 12 month (range, 1 to 24)
Results: Of the 335 patients, MACE (cardiac death, non-fatal MI, re-admission due to unstable angina or heart failure) was developed in 37 patients (11 %). MACE was occurred in 2 (2 %) of 118 patients of group 1, 15 (10 %) of 144 patients of group 2 and 20 (27 %) of 73 patients of group 3 (p< 0.001). Even after adjusting for the conventional risk factors [age, gender, BMI, HTN, DM, smoking, LVEF, type of AMI], group 3 had a 5.4-fold higher risk for MACE than group 1. (Group 2: HR 2.5 [95% CI 0.54-12.2], P = 0.241 and Group 3: HR 5.4 [1.09-26.5], P = 0.038).
Conclusion: Combination of inflammatory, cardiorenal and metabolic biomarkers has graded incremental effects in predicting cardiovascular events in patients with AMI, independent of conventional clinical risk factors.



3:00 p.m.

1010-76 **Impact of Diabetes Mellitus on Intravascular Ultrasound Findings in Patients with Acute Myocardial Infarction with Plaque Ruptures**

Young Joon Hong, Myung Ho Jeong, Jong Won Chung, Doo Sun Sim, Jae Youn Moon, Ju Han Kim, Hyun Ju Yoon, Jeong Gwan Cho, Jong Chun Park, Jung Chaee Kang, Chonnam National University Hospital, Gwangju, South Korea

Background:Plaque rupture and subsequent thrombus formation is the most important mechanism leading to an acute myocardial infarction (AMI). Previous pathological study showed diabetic patients had a larger content of lipid-rich atheroma and macrophage infiltration compared with nondiabetic patients. This is consistent with a greater probability of coronary plaque rupture in diabetic patients. However, data on the intravascular ultrasound (IVUS) findings in diabetic patients with AMI with plaque rupture are lacking.
Methods: The aim of this study was to assess the impact of diabetes mellitus on IVUS findings in 112 AMI patients (58 ST segment elevation and 54 non-ST segment elevation MI; 47 diabetic and 65 nondiabetic patients) with plaque ruptures. IVUS findings included ruptured plaque (a cavity that communicated with the lumen with an overlying residual fibrous cap fragment), multiple ruptured plaques (different plaque ruptures separated by a >5-mm length of artery containing smooth lumen contours), and a thrombus (discrete intraluminal filling defects).
Results: Baseline high-sensitivity C-reactive protein (4.6±4.6 mg/dl vs. 2.4±4.2 mg/dl, p=0.050) and triglyceride levels (158±84 mg/dl vs. 127±52 mg/dl, p=0.041) were significantly higher in diabetic patients compared with non-diabetic patients. Reference segment plaque burden was greater in diabetic patients compared with non-diabetic patients (37±10% vs. 31±12%, p=0.006). The presence of multiple plaque ruptures (60% vs. 29%, p=0.001) and thrombus (72% vs. 52%, p=0.032) were more common in diabetic patients compared with non-diabetic patients. Plaque cavity was significantly larger (2.6±1.6 mm2 vs. 2.2±1.2 mm2, p=0.046) and ruptured plaque length was significantly longer (3.0±1.6 mm vs. 2.5±1.3 mm, p=0.031) in diabetic patients compared with non-diabetic patients.
Conclusions: Diabetic AMI patients with IVUS-evident plaque ruptures have more plaque vulnerability (more frequent multiple plaque ruptures and more thrombus) accompanied with higher inflammatory status compared with non-diabetic AMI patients with plaque ruptures.

3:00 p.m.

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. Dundon, Luan T. Huynh, Stephen G. Worthley, 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 Syndromes 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 analysis revealed that an invasive 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<0.0001), 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, Funen Hosptal, 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, paticularly due to post-MI congestive heart failure (HF). We hypothesized that increased neurohormornal activation, expressed by elevated levels of 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 using a regional 16-segment wall motion score index (WMSI), and diastolic function using the ratio of early transmitral flow velocity to early 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 WHO criteria, categorised as having normal glucose tolerance (NGT), impaired glucose homeostasis (IGH), or newly detected DM. Patients were followed a median of 21 months (IQR: 16-28 months). Primary endpoint was death or hospitalization for heart failure.
Results: The prevalence of NGT, IGH, new DM, and known DM was 35%, 28%, 23%, and 14% respectively. Using linear regression, we found a significant linear increase in NT-proBNP levels with increasing degree of dysglycemia (Ptrend<0.001). After adjustment for age, gender, pre-existing HF, WMSI, E/e', and Killip class at admission, this association remained statistically significant (Ptrend=0.02) also after exclusion of patients with a prior history of DM (Ptrend=0.04). After adjustment for the same variables, both NT-proBNP and 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 neurohormonal activation beyond what can be explained from estimates of left ventricular dysfunction and clinical 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 orma OULDZEIN, Jr., Remy CAGNAC, Jr., Jerome Roncalli, Sr., Didier CARRIE, 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 (% 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 3 days after ACS, before any interventional procedure. A plaque rupture was recognized 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 and arterial remodeling index. Patients were divided into two 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 (49.8% ± 12.3 vs 39.8% ± 12.1, p<0.0005), 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 5.6 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.

1010-80 **Genetic Variability Of Platelet Glycoprotein Ia Determined The Release Of Soluble CD40-Ligand And P Selectin During Myocardial Infarction**

Charalambos Antoniades, Dimitris Tousoulis, Carmen Vasiliadou, Kyriakoula Marinou, George Latsios, Nikolas Koumallos, Elli Stefanadi, Kostas Toutouzas, Gerasimos Siasos, Nikos Papageorgiou, Christodoulos Stefanadis, University of Athens, Athens, Greece

Background: Platelet glycoprotein Ia (GPIa) mediates platelet adhesion to collagen, a major step in platelets activation during the acute phase of myocardial infarction (MI). Activated platelets release the soluble forms of CD40-ligand (sCD40L) and P-selectin (P-Sel). We investigated the role of genetic polymorphisms C807T and G1648A on GPIa gene, on the risk for MI and the release of sCD40L and sP-sel during the acute phase of MI and one year after the event.
Methods: The study population consisted of 630 young subjects (aged 49.0±3.0 years): 219 pts with premature MI and 411 controls. A sub-population of 67 pts and 232 matched controls was followed-up prospectively for 1 year. Distribution of C807T and G1648A were determined by PCR, and plasma sCD40L and P-Sel by ELISA.
Results: The genotypes distribution were for 807TT/CT/CC: 34/112/73 in pts and 33/229/149 in controls (p<0.05) and for 1648GG/AG/AA: 161/50/8 in pts and 315/84/12 in controls (p=NS). The adjusted risk for MI in 807TT was 2.301(1.189-4.540) p=0.011. During the acute phase of MI, both sCD40L and P-sel were higher in 807CT+TT (12.77±1.22pg/ml and 68.2±4.9ng/ml) compared to CC (7.12±0.93pg/ml and 39.9±3.67ng/ml respectively, p<0.01 for both). One year after the event, although sCD40L and P-sel were decreased in all genotypes, they remained higher in CT+TT (8.73±0.97pg/ml and 51.1±3.6ng/ml) compared to CC(4.35±0.93pg/ml and 37.2±2.6ng/ml respectively, p<0.01 for both). In controls, sCD40L and P-sel was not different in CC (4.19±0.48pg/ml and 31.1±3.1ng/ml respectively) compared to CT+TT (5.3±0.33pg/ml and 35.8±1.8 p=ns for both). G1648A had no effect on sCD40L and P-sel levels.
Conclusions: Genetic polymorphism C807T on platelet GPIa is a risk factor for premature MI, and it affects the release of sCD40L and P-selectin during the acute phase of MI. The effect of this genotype on sCD40L and p-sel is still present one year after the event. These findings suggest that C807T polymorphism may modify platelets activation in patients with coronary atherosclerosis, especially during the acute phase of myocardial infarction.

3:00 p.m.

1010-83 **Natural History of the Thin-Cap Fibroatheroma Assessed by Optical Coherence Tomography in vivo**

Ryotaro Yamada, Hiroyuki Okura, Teruyoshi Kume, Takahiro Kawamoto, Yoji Neishi, Eiji Toyota, Yoshinori Miyamoto, Koichiro Imai, Nozomi Watanabe, Kiyoshi Yoshida, Kawasaki Medical School, Kurashiki, Japan

Background: The precursor lesion for plaque rupture is known as thin cap fibroatheroma (TCFA). However, natural history of TCFA in vivo is still unclear. Therefore, the purpose of this study was to evaluate natural history of TCFA in vivo by using optical coherence tomography (OCT) and intravasucular ultrasound (IVUS) during 6 months follow-up.
Methods: Forty-five coronary arterial segments from 15 patients with acute coronary syndrome were examined by OCT and IVUS. TCFA and thick cap fibroatheroma were detected and followed up for 6 months. TCFA was defined as a plaque with a minimum fibrous cap thickness < 65μm by OCT and thick-cap fibroatheroma >= 65μm.
Results: Twelve TCFAs were identified in 7 patients (47 %). Among these patients, 4 (57%) had 1 TCFA, 3 (43%) had 2 TCFAs, and 1 (14%) had 3 TCFAs. Three of 12 TCFAs were treated with stenting because of significant stenosis. Six TCFAs were followed up serially by angiography and IVUS. There were no significant differences in volumetric IVUS assessment between TCFA and thick cap fibroatheroma at the initial examination. However, plaque burden of TCFA was significantly higher than that of thick cap fibroatheroma 6 month later (Table).
Conclusions: This is the first report to reveal natural history of TCFA assessed by OCT. Further large long-term investigation will be needed for a more comprehensive pathophysiologic approach towards natural history of vulnerable plaque.

	TCFA (n=6)	Thick cap fibroatheroma (n=12)	p
0 Month			
EEM CSA, mm^3/mm	13.0±5.1	13.0±4.0	ns
Lumen CSA, mm^3/mm	5.5±2.7	6.9±2.7	ns
P+M CSA, mm^3/mm	7.4±2.8	6.2±2.1	ns
Plaque burden (%)	58±9	48±9	ns
6 Months			
EEM CSA, mm^3/mm	13.8±6.1	13.1±3.4	ns
Lumen CSA, mm^3/mm	6.0±3.2	7.1±2.1	ns
P+M CSA, mm^3/mm	7.8±3.2	6.0±1.7	ns
Plaque burden (%)	57±9	46±6	0.0087
⊿ P+M CSA, mm^3/mm	0.35±1.1	-0.16±1.3	ns
%⊿P+M CSA (%)	4.7±13.3	0.7±20.3	ns

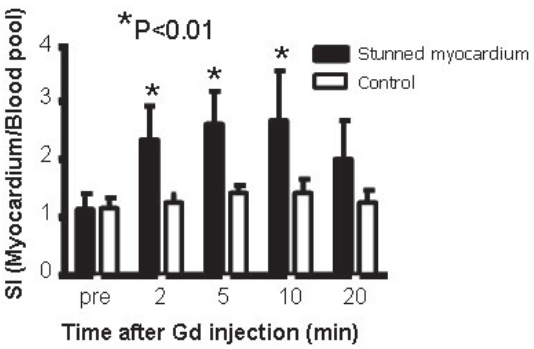
EEM=external elastic membrane, CSA=cross-sectional area
P+M=plaque plus media

3:00 p.m.

1010-84 **Early Phase of Gadolinium Enhancement and T2-weighting Imaging on Cardiac Magnetic Resonance can Detect Ischemic Stunned Myocardium**

Yoko Masukata, Teruo Noguchi, Jun Tanaka, Rika Kawakami, Hiroshi Nonogi, Yoichi Goto, Naoaki Yamada, National Cardiovascular Center, Suita, Japan

Background: Although late gadolinium-enhancement (LGE) by cardiac magnetic resonance (CMR) can visualize myocardial infarction, this technique cannot distinguish stunned myocardium (SM) from normal myocardium. To address this, we measured the signal intensity (SI) of stunned myocardium at the early phase of LGE (i.e., 2-5 min after contrast injection) and to evaluate the usefulness of T2-weighting image (T2WI). **Methods:** Cardiac cine, T2WI, and LGE were performed in 20 patients with ischemic SM and 10 age-mated controls. LGE was evaluated at 2, 5, 10, 20 minutes after contrast injection. To measure SI in myocardium, we put region of interest on the myocardium segments #1, 2, 3, 4, 5 of the American Heart Association, and on blood pool, and calculated myocardium-blood pool ratio. **Results:** In SM group, conventional LGE representing myocardial infarction was not observed. However, at the early phase LGE SM region was visualized as hyperenhancement, whereas such hyperenhancement was not observed in controls. Myocardium-blood pool ratio in SM was significantly higher than that in controls. This hyperenhancement region agreed well with the region of high signals on T2WI. Follow-up CMR demonstrated complete resolution of abnormal wall motion and disappearance of hyperenhancement at the early phase of LGE and on T2WI within one month. **Conclusion:** Stunned myocardium is visualized by the early phase of LGE and T2WI. Thus, combination of these techniques is useful to detect a reversible myocardial damage.



3:00 p.m.

1010-85 **Prehospital Wireless Transmission of STEMI Electrocardiograms to a Cardiologist Reduces Door-to-PCI Times to Less than One-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 times 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 (p <0.0001) and Self-transport (p <0.0001) groups during both the Intervention 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.

	Pre-intervention	Intervention	Follow-up
Time Period	2001-2003	2003-2005	2005-2007
Self-transport Patients			
- Number of Patients	73	94	73
- Door-to-PCI Time in minutes (median)	106	96	82
EMS Patients			
No ECG Transmission			
- Number of Patients	48	37	58
- Door-to-PCI Time in minutes (median)	101	78	65
ECG Transmission			
- Number of Patients	~	24	15
- Door-to-PCI Time in minutes (median)	~	50	39

3:00 p.m.

1010-86 **Benefits of Drug Eluting versus Bare Metal Stents in Patients with Renal Dysfunction are Independent of Target Lesion Revascularization**

Saurabh Gupta, Jeffrey L. Anderson, Bejamin D. Horne, Tami L. Bair, Heidi T. May, Joseph B. Muhlestein, Intermountain Medical Center, Murray, UT

Background: In most patient subpopulations, drug-eluting stents (DES) provide significant benefits over bare metal stents (BMS) for coronary artery restenosis and other major adverse cardiovascular events (MACE). However, the effect of DES in patients with renal dysfunction is not known.
Methods: Baseline clinical information was obtained from 2695 consecutive patients undergoing coronary artery stent deployment at LDS hospital after the availability of DES. Patients with unavailable serum creatinine values (n=48) or those receiving both DES and BMS (n=272) were excluded. In the remaining 2375, clinical characteristics and glomerular filtration rate (GFR, MDRD formula) were recorded. Patients were followed for 6 months for death, MI, and target lesion revascularization (TLR) or the composite (MACE). A GFR < 60 ml/min was designated as impaired renal function. Outcomes were stratified by GFR [≤60 ml/min (n= 632) vs. >60 ml/min (n= 1742)].
Results: Age averaged 64±12 years and 75% were male. Among those with GFR>60 ml/min, DES were superior to BMS for MACE (9.8% vs. 17.3%, p<0.001), TLR (4.8% vs. 7.0%, p=0.077), MI (4.9% vs. 7.8%, p=0.019) and death (1.6% vs. 4.4%, p=0.001). Among patients with GFR ≤60 ml/min, DES were superior to BMS for MACE (13.5% vs. 21.4%, p=0.011), TLR (4.2% vs. 8.0%, p=0.049), and MI (4.9% vs. 11.4%, p=0.003); however, no significant differences were observed for death (6.3% vs. 8.6%, p=0.29). Moreover, the rates of TLR were independent of baseline GFR for both BMS (7.0% vs. 8.0%) and DES (4.8% vs. 4.2%).
Conclusion: The benefits of DES were confirmed in a large population of patients with normal and also with impaired renal function (6-month MACE was decreased in both renal function categories). The study was not powered to specifically show improved death rates with DES among those with impaired renal function although the trend was favorable. Rates of TLR did not vary by renal insufficiency in the two stent types. These findings suggest mechanisms other than TLR may be responsible for increased adverse outcomes with BMS in impaired renal function patients. If confirmed, these results may have important clinical implications in the choice of stent type for this high-risk patient group.

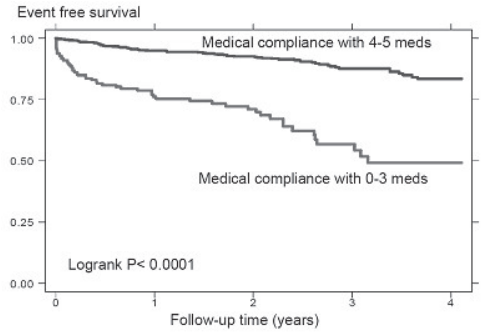
3:00 p.m.

1010-87 **Long-term compliance with guideline-based medical therapies is the strongest predictor of event-free survival following acute coronary syndromes (ACS) and myocardial infarction (MI)**

Amit P. Amin, Ekanka Mukhopadhyay, Sandeep Nathan, Sirikarn Napan, Russell F. Kelly, Rush University Medical Center, Chicago, IL, Cook County Hospital, Chicago, IL

Background: While acute medical therapies significantly improve in-hospital outcomes in patients (pts) with ACS/MI, the impact of sustained compliance with evidence-based medical therapies remains less clear.
Methods: 878 consecutive pts admitted from 2003-04 to a large academic center with high-risk ACS/MI, were followed for compliance with 5 key classes of medical therapy (aspirin, clopidogrel, statins, beta blockers and ACEI/ARB). The effect of medical compliance on the primary composite outcome, mortality and MI, was explored using Kaplan-Meier and Cox regression analyses.
Results: Of 878 pts (66% male, 54% DM), 134 (15.3%) presented with STEMI, 390 (44.4 %) with NSTEMI and 354 (40.3%) with unstable angina. 566 pts (64.5%) underwent revascularization (PCI 406 (46.3%), CABG 160 (18.2%)) and 312 (35.6%) were medically managed. Outpt follow-up was available in 92% of pts. 100 (11.4%) pts died, and 25 (2.9%) had recurrent outpt MI at median follow-up of 2.2 years. In a stepwise Cox model adjusting for risk covariates, medical compliance (per incremental therapy) was the

strongest factor associated with event-free survival (HR 0.57, P<0.0001, 95%CI 0.51-0.63). The benefit was amplified with sustained compliance with >/= 4 medical therapies (Figure 1).



Conclusions: Long-term compliance with 5 key medical therapies post-ACS is strongly and independently associated with event-free survival. The time-dependent relative contributions of each individual class are currently being investigated.

3:00 p.m.

1010-88 **Polymorphism of endothelial NOS gene promoter is associated with endothelial dysfunction, increased arterial stiffness and has negative prognostic impact after ACS**

Yaroslav M. Lutay, Sr., Viktor Dosenko, Sr., Alexander Parkhomenko, Sr., Institute of Cardiology, Kiev, Ukraine, Institute of Physiology, Kiev, Ukraine

Background: an endothelial nitric oxide synthase (eNOS) gene polymorphism (-786T>C) in promoter region has been associated with cardiovascular disease. We investigated whether carriage of the polymorphism was associated with functional changes in the endothelium, arterial stiffness and how it affected prognosis in patients with ACS.
Methods: 332 patients with ACS (142 patients without ST elevation and 190 patients with ST elevation ACS) and 83 controls were investigated. The eNOS gene polymorphism has been analyzed by PCR-RFLP (restriction fragment length polymorphism) analysis. Endothelium-dependent, flow-mediated brachial artery dilatation (FMD) was measured using high-resolution ultrasound. Carotid-femoral and carotid-radial pulse wave velocity (PWV) were measured as an index of aortic stiffness using an automated non-invasive device (Complior®)
Results: A significant difference in genotype distribution was observed between patients and controls. Pathological CC genotype was more often determined in ACS patients (16,6% vs. 6,0%, p<0,01). The multivariate analysis showed that C/C genotype in the eNOS gene promoter was associated with increased risk of recurrent ischemic events (death/ myocardial infarction) during one-year follow-up. Homozygosity for the CC variant of the eNOS gene promoter in ACS patients was associated with lower flow-mediated brachial artery dilatation (6.4±1.4% vs 9.0±0.7%, p<0.05) CC genotype carriers had significantly higher carotid-radial PWV than patients with TT genotype (9.4±0.16 vs 8.9±0.13 m/sec, p<0.05). Carotid-femoral PWV did not differ between groups.
Conclusions: CC genotype of eNOS gene promoter may predispose to the development of ACS and among ACS patients this genotype is associated with poor prognosis that can be explained by more pronounced endothelial dysfunction and increased arterial stiffness.

ACC.POSTER CONTRIBUTIONS

1017

Unstable Ischemic Syndrome--Clinical; Acute Myocardial Infraction--Therapy

Monday, March 31, 2008, 9:00 a.m.-12:30 p.m.
McCormick Place, South Hall

11:00 a.m.

1017-41 **ST Segment Deviation Resolution is an Indicator for Coronary Artery Patency Prior to Primary Percutaneous Coronary Intervention in Patients With Acute Myocardial Infarction**

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

Background: Pre-procedural Thrombolysis in Myocardial Infarction (TIMI) flow is known to be an independent predictor of long-term mortality in high-risk patients with ST Elevation Myocardial Infarction (STEMI) undergoing primary Percutaneous Coronary Intervention (PCI). We evaluated whether pre-procedural ST segment deviation Resolution (STR) adequately correlates with TIMI flow at first dye injection.
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 the12-lead ECG recorded immediately prior to PCI. TIMI flow through the culprit vessel was determined at first angiographic flim 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.

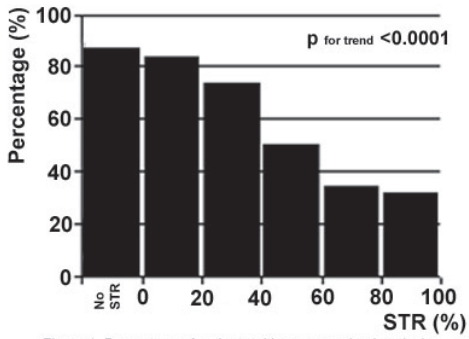


Figure 1. Percentage of patients with pre procedural occlusion as a function of degree of STR

11:00 a.m.

1017-42 **A Propensity Score Analysis of the Benefit of Upstream Platelet Glycoprotein IIb/IIIa Receptor Antagonists in Acute Coronary Syndromes - Insights From the TRACS Registry**

Amit P. Amin, Sandeep Nathan, Yasmeen Golzar, James E. Calvin, Jr., Rush University Medical Center, Chicago, IL, Cook County Hospital, Chicago, IL

Background: In patients (pts) with high-risk acute coronary syndromes (ACS) who undergo an early, invasive strategy, current guidelines recommend glycoprotein IIb/IIIa inhibitors (GPI), administered either "upstream" prior to angiography or "downstream" in the catheterization laboratory during PCI however the optimal approach remains unknown. We examined the effect of upstream GPI use via propensity score analysis in a large ACS registry.
Methods: The Registry of Acute Coronary Syndromes (TRACS) is a prospective registry of 3,468 ACS pts from 9 institutions, established to track quality of care. Pts receiving upstream GPI (in the emergency room, CCU or chest pain unit) constituted "early GPI use" group vs. cath lab use comprising the "deferred/selective" group. In-hospital death was the primary outcome variable. A propensity score predicting use of early GPI was developed from a logistic model with early GPI as the dependent variable and male gender, age ≥ 65, ST depression, TIMI score, diabetes and troponin release as independent variables.
Results: Overall, 1,376 (40%) pts received GPI of which, 294 (8.5%) received GPI in the ER, 249 (7.2%) received GPI prior to cardiac catheterization (in the CCU or chest pain unit) comprising the "early GPI use" group (n= 543, 15.7%). A propensity score predicting the use of early GPI had an ROC AUC of 0.63 and was divided into quintiles for further covariate adjustment. A simple multivariate logistic model controlling only for the propensity score quintiles showed that early GPI use was strongly associated with survival benefit (OR 0.4, p=0.013, 95% CI 0.19-0.82). A more comprehensive multivariable logistic model controlling for additional covariates like gender, diabetes, dyslipidemia, prior MI, ST depression, TIMI score, revascularization, aspirin, beta-blocker and heparin use in addition to propensity score quintiles, showed that early GPI use was independently associated with survival (OR 0.47, p=0.04, 95% CI 0.22-0.99).
Conclusions: This propensity score analysis in a large ACS registry reveals independent in-hospital mortality benefit with upstream GPI use even after adjusting for important covariates.

11:00 a.m.

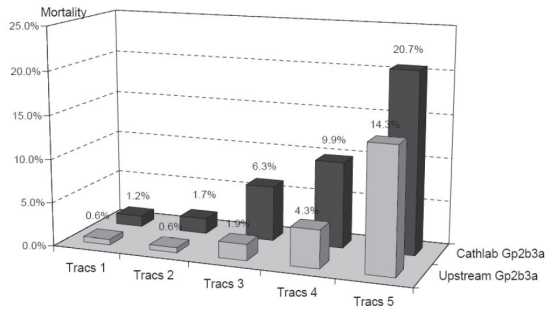
1017-43 **The TRACS Score Predicts Benefit of Upstream Glycoprotein IIb/IIIa Use in Acute Coronary Syndromes**

Sandeep Nathan, Amit P. Amin, James E. Calvin, Jr., Rush University Medical Center, Chicago, IL, Cook County Hospital, Chicago, IL

Background: The TRACS score is a simple scoring system for predicting mortality in acute coronary syndromes (1). We attempt to evaluate the relative benefit of upstream glycoprotein IIb/IIIa (GPI) use across categories of the TRACS score.
1. J Am Coll Card 2006;47; Issue 4 Suppl A:1018-227·224A.
Methods: The Registry of Acute Coronary Syndromes (TRACS) is a registry of 3,468 ACS patients (pts) from 9 institutions. Pts receiving GPI in the ER, CCU or chest pain unit constituted the "upstream" group. In-hospital death was the primary outcome variable. The TRACS score is a validated scoring system based on multiple clinical variables and

cardiac biomarker postivity 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 0.22-0.99). 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 Arida, James K. McCord, Akshay Khandelwal, Steven Mast, Karthik Iyer, Glenn Tokarski, Nabil Khoury, Aaron Kugelmass, Henry Ford Heart and Vascular Institute, Detroit, MI

Background: The benefit of primary angioplasty for treatment of ST Elevation Myocardial Infraction (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 among 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 activation 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.

ECG Group	Number of patients	Door to activation time (minutes)
Acute MI	277	12 ± 13
MI unknown onset	69	43 ± 51
LBBB	9	14 ± 10
No change	6	17 ± 20
Other	31	68 ± 115

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 Satterfield, 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 without CHD (age 73.5±2.9 years, 55% females, 41% blacks) in the Health ABC study. CHD was defined as history of myocardial infarction (MI) or angina or coronary revascularization whereas new coronary event was defined as hospitalization for MI or angina. Incident HF was defined as hospitalization for new onset HF.

Results: Overall 91/477 (19.1%) participants with and 153/2320 (6.6) without CHD developed HF during the 6.5±1.8 yr follow-up (HR 3.25, p<0.001). In both groups systolic blood pressure, serum creatinine and fasting glucose levels, and continued smoking were independent predictors of new HF. In patients without CHD, age, increased heart rate, left ventricular hypertrophy, and low albumin levels were additional independent predictors. Among the 153/2320 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±2.1 yr follow-up period post-HF development, participants without prior coronary event had higher mortality as compared to those who did (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=0.309). In comparison, participants with baseline CHD who developed HF had 18% per year mortality 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 maybe 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 Slivka, Jana Williams, Margo Minissian, Donna Polk, C. Noel Bairey 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 conductivity.

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 individuals 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 sensitivity, specificity, 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 intervention 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 Yong Suh, Cheol Ung Choi, Jin Oh Na, Eung Joo Kim, Seung-Woon Rha, Chang Gyu Park, Hong Seog Seo, Dong Joo Oh, Cardiovascular Center Korea University, Guro Hospital, Seoul, South Korea, Nuclear Medicine, Korea University Guro Hospital, Seoul, South Korea

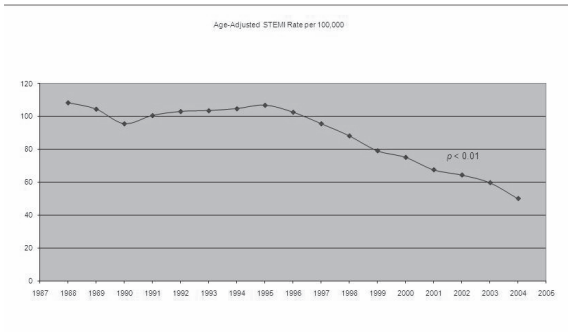
Background: A systematic plaque instability is suggested in patients with acute coronary syndrome. Plaque inflammation could be assessed by 18F-fluorodeoxyglucose Positron Emission Tomography (18F-FDG PET). We investigated whether carotid plaque inflammation could be related to coronary plaque instability using 18F-FDG PET. **Methods:** In 50 (male 14, 48.1±7.7 yrs) patients who were newly diagnosed as acute coronary syndrome (28 patients, male 6, 46.8±7.9 yrs) or stable angina (22 patients, male 13, 49.5±9.8), 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 18F-FDG injection and the multislice CT angiogram were acquired at 180 min on the Philips GEMINI TF scanner with 16 slice CT. The maximum standardized uptake values (SUVs) were measured in individual plaques. **Results:** In all patients, carotid plaque with increased 18F-FDG 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 (3.19 to 5.27) vs. 2.87±0.98 (2.47 to 3.62), p=0.003). 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.

11:00 a.m.

1017-48 Nationwide trends in the incidence of acute ST elevation myocardial infarction (STEMI) in the United States

Mohammad Reza Movahed, Mehrtash Hashemzadeh, Mazen Jamal, University of Arizona Sarver Heart Center and Southern Arizona VA Health Care System, Tucson, AZ

Background: Advances in the prevention and treatment of atherosclerosis risk factors have been dramatic in the last ten years. The goal of this study was to evaluate any decline in the age adjusted incidence of acute ST elevation myocardial infarction (STEMI) 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 ±13.69 years old. Male has almost twice age adjusted STEMI rate than female (male: 62.4%, female 37.6%). From 1988 the age-adjusted rate for all 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 steadily 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.



11:00 a.m.

1017-49 Lack of Benefit with PCI for Total Occlusions in Stable Patients Following Myocardial Infarction is Time Independent: Results from the Occluded Artery Trial (OAT)

Venu Menon, Camille A. Pearte, Christopher E. Buller, Ph. Gabriel Steg, Sandra A. Forman, Harvey D. White, Paolo N. Marino, Demosthenes G. Katritsis, Paulo Caramori, Ricardo Lasevitch, Krystyna Loboz-Grudzien, Aleksander Zurakowski, Gervasio A. Lamas, Judith S. Hochman, Cleveland Clinic, Cleveland, OH, New York University School of Medicine, New York, NY

Background: The Occluded Artery Trial (OAT) (n=2201) showed no benefit for routine PCI (n=1101) over medical therapy (MED) (n=1100) alone in stable post-MI patients with late occluded infarct-related arteries up to 28 days post MI. MI onset was protocol defined as Day 1 and the earliest time to study entry was 3 calendar days after MI onset, which could be as early as 24 hours (23.59 pm Day 1 - 00.01 hours Day 3) post MI. The potential for selective early benefit led us to explore outcomes with PCI over MED in the < 3 days; < 7days, and > 7days time windows.
Results: Earlier time to randomization was associated with higher 48-month life table event rates of death, MI, and class IV CHF; (adj HR 1.04/day: 95% CI 1.02-1.06; p<0.001). The 48-month event rates for < 3 days, < 7days and > 7days post MI enrolled patients were similar for PCI vs. MED.

48-Month Life Table Event Rates (%)									
	≤ 3 days Post MI			≤ 7 days Post MI			> 7 days Post MI		
	PCI (n=168)	**MED** (n=163)	**P**	**PCI** (n=492)	**MED** (n=483)	**P**	**PCI** (n=609)	**MED** (n=617)	**P**
Death/MI/CHF	18.3	17.6	0.71	18.8	17.4	0.31	15.0	13.4	0.74
Death	7.9	7.9	0.88	9.4	10.7	0.91	9.4	8.5	0.90
MI	6.6	7.2	0.90	7.5	5.9	0.20	5.7	3.7	0.27
CHF	6.9	6.2	0.76	5.5	5.1	0.77	3.6	3.7	0.64

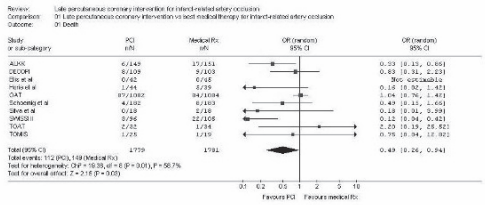
There was no interaction between time to randomization defined as a continuous (p=0.55) or categorical variable with a cut-point of 3 days (p=0.98) or 7 days (p=0.64) post MI and treatment effect.
Conclusions: Consistent with overall OAT trial findings, patients enrolled in the < 3 days and < 7day time windows derived no benefit with PCI over MED. Although earlier enrolled patients were at higher risk of events, there was no interaction between time to randomization and treatment effect. Thus, the results of OAT are broadly applicable over the entire enrollment window.

11:00 a.m.

1017-50 Survival And Cardiac Remodeling Benefits In Patients Undergoing Late Percutaneous Coronary Intervention Of The Infarct-Related Artery: Evidence From A Meta-Analysis Of Randomized Controlled Trials

Antonio Abbate, Giuseppe GL Biondi-Zoccai, Darryn L. Appleton, Paul Erne, Andreas W. Schoenenberger, Michael J. Lipinski, Pierfranseco Agostoni, Imad Sheiban, George W. Vetrovec, Virginia Commonwealth University Pauley Heart Center, Richmond, VA

Background. There is uncertainty about the role of late PCI in stable patients with AMI. The aim of this study was to perform a systematic review and meta-analysis of randomized trials comparing percutaneous coronary intervention (PCI) with medical therapy in patients randomized >12 hours after acute myocardial infarction (AMI).
Methods. PubMed, CENTRAL, and other databases were searched (July 2007). Studies were included if comparing PCI with medical management, randomizing hemodynamically stable patients >12 hours and up to 60 days after AMI. Odds ratios (OR) were pooled for dichotomous outcomes, with all-cause mortality as the primary end-point. Left cardiac remodeling parameters were pooled with generic-inverse-variance weighting.
Results. We retrieved 10 studies enrolling 3560 patients, with median time from AMI to randomization of 12 days (range 1-26), and follow-up of 2.8 years (42 days-10 years). Randomization allocated 1779 subjects to PCI and 1781 to medical treatment. There were 112 (6.3%) and 149 (8.4%) deaths in the 2 groups, respectively, yielding significantly improved survival in the PCI group (OR=0.49 [0.26-0.94], P=0.030). These benefits were associated with similarly beneficial effects on cardiac remodeling, such as improved left ventricular ejection fraction in the PCI group (+4.4% change [1.1 to 7.6], P=0.009).
Conclusions. PCI of the IRA performed late (12 hours to 60 days) after AMI is associated with significant improvements in cardiac function and survival.

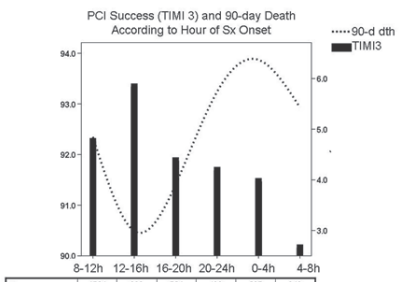


11:00 a.m.

1017-51 Procedural Delay does not Explain the Circadian Variation Observed in Outcomes of Primary PCI for STEMI: Insights from the APEX-AMI Trial

Kiranbir Josan, Cynthia M. Westerhout, Arnoud WJ van 't Hof, William W. O'Neill, David R. Holmes, Jr., Petr Widimsky, Witold Ruzyllo, Christopher B. Granger, Paul W. Armstrong, APEX AMI Investigators, University of Alberta, Edmonton, AB, Canada

Background: Evening and early morning onset of ST-elevation myocardial infarction (STEMI) has been linked with worse outcomes in patients undergoing reperfusion. The extent to which biologic versus process of care factors modulate this phenomenon is unknown. We hypothesized that process of care issues in patients undergoing primary PCI i.e. longer door to balloon times at night would result in worse procedural and clinical outcomes.
Methods: Risk-adjusted post-PCI TIMI 3 flow and 90-day mortality (overall 3.6%) were examined by hour of symptom onset (Sx onset) in 4835 STEMI patients enrolled in APEX-AMI (testing pexelizumab, a complement inhibitor). Hour of sx onset was classified as "daytime " (08.00-20.00h) or "nighttime " (20.00-08.00h).
Results: Of 4835 patients, 64.0% had Sx onset during daytime hours. Nighttime Sx onset was associated with lower rates of successful reperfusion (i.e., post-PCI TIMI Flow 3) and higher 90-day mortality rates (figure). Interestingly whereas nighttime Sx onset was associated with longer delays from Sx onset to hospital arrival, door to balloon times were consistent regardless of time of day.
Conclusion: In this large, contemporary well treated STEMI cohort undergoing primary PCI, Sx onset and outcomes exhibited a clear circadian rhythm. Patient care-seeking behaviors, rather than procedural delays, appear to be the primary modulator of longer times to reperfusion.

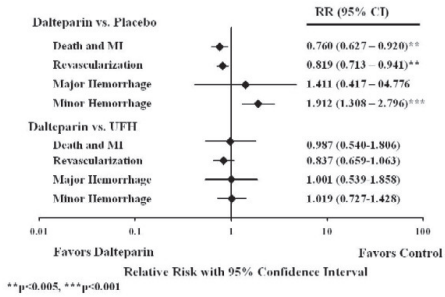


11:00 a.m.

1017-52 Low Molecular Weight Dalteparin As An Adjunct In Treatment Of Acute Myocardial Infarction: A Meta-Analysis

Amol A. Bahekar, Rohit Arora, Sarabjeet Singh, Ahmad Khraisat, Janos Molnar, Param Puneet 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 homogenous and the random effect model was used when the studies were heterogenic. 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: 0.760; CI: 0.627-0.920). There was an increased risk of minor hemorrhage (RR: 1.912; CI: 1.308-2.796) but not 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.



11:00 a.m.

1017-53 Randomized trial of early vs. late abciximab 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 Paradossi, 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 (PPCI). Our aim was to demonstrate that early abciximab (before transfer from remote hospital to cath lab) compared to late abciximab (during PPCI) 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 PPCI >45 minutes, were prospectively randomized to either Early (57 pts) or Late (50 pts) abciximab administration. Four days after PPCI, 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.
Results: The 2 groups had similar baseline clinical characteristics. Baseline TIMI 2-3 flow (38.5% vs. 31.6%, P>0.2), final TIMI 3 flow (90.4% vs. 94.7%, P>0.2), and ST elevation resolution >70% 60 minutes after PPCI (71.2% vs. 68.4%, P>0.2) were not significantly better in the Early group. Preliminary MRI data (Table) show no significant difference in initial and 6-month perfusion defects, although a trend to a greater reduction in final infarct size is observed in the Early group (P=0.09).
Conclusions: Preliminary MRI data show that early abciximab administration is not associated with smaller infarct size after 6 months, although a greater myocardial salvage is observed.

	Pre-discharge			6 months			
	LVEF, %	**DE, % of myocardium**	**Transmurality of DE, %**	**LVEF, %**	**DE, % of myocardium**	**Transmurality of DE, %**	**Change in DE,%**
Early (n=30)	53±11	22±11	27±14	53±9	14±9	17±13	-8±5
Late (n=18)	54±11	17±12	21±15	56±13	12±10	15±13	-5±7
P	>0.20	0.18	>0.20	>0.20	>0.20	>0.20	0.09

11:00 a.m.

1017-54 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 Siudak, Tomasz Rakowski, Artur Dziewierz, Wojciech Zasada, Michal Brzezinski, Magnus Janzon, 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 (PPCI) during night hours.
Methods: Consecutive 1,650 STEMI patients treated with PPCI 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 295+/-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 PPCI for STEMI patients in the setting of hospital networks during nightshift 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
Clopidogrel loading dose > 300 mg	30.1%	34.1%	0.169
Thrombolysis	3.1%	7.8%	<0.0001
Early abciximab	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	1.5%	1.8%	0.653

11:00 a.m.

1017-55 Bypassing the Emergency Room After Pre-Hospital ECG Transmission as a Major Contributor to Reduced Door-to-Balloon Times in Patients With Acute ST-Elevation Myocardial Infarctions

Dorothe Ahlersmann, Karl-Heinrich Scholz, Holger Duwald, Rolf Nitsche, Georg von Knobelsdorff, Reinhard Hilgers, Friederike Keating, St. Bernward Hospital, Hildesheim, Germany, University of Vermont, Burlington, VT

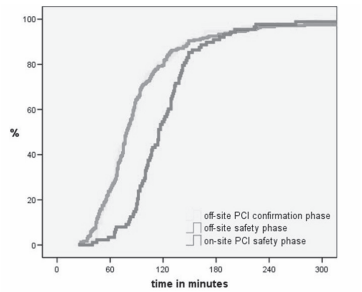
Background: Streamlining diagnosis and treatment of patients with ST-elevation myocardial infarction (STEMI) reduces time to revascularization. We prospectively examined the effects of a strategy to bypass the emergency room in those patients in whom the diagnosis was established pre-hospital with a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

11:00 a.m.

1017-56 Percutaneous Coronary Intervention with Off-site Cardiac Surgery Backup for Acute Myocardial Infarction as a Strategy to Reduce Door-to-Balloon Time

Victor A. Umans, Hans O. Peels, Hans de Swart, Raymond Hautvast, 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 started the first PCI with off-site surgery program in the Netherlands in 2002 and report 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, 540consecutive 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.



11:00 a.m.

1017-57 Impact of Spontaneous Reperfusion in Diabetics with Acute Myocardial Infarction

Kevin R. Bainey, 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 reperfusion (SR) in STEMI is known to improve clinical outcome, yet its incidence and impact amongst diabetics is unclear. Accordingly, in the APEX AMI study we undertook 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 primary clinical outcomes according to the presence or absence of SR in the total population, diabetics, and non-diabetics.

	All patients		Diabetics		Non- Diabetics	
	SR	No SR	SR	No SR	SR	No SR
N=	568	4376	70	694	498	3682
∑ST at baseline (mm)	11.5 (8-16.5) [a]	13 (9-19)	10.3 (7.5-15.3)	12 (8.5-17.5) [b]	11.5 (8.4-16.5) [a]	13.5 (9.5-19.5)
Symptom onset to PCI (hrs)	3.2 (2.4-4.5)	3.4 (2.5-4.5)	3.9 (2.6-4.8)	3.6 (2.8-4.9) [b]	3.2 (2.4-4.3)	3.3 (2.5-4.4)
Baseline blood glucose ≥ 7.8 mmol/l %	40.7 [a]	53.5	83.6	89.5	34.2 [a]	46.6 [b]
Post PCI TIMI 3 flow %	99.6 [a]	89.4	98.6 [a]	84.9 [b]	99.8 [a]	90.3
≥ 70% ST Resolution 30 min post PCI %	54 [a]	49.5	45.7	37.9 [b]	55.2	51.7
90-day death %	2.5	4.0	4.3	6.1 [b]	2.2	3.6
90-day death/shock/CHF %	5.1 [a]	9.8	10.0	14.9 [b]	4.4 [a]	8.9
[a] denotes p<0.05 for comparison of SR versus No SR within each category, [b] denotes p<0.05 for comparison of diabetics without SR versus their counterpart with non-diabetics						

Patients without SR had worse epicardial flow, higher baseline blood glucose and tended towards less ST resolution post PCI than those with SR, especially in diabetics. Multivariable analysis identified SR, complete ST resolution post PCI and baseline glucose <7.8mmol/l as independent predictors of the 90 day composite clinical outcome.
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. By contrast, diabetics without SR have achieve diminshed epicardial patency with impaired microvascular perfusion post PCI likely contributing to their worse clinical outcomes.

11:00 a.m.

1017-58 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

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 fibrinolytics 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 18% 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.
Conclusions: Almost half of STEMI pts treated with fibrinolytics 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.

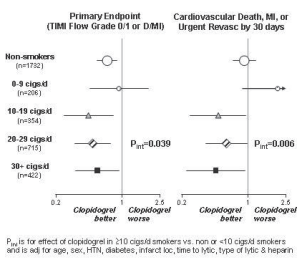
*OR adjusted for age, sex, BMI, renal insufficiency, signs of HF				
	No excess dosing (n=317)	**Mild excess dosing (n=231)**	**Major excess dosing (n=137)**	**P Value**
Major bleeding				
Unadjusted rates	12.4%	18.7%	19.2%	0.004
Adjusted OR (95% CI)*	--	0.96 (0.41, 2.27)	0.87 (0.38, 2.15)	0.86
Transfusion				
Unadjusted rates	4.7%	8.6%	13.5%	0.0002
Adjusted OR (95% CI)*	--	0.89 (0.41, 1.92)	1.39 (0.61, 3.14)	0.90

11:00 a.m.

1017-59 The Smoker's Paradox with a Clopidogrel Twist: Insights from CLARITY-TIMI 28

Nihar 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

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 1.5d. 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 v. 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: 1732 patients were not current smokers and 1697 were, the latter consisting of 206 light (1-9 cigs/d, median=5), 354 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 ≥10 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.



11:00 a.m.

1017-60 **Constrasting ex Vivo and in Vitro Effects of Pexelizumab on Complement Activation and Cell Apoptosis in Patients With ST-Segment Elevation Myocardial Infarction Undergoing Primary PCI: A Substudy of The APEX-AMI Trial**

Catherine Martel, Benoit Labarthe, Jacinthe Rivard, Marta Ghitescu, Arnaud Bonnefoy, Pierre Théroux, Montreal Heart Institute, Montreal, QC, Canada, University of Montreal, Montreal, QC, Canada

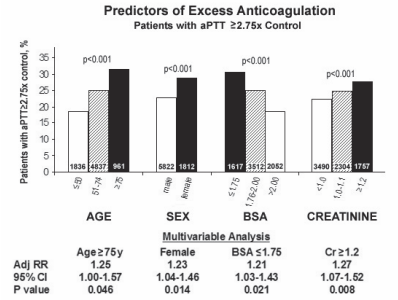
Background: Complement (C) activation and apoptosis are involved in the pathophysiology of STEMI. Yet, Pexelizumab (PEX), a MAb to C5 designed to prevent activation of terminal complement (Term C), failed to benefit STEMI patients enrolled in the APEX-AMI trial. We therefore explored why and examined C activation and cell apoptosis in patients treated with PEX or placebo.
Methods: Blood was obtained from 45 patients enrolled at MHI 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, Bb, and MBL (proximal C), and C5a, 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 annexinV. 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 C5a 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 ng/ml, NS). sC5b-9 values, however, increased more with PEX (743 to 1892 ng/ml, p=0.003) than with placebo (858 to 1473 ng/ml, NS). 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 ng/ml vs. 3505 to 4259 ng/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≤0.0001), PEX had no detectable direct 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 C5a 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.

11:00 a.m.

1017-61 **Predictors of Excessive Anticoagulation with Unfractionated Heparin in STEMI**

Susan Cheng, David A. Morrow, Sarah Sloan, Elliott M. Antman, Marc S. Sabatine, TIMI Study Group, Division of Cardiovascular Medicine, Brigham and Women's Hospital, Boston, MA

Background: Although weight-based nomograms are used to guide unfractionated heparin (UFH) dosing, additional patient characteristics may affect the ability to achieve a therapeutic activated partial thromboplastin time (aPTT).
Methods: ExTRACT-TIMI 25 enrolled 20,506 STEMI patients; half were randomized to UFH, dosed per the ACC/AHA wt-based nomogram w/ centrally monitored aPTTs. We used multinomial logistic regression to determine the independent association between patient characteristics and achieving target aPTT.
Results: 7634 patients received UFH and had an aPTT w/in 4-8 h of starting therapy. Despite 99% compliance with recommended dosing, only 29.5% of initial aPTTs were therapeutic (1.5-2x control); 11.1% were excessively low (<1.25x), requiring re-bolusing; and 24.2% were excessively high (>=2.75x), requiring temporary UFH cessation. Excessively high initial aPTTs were significantly more likely to occur in patients who were age >=75, female, with BSA <=1.75 m2, or with creatinine >=1.2 mg/dL (Fig) and were associated with a significantly increased risk of TIMI major or minor bleeding by 48 h (adj OR 1.83; P=0.011).
Conclusion: The standard weight-based UFH nomogram in STEMI often fails to achieve initial therapeutic anticoagulation. Excess anticoagulation is more likely among patients who are older, female, of smaller body size, or with renal impairment, and is associated with increased bleed risk. These findings should be considered when dosing UFH in support of lytic therapy.



11:00 a.m.

1017-62 **Does Statin Pre-treatment Promote Thrombolysis in Patients With Acute Myocardial Infarction Treated With Thrombolytic Therapy?**

Masayoshi Kiyokuni, Masami Kosuge, Toshiaki Ebina, Kiyoshi Hibi, Kengo Tsukahara, Jyunn Okuda, Noriaki Iwahashi, Toshiyuki Ishikawa, Kazuaki Utino, Satoshi Umemura, Kazuo Kimura, Yokohama City University Medical Center, Yokohama, Japan

Background: Statins promote vascular thrombolysis. We hypothesize that statin pre-treatment provides a more efficient response of the infarct-related artery to thrombolytic therapy, resulting in smaller infarct size in patients with acute myocardial infarction (AMI).
Methods: We studied 319 patients with first AMI within 12 h after symptom onset. All patients underwent thrombolysis, and rescue or immediate percutaneous coronary intervention (PCI) was performed on the basis of angiographic findings. Patients were classified into 2 groups: 39 who had received statin before AMI onset (statin group) and 280 who had not (non-statin group). QRS score, a marker of transmural damage, was measured by ECGs at admission and 1 h after recanalization.
Results: Age, time from onset to admission (110 vs 108 min), preinfarction angina, door to needle time, and the rate of PCI (79 vs 68%) did not differ between statin and non-statin groups. Statin group had higher rates of women (36 vs 10%), hypertension (74 vs 55%), hyperlipidemia (100 vs 54%), diabetes mellitus (47 vs 26%), non-anterior AMI (63 vs 47%), and a smaller QRS score on admission (1.9+3.4 vs 3.1+3.3) and 1 h later (3.1+4.2 vs 5.0+3.9) (all p<0.05). Initial TIMI grade 3 rate did not differ between the groups (31 vs 31%). Among 123 patients with initial TIMI grade 0/1, TIMI grade >2 (70 vs 35%, p=0.03) was more frequently observed in statin group until the first balloon inflation. Final TIMI grade 3 rate was higher in statin group (95 vs 85%, p=0.09). Peak creatine kinase was lower in statin group (2187+1967 vs 3383+3401 IU/L, p=0.03). When restricted to patients with anterior AMI, QRS scores on admission (2.2+2.2 vs 4.4+3.4, p=0.03) and 1 h later (3.4+3.5 vs 6.3+3.7, p=0.02) and peak creatine kinase (2758+2910 vs 4170+3995, p=0.21) were lower in statin group. Multivariate analysis showed that statin pre-treatment was an independent predictor of a smaller infarct size, defined as a peak creatine kinase level of <3000 IU/L(OR 2.87, 95%CI 1.06-6.10, p=0.039).
Conclusions: Smaller infarct size in patients with statin pre-treatment may result from partly promoting thrombolysis and directly protecting myocardium by statin in AMI treated with thrombolytic therapy.

11:00 a.m.

1017-63 **Platelet Responsiveness to Aspirin Loading in Patients with ST Elevation Myocardial Undergoing Primary Percutaneous Intervention is Associated with Myocardial Reperfusion and Clinical Outcome**

Shlomi Matetzky, Paul Fefer, Boris Shenkman, Michael Shechter, Levi Nitza, David Varon, Naphthali Savion, Hanoch Hod, Sheba Medical Center, Tel Hashomer, Israel, Hadassah University Hospital, Jerusalem, Israel

Background: In patients treated with aspirin in the setting of primary prevention, as well as in patients with stable coronary artery disease, and patients undergoing elective percutaneous coronary intervention (PCI), laboratory resistance to aspirin is associated with a higher incidence of adverse events. Nevertheless, the responsiveness to aspirin in acute myocardial infarction (AMI) and its implications have not yet been investigated.
Methods: The study comprised 76 aspirin naïve patients who underwent primary PCI (PPCI) for ST-elevation MI (STEMI). Platelet reactivity was assessed 30-60 mins after a loading dose of 300mg chewable aspirin, by conventional aggregometry and Impact R, where platelet reactivity to arachidonic acid (AA) was expressed by platelet deposition under flow conditions.
Results: Patients were stratified using the median value of AA-induced platelet aggregation (PA) (49%) to good responders to aspirin (n=38), who had a median AA-induced PA of 33% (25-41), and poor responders to aspirin (n=38), who had a median AA-induced PA of 77% (70-84). Similarly, good compared with poor responders had higher surface coverage by Impact R (3.9±2.6 vs. 2.2±1.3, p=0.003). Good versus poor responders were similar regarding baseline demographic, clinical and angiographic characteristics. However, good responders were more likely to demonstrate early ST-segment resolution ≥70% after PPCI (84% vs 54%, p <0.01), suggestive of better myocardial reperfusion. Good compared to poor responders had a lower incidence of adverse cardiovascular events (re-infarction, need for re-intervention, congestive heart failure and/or death) throughout a 6-month follow-up (11% vs 24%, respectively; p<0.11).
Conclusions: Ex vivo poor platelet responsiveness to aspirin loading in STEMI patients is associated with a worse prognosis in patients undergoing PPCI.

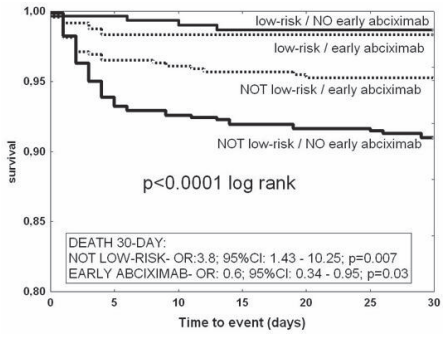
11:00 a.m.

1017-64 **Early Abciximab Administration Before Primary Percutaneous Coronary Interventions Reduces Mortality but Not in Low-Risk Patients: Results From EUROTRANSFER Registry on ST-Elevation Myocardial Infarction Patients**

Tomasz Rakowski, Artur Dziewierz, Zbigniew Siudak, Waldemar Mielecki, Jacek Legutko, Magnus Janzon, Ralf Birkemeyer, Rafal Depukat, Dariusz Dudek, Jagiellonian Unversity Medical College, Krakow, Poland

Background: Early abciximab administration before primary percutaneous coronary intervention (PPCI) for ST-elevation myocardial infarction (STEMI) is recommended in guidelines. However, the randomized trials provide conflicting results. Target population which benefits from this strategy has to be defined.

Methods: Consecutive 1,650 STEMI patients treated with PPCI were enrolled in 7 European countries from Nov 2005 to Jan 2007 and were stratified into "not low-risk" (NLR n=1107; 67%) and "low-risk" (LR n=543; 33%) groups according to the Thrombolysis In Myocardial Infarction criteria. Abciximab was administered early (before admission to cath lab) in 44% of not low-risk and 44% of low-risk patients.
Results: Higher rate of infarct-related artery patency in baseline angiography (TIMI 2+3- NLR: 30.2 vs 21.3% p<0.001; LR: 35.8% vs 26.1% p=0.01), as well as better ST-segment resolution >50% after PPCI (NLR: 74.1 vs 63.2% p<0.001; LR: 88.8 vs 75.6% p=0.01) were found after early abciximab in both risk groups. Mortality reduction after early abciximab was found only in NLR group. In multivariate Cox regression NLR profile and lack of early abciximab administration were independent predictors of 30-day death (Figure).
Conclusions: Early abciximab administration before transfer for PPCI in STEMI results in more frequent infarct-related artery patency before PPCI, better myocardial perfusion after PPCI regardless of patients' risk profile but mortality reduction is present only in not low-risk group.



11:00 a.m.

1017-65 **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, Sadia Khan, Linda Sharples, Cameron Densem, 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: Patient demographics were matched between groups (mean age: control: 62.5 yrs, remote IPC: 63.8 yrs; diabetes: control: 15/88, remote IPC: 21/92). Interval between remote IPC and coronary balloon inflation was 68 ± 29 minutes. Baseline mean cTnI was below the lower limit of detection in both groups, but 24-hour mean cTnI was lower in the remote IPC group. 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.

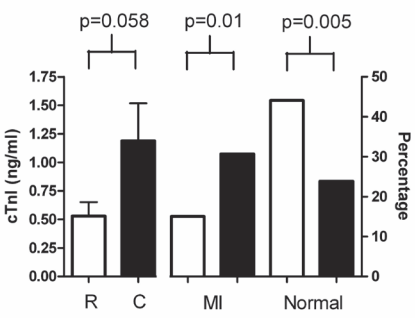


Figure: Mean cardiac troponin I level (SEM), percentage of patients with procedure related myocardial infarction (MI) and normal cTnI levels (Normal) in control (C, black bars) and remote IPC (R, white bars) after elective PCI.

11:00 a.m.

1017-66 **Effect of Chronic Statin Therapy on Hospital Course in Patients With Acute Myocardial Infarction**

Timm Bauer, Oliver Koeth, Claus Juenger, Tobias Heer, Anselm Gitt, Ralf Zahn, Jochen Senges, Michael Boehm, Uwe Zeymer, ACOS-registry group, Herzzentrum Ludwigshafen, Ludwigshafen, Germany, Uniklinikum Saarland, Homburg/Saar, Germany

Background: Chronic treatment with statins reduces the risk of adverse clinical outcomes in patients with coronary artery disease. It is less clear whether prior statin therapy benefits patients who develop an acute myocardial infarction.
Methods: We analyzed data of consecutive patients with ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) who were prospectively enrolled in the German Acute Coronary Syndromes registry between July 2000 and November 2002. Aim of the study was to investigate the impact of a prior statin therapy on hospital course in patients presenting with acute myocardial infarction (AMI) in clinical practice.
Results: Overall 14661 patients were included and we compared those who were on chronic statin treatment (n=2322, 15.8%) to those who were not (n=12339, 84.2%). Pretreated patients were older (68.2 versus 66.9 years, p<0.01), had a higher incidence of prior myocardial infarction (46.2 versus 15.2%, p<0.0001), percutaneous coronary intervention or coronary artery bypass grafting (41.5 versus 8.3%, p<0.0001) as well as diabetes mellitus (36.6 versus 26.7%, p<0.0001). Patients with prior statin use were less likely to suffer from prehospital resuscitation (2.2 versus 5.0%, p<0.05) and STEMI (46.3 versus 58.6%, p<0.0001) and had more often NSTEMI (53.7 versus 41.4%, p<0.0001) and lower peak CK levels (364 versus 566U/l, p<0.0001). In the propensity score analysis a strong tendency towards a reduction of in-hospital death could be observed in statin users (OR 0.83, 95% CI 0.69-1.00). The benefit was higher in elderly (NNT to prevent one death 44), diabetics (NNT 44) and in patients with known coronary artery disease (NNT 29).
Conclusions: In clinical practice chronic use of statins is associated with smaller myocardial infarction size and borderline significant reduction of hospital mortality.

11:00 a.m.

1017-67 **Transfer for Primary Percutaneous Coronary Intervention in Patients With ST Elevation Myocardial Infarction: Not All Delays Are Created Equal**

Michael D. Miedema, Marc C. Newell, Scott W. Sharkey, Wes R. Pedersen, Katie M. Menssen, Sue Duval, David M. Larson, Timothy D. Henry, Minneapolis Heart Institute Foundation at Abbott Northwestern Hospital, Minneapolis, MN

Background: Primary percutaneous coronary intervention (PCI) is the preferred treatment for ST-elevation myocardial infarction (STEMI), if it can be performed in a timely manner. Prolonged treatment times are associated with increased mortality.
Methods: The Level 1 STEMI program is a standardized protocol designed for PCI in STEMI patients including transfer from 31 rural and community hospitals. We divided treatment times into 3 segments: in door-out door >45 min at community hospital (CH), transfer (Tr) >30 min, and door-to-balloon > 30 min at PCI center (PC) were considered delays and the specific reason for delay was documented prospectively.
Results: From 03/2003 to 11/2006, 1,014 patients were transferred for PCI. In-hospital (4.9% vs 2.8%, p-value 0.13) and 1 year mortality (8.2% vs 4.5%, p-value 0.04) was greater in patients with total door-to-balloon >90 minutes. The associations between in-hospital mortality and the specific reason for delay for each segment are shown in Table 1.
Conclusions: Mortality is higher in STEMI patients with prolonged treatment time but varies significantly according to the reason for delay. Delays were most frequent at the CH where awaiting transfer, ED delay and non-diagnostic EKG were frequent but did not increase mortality. In contrast, delays due to cardiac arrest or cardiogenic shock significantly increased mortality at both CH and PC. Delays during Tr did not increase mortality while PC delays had the highest mortality. All delays are not created equal.

Community hospital	Mortality	Transfer	Mortality	PCI center	Mortality
Total # of delays (n=663)	35 (5.3%)	Total # of delays (n=288)	8 (2.8%)	Total # of delays (n=165)	14 (8.5%)
Awaiting transport (n=293)	11 (3.8%)	Distance (n=209)	7 (3.4%)	Cath lab team delay (n=58)	3 (5.2%)
ED delay (n=124)	4 (3.2%)	Traffic (n=29)	0 (0.0%)	Complex procedure (n=53)	4 (7.3%)
Diagnostic dilemma (n=90)	6 (6.7%)	Weather (n=25)	0 (0.0%)	Unknown (n=38)	5 (13.2%)
Non-diagnostic EKG (n=78)	0 (0.0%)	Unknown (n=25)	1 (4.0%)	Cardiogenic shock/ cardiac arrest (n=8)	2 (25.0%)
Cardiogenic shock/ cardiac arrest (n=47)	12 (25.5%)				
Unknown (n=31)	2 (6.5%)				

11:00 a.m.

1017-68 Are Staged Interventions Really Necessary in Patients Presenting With Acute Myocardial Infarction and Multi-Vessel Disease and Treated With Primary Percutaneous Coronary Intervention?

Tami L. Bair, Jeffrey L. Anderson, Heidi T. May, Benjamin D. Horne, Donald L. Lappé, Joseph B. Muhlestein, Intermountain Medical Center, Murray, UT

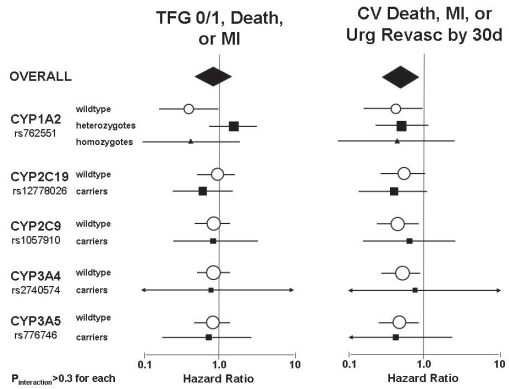
Background: The most recent (2005) ACC/AHA/SCAI guidelines for percutaneous coronary intervention (PCI) state that, when performing primary PCI for acute myocardial infarction (AMI) with multi-vessel disease, "Elective PCI should not be performed in a non-infarct-related artery at the time of primary 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=0.22, 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=0.28, 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.

11:00 a.m.

1017-69 Sequence Variations in CYP Metabolism Genes and Cardiovascular Outcomes following Treatment With Clopidogrel: Insights From the CLARITY-TIMI 28 Genomic Study

Jessica L. Mega, Joseph V. Thakuria, Christopher P. Cannon, Marc S. Sabatine, Brigham & Women's Hospital, Boston, MA

Background: Clopidogrel is a pro-drug that requires oxidation by cytochrome P450 (CYP) enzymes to generate an active metabolite. Gene sequence variations in the CYP pathway have been associated with variability in clopidogrel responsiveness, as measured by platelet aggregation. The clinical significance of these observations is unknown.
Methods: CLARITY-TIMI 28 randomized STEMI patients undergoing fibrinolysis to clopidogrel (300 mg loading dose, then 75 mg daily) or placebo. Patients were to undergo angiography at 48-192 h and were followed for 30 d for clinical events. Genotyping was performed using an Illumina GoldenGate Assay.
Results: 465 patients were genotyped for 5 commonly studied SNPs: CYP1A2*1F (rs762551), CYP2C9*3 (rs1057910), CYP3A4*1B (rs2740574), CYP3A5*3 (rs776746), 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 of cardiovascular death, MI, or urgent revascularization by 30 d (Fig). Likewise, there was no observed heterogeneity for the relationship between genotype, treatment, and bleeding (Pinteraction >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.



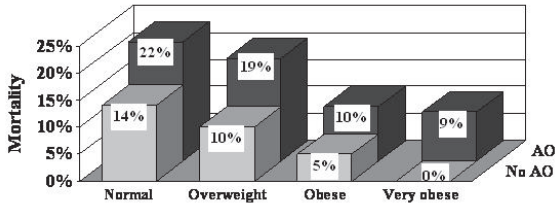
11:00 a.m.

1017-70 Relation of Body Mass Index and Waist Circumference to Mortality After Acute Myocardial Infarction

Marianne Zeller, Philippe G. Steg, Laurent Mock, Jean-Claude Beer, Yves Laurent, Pierre Sicard, Luc Janin-Manificat, Anne-Cecile Lagrost, Hamid Makki, Luc Rochette, Yves Cottin, Cardiology department, CHU, Dijon, France

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 2229 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 ¼ 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(95%CI): 0.95(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.

Figure : Mortality according to both BMI and WC categories



11:00 a.m.

1017-71 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

Jean-Claude Beer, Laurent Mock, Pierre Sicard, Michel Vincent-Martin, Isabelle L'huillier, Yves Laurent, Anne-Cecile Lagrost, Marianne Zeller, Yves Cottin, Cardiology department, CHU, Dijon, France

Background: The impact of ECG modifications during non ST segment elevation myocardial infarction (NSTEMI) deserves to be better specified. The goal of our study was to evaluate characteristics and outcomes of NSTEMI patients in the absence of significant ECG changes during the course of MI.
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 either ST depression >= 1 mm, or T wave inversion in 2 or more consecutive leads.
Results: Among the 829 patients included, 85 (10%) were ECG -. Patients from the ECG- group were younger (61(51-72) vs 69(56-76) y; p=0.002), more frequently men (85 vs 70%, p=0.006), with a better LVEF (p=0.002), a lower troponin Ic peak, and lower levels of CRP and Nt-ProBNP on admission (p<0.001) than the ECG+ group. Angiographic data showed an increased proportion of patient with normal coronary arteries in the ECG - group (21 vs 9%; p=0.002) and more patients with single vessel disease than in the ECG + group. Acute treatments were similar for the 2 groups, except for diuretics (p=0.004), which were more frequently used in the ECG+ group. Also, reperfusion therapy (PCI or CABG) was more frequently used in the ECG+ group. Mortality at one year was markedly reduced in the ECG- when compared to the ECG+ group (2 vs 11%, p=0.023). Multivariate analysis showed that the absence of significant ECG changes remained associated with improved long-term survival, even after adjustment for potential co-variates.
Conclusions: Our observational study on a population with NSTEMI shows that the absence of modifications in ECG printouts throughout the hospital phase identifies a subgroup of low risk patients at one year follow-up.

11:00 a.m.

1017-72 **Improving Door-to-Balloon Time in ST-Elevation Myocardial Infarction**

Sun K. Scolieri, Joon S. Lee, Suresh Mulukutla, Vincent N. Mosesso, Donald M. Yealy, Charissa B. Pacella, Kathleen Zell, UPMC 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 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 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, cath lab staff, interventional fellow and attending. 4) Defined time expectations for triage to ECG time, decision to activate cath lab, transfer time. 5) Detailed real time feedback of each component of D2B to all caregivers involved within 1 day of patient encounter. The baseline group consisted of 63 consecutive STEMI 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 108.3±34.7 to 72.2± 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 (GAP-D2B) 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.

11:00 a.m.

1017-73 **Left Ventricular Remodeling and Heart Failure in Elderly Patients With Acute Myocardial Infarction Treated With Primary Angiopalsty**

Nazario Carrabba, Guido Parodi, Renato Valenti, Gentian Memisha, Umberto Signorini, Angela Migliorini, David Antoniucci, Division of Cardiology, Florence, Italy

Background: The ability of primary percutaneous coronary intervention (PCI) to salvage ischemic myocardium and to prevent left ventricular (LV) remodeling in elderly patients (pts) with acute myocardial infarction (AMI) is questioned.
Aim: To assess the impact of aging on LV remodeling and subsequent heart failure (HF) after primary PCI.
Methods: For this purpose, 512 consecutive pts with AMI successfully treated with primary PCI underwent serial 2D echo at admission, at 1 and 6 months. LV volumes, ejection fraction (EF) and wall motion score index (WMSI) were measured. Pts were divided in two groups: younger pts (<70 years, n= 361), and elderly pts (≥70 years, n= 151). LV remodeling was defined as an increase >20% in end-diastolic volume (EDV) from baseline to 6-months. HF was defined as the presence of Killip class >I.
Results: Elderly pts showed a higher prevalence of female gender (36% vs 15%, p<.0001), multivessel disease (66% vs 52%, p=.003), and a longer time to reperfusion (247 ± 126 min vs 202 ± 93 min, p<.0001) 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=.00002 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 after 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.

11:00 a.m.

1017-74 **Modification of Traditional ECG Evolution of Myocardial Infarction by Early Intervention: Analysis of the CZECH Registry of Acute Coronary Syndromes**

Milka Klinceva, Petr Widimsky, Michal Zelizko, Petr Jansky, Frantisek Tousek, Michal Aschermann, Cardiocentrum Vinohrady, Prague, Czech Republic

Background: Early reperfusion therapy and especially primary percutaneous coronary intervention (PCI) changed the classical electrocardiographic scheme of the myocardial infarction (MI) evolution: ST elevation myocardial infarction (STEMI) can be turned into a nonQ wave MI (nonQMI) and conversely a non-ST elevation MI (nonSTEMI) may occasionally develop into Q wave MI (QMI) when reperfusion is not performed in time or is not successful. The aim of this study was to analyze these ECG changes in the real life setting in a country with very high use of very early PCI.
Methods: The data from the CZECH Registry of Acute Coronary Syndromes (ACS) were analyzed. A total of 722 patients were admitted for ACS that developed Q or nonQMI at discharge ECG. Patients were divided into 4 groups (STEMI - QMI, STEMI - nonQMI, nonSTEMI - QMI and nonSTEMI - nonQMI). The clinical and angiographic differences between Q and nonQMI admitted to the hospital for STEMI or NonSTEMI were examined.
Results: ST elevation developed into a nonQMI in 20% of the patients (93/456) and into a QMI in 80% of patients (363/456). Patients that developed a nonQMI comprised mostly females (p=0.02), patients who suffered from heart failure (p=0.01), and half of the patients had an ejection fraction more than 50% (p<0.001) and an uncomplicated outcome (p=0.01).
NonSTEMI developed into a QMI in 11% of the patients (29/266) and into a nonQMI in 89% of patients (237/266).
The patients with QMI were mostly men (p=0.03), more persistent smokers (p<0.001), had less diabetes mellitus (p=0.02), received less aspirin before hospital admission (p=0.05), suffered more heart failure (p=0.03), had more complicated outcome (p=0.01) and underwent more often primary PCI (p=0.04).
There were no differences in the time from the onset of the symptoms to the coronary angiography and in-hospital mortality between the QMI patients and the nonQMI patients admitted as either STEMI or nonSTEMI.
Conclusions: Nationwide implementation of early interventional treatment of acute coronary syndromes leads to the abolishment of ECG ,,transmurality" in 20% of STEMI. On the other hand, no use or late use of the intervention causes 11% of the nonSTEMI to evolve into STEMI patients.

11:00 a.m.

1017-75 **Coordinated Inter-Hospital Transfer Program Improves Quality of Care Delivered to ST Elevation Myocardial Infarction Patients Presenting in Rural Communities**

Frank V. Aguirre, Joji J. Varghese, Anushree Agarwal, Leah Turner, Lisa Page, Sheryl Friedrich, Jayne Thompson, Diane Tebrugge, Wilfred Lam, Michael Kelley, Frank Mikell, Prairie Cardiovascular Consultants. Ltd, Springfield, IL, Southern Illinois University School of Medicine, Springfield, IL

Background: Inter-hospital transfer of ST elevation myocardial infarction (STEMI) patients (pts) for primary percutaneous revascularization (PPCI) are increasingly being established in United States. The clinical utility and financial impact of these programs have been questioned because of inherent delays leading to prolonged door-balloon times and increased resource utilization. In this study, we examined the impact of a coordinated inter-hospital transfer program on overall process of STEMI care and financial outcomes.
Methods: In 2005, we established a STEMI inter-hospital PPCI program between 6 STEMI-Referral hospitals and 2 STEMI-Accepting hospitals in Central Illinois. Between 2005 and 2007, 188 STEMI-confirmed pts have been treated (STAT Heart). Before initiation of this program (2003-2004), 389 STEMI-confirmed pts were transferred for care (Pre STAT Heart).
Results:

Comparison of Variables before and after initiation of STAT Heart Program			
	STAT Heart (n= 188)	Pre STAT Heart (n=389)	p-value
Primary PCI (%)	87	10	<0.0001
Thrombolytics (%)	8.5	62.7	0.001
No initial reperfusion strategy (%)	0	19.3	<0.0001
Door - Needle(median minutes)	28 (23, 35)	35 (22, 57)	ns
Door - Balloon (median minutes)	117 (99, 137)	235 (199, 313)	<0.0001
Bleeding Complications (%)	3.7	13.1	<0.0001
Death+ReMI+Stroke (%)	4.8	8.7	<0.0001
Length of Stay (mean±SD)	3.8±4	5.4±9	<0.0001
Total cost in $ (mean±SD)	19708.3±15108.4	26839.3±3638.3	<0.0001

Helicopter was used for inter-hospital transport in 68.1% STAT Heart patients vs 44.2% patients in pre STAT Heart (p=<0.0001).
Conclusions: As compared to Pre-STAT Heart, the establishment of this coordinated rural inter-hospital STEMI transfer program significantly reduced door-balloon times, length of hospitalization and contributed to achievement of greater number of patients recieving reperfusion therapy with resultant improvement in in-hospital clinical outcomes . Despite, increased resource utilization (i.e. PPCI and helicopter transport), total hospital cost were significantly reduced.

11:00 a.m.

1017-76 **Bleeding and Ischemic Events Run Parallel in NSTEMI Patients**

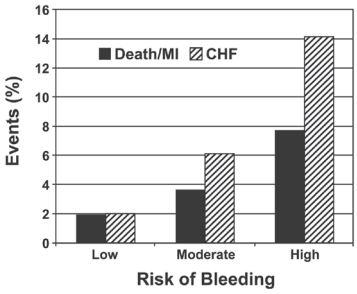
Karen P. Alexander, Richard G. Bach, Anita Y. Chen, Sumeet Subherwal, Brian F. Gage, Sunil V. Rao, W. Brian Gibler, Charles V. Pollack, Jr., E. Magnus Ohman, Matthew T. Roe, Eric D. Peterson, Duke Clinical Research Institute, Durham, NC, Washington University in St. Louis School of Medicine, St. Louis,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

Background: Bleeding and ischemia are both important considerations when selecting among treatment options for NSTEMI patients (pts). The ability to distinguish between these risks at the pt level has not been explored.
Methods: The CRUSADE Bleeding Score combines 9 patient characteristics, lab values, and vital signs (HCT, CrCl, heart rate, systolic BP, weight, diabetes, peripheral vascular disease, signs of HF, female sex) by assigning a weighted value for each variable in a

nomogram predicting risk for in-hospital bleeding (score range 1-100). With the score, 71,277 CRUSADE pts were stratified into tertiles of bleeding risk (low risk 1-16, moderate risk 17-32, high risk 33-88 points). Patient characteristics and in-hospital outcomes were assessed across tertiles.

Results: Major bleeding occurred in 3.3% of low-risk (n=23,693), 8.1% of moderate-risk (n=22,780), and 16.9% of high-risk (n=23,259) groups. Mean age (57.4, 67.5, 76.1 y), female sex (10.6, 44.0, 64.7%), comorbidity (diabetes: 13.6, 33.2, 51.8%; renal insufficiency: 1.3, 6.8, 32.5%), and disease acuity (heart rate: 75.8, 86.4, 97.2 bpm; signs of CHF: 2.1, 15.9, 51.1%) all increase respectively from low- to high-risk groups. In-hospital death or MI and CHF are shown (Figure, p<.0001).

Conclusions: Patients at high-risk for bleeding are also at high risk for ischemic events and CHF, largely due to their shared predictors. These outcomes, therefore, should not be viewed in isolation when selecting treatments for this population.



11:00 a.m.

1017-77 **Clinical Characteristics and In-Hospital Outcomes of Patients Undergoing Rescue Percutaneous Coronary Intervention Compared to Primary Percutaneous Intervention**

Sukesh C. Burjonroppa, Paul D. Varosy, Matthew Roe, Eric Peterson, Fang-Shu Ou, Sunil V. Rao, Mandeep Singh, Kendrick A. Shunk, For the National Cardiovascular Data Registry, University of California San Francisco, San Francisco, CA, Duke Clinical Research Institute, Durham, NC

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 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 30,690 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. Clinical characteristics and in-hospital outcomes are shown in Tables 1 and 2.

Conclusion: When compared to the primary PCI cohort, rescue PCI patients were at higher risk of heart failure, stroke and death. The risk of bleeding did not differ despite more than half the rescue patients receiving potent anti-platelet regimens in the setting of fibrinolytic therapy.

Table1. Clinical characteristics

	Primary PCI (n=30690)	Rescue PCI (n=2829)	p Value
Age	61±13	59±12	<0.0001
Male	21620(70)	2102(74)	<0.0001
Caucasian	26469(86)	2496(88)	<0.0001
BMI	28.7±6	29.1±6	0.03
Diabetes	6452(21)	568(20)	0.03
Cerebrovascular disease	2096(6.8)	146(5.2)	0.005
Peripheral Vascular disease	2011(6.6)	144(5.1)	0.02
Smoking	20423(66.5)	1982(70)	<0.0001
Prior PCI	5254(17)	425(15)	0.005
IABP	3331(11)	372(13)	<0.0001
LVEF	46.1±12.7	45.2±12.4	0.04
Table 2. In-hospital outcomes			
Mortality	1570(5.35)	170(6.2)	0.006
Cardiogenic shock	993(3.3)	124(4.5)	0.14
Congestive heart failure	941(3.1)	138(5.0)	0.0001
Stroke	167(0.6)	54(2.0)	0.0001
Tamponade	108(0.4)	35(1.3)	0.47
Post procedure TIMI 3 flow	28450(92.7)	2583(91.3)	0.004
No reflow phenomenon	943(3.1)	156(5.5)	<0.0001
Acute closure	317(1)	47(1.7)	0.008
Bleeding	1586(5.2)	158(5.7)	0.97

Age, BMI, and LVEF are presented as mean ± STD.
The remainder are presented as frequency (percentage)

11:00 a.m.

1017-78 **Modulating Effects of Intravenous Recombinant Human Brain Natriuretic Peptide on Activation of Neuroendocrine Systems in Acute Myocardial Infarction Patients With Cardiac Dysfunction**

Xianghua Fu, Shiqiang Li, Weize Fan, Xinna Fan, Xinshun Gu, Yunfa Jiang, Ling Xue, Ling Xue, Guozhen Hao, 2nd Hospital of Hebei Medical University, Shijiazhuang, People's Republic of China

Background: To compare the modulating effects of intravenous injection of recombinant human brain natriuretic peptide (rhBNP) versus nitroglycerin (NIT) on neurohormonal activation in the early stage of patients of acute myocardial infarction with cardiac dysfunction (AMI-CDF) through a prospective study.

Methods: Forty-two anterior wall AMI-CDF patients within 12 to 24 hours from the onset were randomized into rhBNP group(n=21, 1.5μg ·kg-1 bolus, 0.0075μg·kg-1·min-1 for the first 3 hrs and 0.015-0.03μg·kg-1·min-1 infusion for following 21 hrs)and NIT group(n=21, 10 to 100μg ·min-1 infusion for 24 hours, Blood samples were taken at baseline, 6h, 24h after administration and 6h postinfusion to measure epinephrine(E), norepinephrine (NE), rennin(R), angiotensin II (AII) and aldosterone(Ald)

Results: The plasma concentration levels of E, NE, R, AII, and Ald, which were no significant differences at baseline between the two groups, were significant reduced 6h after the administration of rhBNP (240.28±77.05 vs 1191.46±360.07 pg·ml-1, 8.82±4.78vs14.20±6.42ng ·ml-1, 4.82±1.88 vs 7.69±2.75 ng·ml-1·h-1, 39.82±23.75 vs. 84.60±32.72pg·ml-1, 128.84±71.25 vs. 189.21±120.80pg·ml-1, all P<0.01), and these changes continued during the whole 24 hours of infusion, while in NIT group, they were only slightly decreased at 6h of NIT infusion, then became significant reduction at 24h of NIT infusion, but still obviously higher than those in rhBNP group (E: 685.08±176.29 vs. 216.85 ±62.47pg ·ml-1, NE: 10.64±4.70 vs. 9.28±4.35ng·ml-1, R: 5.26±2.19 vs. 4.08±1.26ng·ml-1·h-1, AII: 62.82±27.45 vs. 36.47±15.62pg·ml-1, Ald: 120.35±84.29 vs. 88.76±56.70pg·ml-1, P<0.05). 6h postinfusion, levels of above neurohormone were still lower than those at baseline in rhBNP group, which except that of NE were still lower than those in NIT group (E: 286.01±67.72 vs. 643.51±162.44pg ·ml-1, R: 4.20±2.01 vs. 5.87±2.40ng ·ml-1·h-1, AII: 56.13±21.82 vs. 78.30 ±29.75pg ·ml-1, Ald: 107.28±49.48 vs. 145.50 ± 77.01 pg ·ml-1, P<0.05).

Conclusion: Intravenous injection of rhBNP results in more rapid, stronger and longer antagonistic action against plasma levels of E, NE, R, AII and Ald than NIT does in AMI-CDF patients.

11:00 a.m.

1017-79 **Role of Embolic Protection Devices in Acute Myocardial Infarction. Is Their Routine Use of Clinical Benefit at Six Months?**

Hector Salazar, Xavier Freixa, Neus Bellera, Ricardo Kiamco, Carlos Fernández, Amadeo Betriu, Mònica Masotti, Thorax Institute - Hospital Clinic, Barcelona, Spain

Background: Thromboembolic debris liberated during primary angioplasty (PCI) might worsen clinical outcomes. Individual randomized control trials (RCT's) on the use of thrombectomy or distal protection and aspiration devices in STEMI have documented improvement in ST-segment resolution or myocardial perfusion. Although no clinical benefit has consistently been demonstrated at 1 month, longer follow-up data are lacking.

Objective: To combine data from all RTC's using these devices in the setting of STEMI. The primary end-point of this investigation was to asses the potential impact on death, reinfarction (reMI), or both at 6 months.

Methods: Data from seven RCT's (X AMINE ST, De Luca, DEAR-MI, ASPARAGUS, DIPLOMAT, EMERALD, PREMIAR) were analyzed. The study population included 1456 patients; of them, 733 were randomized to active treatment whilst the remaining 723 were controls.

Results: Clinical outcomes were as follows:

Conclusion: Embolic protection devices in STEMI patients undergoing PCI does not decrease the risk of death or reinfarction at 6 months. Therefore, routine use of this adjunctive therapeutic armamentarium does not appear warranted at the present time.

	Death	reMI	Death/reMI
Thrombectomy & Aspiration n= 425	1.88% vs. 2.81%*	0.94% vs. 1.4%	2.83% vs. 4.2%
	0.69 (0.2-2.34)**	0.71 (0.14-3.68)	0.66 (0.23-1.9)
Distal protection n= 1031	2.87% vs. 3.7%	1.15% vs. 2.74%	4.03% vs. 6.47%
	0.77 (0.38-1.53)	0.45 (0.18-1.1)	0.61 (0.35-1.06)
All n= 1456	2.6% vs. 3.45%	1.09% vs. 2.3%	3.68% vs. 5.8%
	0.75 (0.41-1.36)	0.5 (0.23-1.1)	0.62 (0.38-1.01)
* Active vs. control	** Odds ratio (95% confidence interval)		

11:00 a.m.

1017-80 **Arterial Access and Door-to-Balloon Times for Primary Percutaneous Coronary Intervention in Patients Presenting with Acute ST-Elevation Myocardial Infarction**

Rick A. Henderson, Ian Gilchrist, 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-balloon; D2B). For patients undergoing primary PCI for acute STEMI, potential benefits of r-PCI as 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 this analysis. Specific time parameters measured included: door-to-ECG, ECG-to-HA activation, HA 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=47 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 contrast used (r-PCI 168cc vs. f-PCI 189cc).
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.

11:00 a.m.

1017-83 **Long-term Outcome of Primary Angioplasty Compared with Fibrinolysis across Age groups: A DANAMI-2 substudy**

Emil L. Fosbol, Jens J. Thune, Henning Kelbaek, Henning R. Andersen, Kari Saunamäki, Torsten T. Nielsen, Leif S. Mortensen, Lars Kober, The 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. Follow-up was 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<0.0001) and composite event rate (adjusted HR=1.47, CI:1.23-1.75, p<0.0001). The long-term superiority of angioplasty over fibrinolysis on the combined outcome 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 <56, 56-65, 66-75 and >75 years, 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.

11:00 a.m.

1017-84 **The Relative Contribution of Clinical Factors, Treatments, Bleeding, and CV Complications to Mortality in 20,323 Patients Receiving Fibrinolysis for STEMI**

Robert P. Giugliano, Roberto R. Giraldez, David A. Morrow, Elliott M. Antman, C. Michael Gibson, Satishkumar Mohanavelu, Sabina A. Murphy, Carolyn H. McCabe, Eugene Braunwald, Brigham and Women's Hospital, Boston, MA

Background: In ExTRACT-TIMI 25, enoxaparin death/MI (9.9 vs 12.0%, P<0.001), ↑ major bleeds (2.1 vs 1.4%, P<0.001) but not ICH (0.83 vs 0.65%, P=0.14), improving net clinical benefit (death/MI/ICH: 10.1 vs 12.2%, P<0.001) c/w UFH in STEMI pts receiving lytic. We explored how pt and clinical factors contributed to mortality.
Methods: We used Cox models to predict death (30d, 1yr) in 20,323 ExTRACT-TIMI 25 pts who rec'd lytic and antithrombin, using 5 covariate groups: pt characteristics, antithrombotic Rx, revasc, major bleed (ICH, non-ICH bleed with hgb >5 g/dL), CV events. We used the Likelihood Ratios (LR) of covariates to estimate their model contribution.
Results: ICH (HR 12.4, LR=295) and non-ICH major bleeds (HR 2.2, LR=14) were associated with 30d death in the unadjusted model (both P<0.001). In the adjusted model, ICH (HR 9.2, P<0.0001) but not non-ICH major bleeds (HR 1.03, P=0.91) were associated with 30d death (Table). Cardiogenic shock (c-shock) strongly influenced the relationship between non-ICH bleeds and death (adj HRs: c-shock/no bleed 19.2, c-shock then bleed 14.6, bleed then c-shock 4.7 [all P<0.001]). 1-year mortality models were qualitatively similar.
Conclusion: Cardiogenic shock, age, ICH, heart rate, and no revascularization predischarge are the strongest independent correlates of death in STEMI pts receiving lytic. Non-ICH major bleeding is not associated with death after controlling for pt and clinical factors, particularly antecedent c-shock, in lytic-treated STEMI pts.

Key Variables from the Cox Model Predicting Death Through 30 Days			
Covariate	HR (95% CI)	LR	Mortality Contribution
Cardiogenic Shock	14.6 (12.6, 17.0)	1691	68%
Age (per decade↑)	1.5 (1.4, 1.6)	362	15%
ICH	9.2 (7.0, 12.1)	135	5.4%
HR (per 10BPM↑)	1.13 (1.09, 1.17)	81	3.3%
No Revasc predischarge	2.1 (1.7, 2.7)	61	2.5%
Severe CHF	2.0 (1.5, 2.6)	29	1.2%
Enoxaparin	0.88 (0.77, 0.99)	3.8	0.2%
Non-ICH major bleed	1.03 (0.65, 1.62)	1.3	0.05%
P<0.0001 for each except enox (P=0.039), non-ICH major bleed (P=0.91). 7 other independent covariates had small (<1%) contributions.			

11:00 a.m.

1017-85 **The Impact of Gender on the Outcomes of Invasive versus Conservative Treatment of Patients with Acute Coronary Syndrome**

Li Ching LEE, Poh Leng, Tiffany Tang, Yee Leng Tan, Han Wen Tee, Luming Shi, Kian Keong Poh, Huay Cheem Tan, Cardiac Department, National University Hospital, Singapore, Singapore

Background: Recent data has suggested that women who presented with non ST-elevation myocardial infarction (NSTEMI) did not benefit from early invasive strategy. We examined the impact of gender difference in patients with NSTEMI with respect to outcomes following invasive versus conservative treatment.
Methods: Patients enrolled in our national MI registry between January 2000 and September 2005 with diagnosis of NSTEMI was retrospectively analyzed. The study end points were mortality rates during hospitalization and at 1 year; and reinfarction at 1 year.
Results: A total of 1472 patients (63.5% female) with NSTEMI were studied. The mean age of men was 62.2±13.6 years old versus 71.5±11.8 years in women. The prevalence of hypertension, hyperlipidaemia, and diabetes mellitus were significantly higher in women. Men were more likely to undergo percutaneous coronary intervention (PCI) than women (OR 2.65, 95% CI 1.99-3.54, p <0.001). Among those who underwent PCI, there was no gender difference in survival and reinfarction rates during hospitalisation and at 1 year. However, there were more in-hospital cardiovascular complications of heart failure, arrhythmias, periprocedural MI in women who underwent PCI (OR =1.82, 95% CI 1.01-3.13, p=0.03). In the medically treated group, the difference was even greater (OR =1.86, 95% CI 1.38-2.45, p<0.001). Compared with medical therapy, PCI was associated with a significant reduction in 1-year mortality or reinfarction in women (HR 15.7, 95% CI 3.8 to 65.1) and men (HR 8.6, 95% CI 4.7 to 15.9). The most important predictor of adverse events for females was diabetes (HR = 0.41; 95% CI= 0.25-0.66).
Conclusions: There is a gender-based difference in the rate of PCI among patients with NSTEMI. Women benefit from an invasive approach but have higher rate of attendant cardiovascular complications. Mortality associated with reperfusion treatment is independent of gender.

11:00 a.m.

1017-86 **Pre-hospital Electrocardiograms: Potential Answer to the Time to Reperfusion Challenge**

Deborah B. Diercks, Joseph Lynch, Michael C. Kontos, John S. Rumsfeld, Anita Y. Chen, W. Brian Gibler, Christopher P. Cannon, Steven D. Wiviott, Charles V. Pollack, Jr., David J. Magid, Matthew T. Roe, University of California Davis School of Medicine, Sacramento, CA, Duke Clinical Research Institute, Durham, NC

Background: Current ACC/AHA guidelines and the nationwide Door to Balloon (D2B) Initiative advocate pre-hospital electrocardiograms (ECGs) to accelerate the identification of patients with ST-segment elevation myocardial infarction (STEMI) by Emergency Medical Services (EMS). However, the current use of pre-hospital ECGs for the triage of STEMI patients has not been evaluated.
Methods: We evaluated nontransfer-in patients with STEMI who received reperfusion therapy (n = 4138) included in the NCDR ACTION registry from 202 U.S. hospitals between January 1, 2007, and June 30, 2007, to determine the use of pre-hospital ECGs (any ECG done prior to arrival in the emergency department [ED]) and the association of pre-hospital ECGs with reperfusion times. Continuous data are presented as median (25th, 75th percentile) times.
Results: Among the analysis population, 2417 patients (58.4%) were transported to the ED by EMS, of whom 728 patients (17.6%) received a pre-hospital ECG. Primary percutaneous coronary intervention (PCI) was performed in 3906 patients (94.4%) while the remainder received fibrinolytic therapy. Median door-to-needle time was significantly shorter among patients with a pre-hospital ECG (18 min [10, 30] vs. 28 min [20, 47], p=0.03). In patients receiving primary PCI, use of a pre-hospital ECG resulted in significantly shorter median D2B times (63 min [49, 83] vs. 81 min [64, 106], p<0.0001).

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 are 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 used, 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.

1017-87 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 into 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. Leukotrien 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 (M±m). [* - <0,05 compared with the 1st day value; ESVI, EF - changes in end-systolic, end-diastolic volume indexes 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; ISI - infarct size index].
Conclusions: These findings suggest that intravenous form of lipoxygenase inhibitor Q in AMI pts with successful reperfusion reduces final infarct size and improves heart function. Obtained cardioprotective effect of Q was accompanied by decreases proinflammatory activation and induces VEGF expression.

	Quercetin gr. (n=54)	Control gr. (n=37)	P
ΔESVI (%)	- 10.1*	- 4.5	
ΔEF (%)	+ 13,3*	+ 8.4	
CK-MB time of peak (h)	8.9±0.3	9.0±0.3	
N time (h)	32.2±1.3	37.1±1.4	P<0.05
ISI (g/equivalent)	45.3±2.1	52.2±2.1	P<0.05
CRP (%)	- 67.4*	- 42.1	
LTC4 (%)	- 30.2*	- 3.9	
vWF (%)	- 38.8*	- 16.0	
VEGF (%)	+ 266.9*	+ 83.3	

11:00 a.m.

1017-88 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 Beygui, Olivier Barthelemy, Raphaelle Dumaine, Nicolas Vignolles, Delphine Brugier, Sophie Gallier, Gilles Montalescot, IHopital Pitie-Salpetriere 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 assigned to receive either 300 mg, 600mg or 900mg of clopidogrel as initial reloading dose. Four hours later, a second loading dose was administered (600, 300 or nothing respectively) to achieve a final loading dose of 900mg 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 20µMol 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 4 hours in patients assigned to an initial load of 300mg vs 600 mg vs 900mg (30.7% vs 40.3% vs 64.0%, 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.

ACC.ORAL CONTRIBUTIONS

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, Luc Janssens, H.R. Andersen, Amadeo Betriu, Stefano Savonitto, Jerzy Adamus, 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 half 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-facilitated 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 ventricular fibrillation > 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 ace 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"

1:15 p.m.

806-6 **SR123781A, a Synthetic Antithrombin-Dependent Thrombin and Factor Xa Inhibitor, in Patients with Non-ST-segment Elevation Acute Coronary Syndromes (NSTEACS): Results of an Active-Controlled, Dose-Ranging Study**

A. Michael Lincoff, Paulo Caramori, Paul W. Armstrong, Fernando A. Cura, Judith S. Hochman, Neal S. Kleiman, Frans Van de Werf, Luis O. Carreras, Dianna L. Bash, John M. Galla, Eric J. Topol, Cleveland Clinic, Cleveland, OH

Background: SR123781A, a synthetic hexadecasaccharide, is a potent antithrombin-dependent inhibitor of factors IIa 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 5000 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						
	SR123781A 0.25mg (N=115)	SR123781A 0.5mg (N=122)	SR123781A 1mg (N=116)	SR123781A 2mg (N=298)	SR123781A 4mg (N=305)	UFH/abciximab (N=287)
1° Endpoint ITT population n=1,243 (p=0.75)	5.2%	4.1%	3.4%	3.7%	4.3%	3.8%
1° Endpoint PCI population n=775 (p=0.94)	7.5%	3.8%	5.4%	4.8%	5.9%	3.3%
TIMI Major Bleeding (p=0.75)	2.6%	1.6%	1.7%	2.4%	1.6%	1.0%
TIMI Major/Minor Bleeding (p=0.43)	3.4%	5.7%	6.0%	5.8%	5.9%	4.9%
PCI thrombotic complications (p = 0.0003 for dose effect)	11.9%	11.3%	6.8%	3.6%	2.4%	2.7%

"Abstract withdrawn by author"

1:30 p.m.

806-7 **Intracoronary Compared with Intravenous Bolus Abciximab Application in Patients with ST-Elevation Myocardial Infarction Undergoing Primary Coronary Intervention**

Holger Thiele, Kathrin Schindler, Josef Friedenberger, Ingo Eitel, Georg Fürnau, 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 90 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.c. versus 24.7% i.v., 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.

1:45 p.m.

806-8 **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 thrombois 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.
Methods: We examined temporal patterns of DES vs. BMS use in patients with non-ST-elevation MI (NSTEMI) by quarter (1/06-6/07) in the CRUSADE and ACTION national registries. CRUSADE ended in December 2006 and transitioned to ACTION, which began data collection in January 2007. NSTEMI patients who underwent PCI during the initial hospitalization were analyzed by quarter among hospitals that submitted data during all 4 quarters of 2006 (CRUSADE) and during both the first and second quarters of 2007(ACTION).
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.

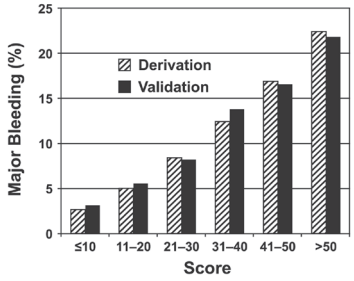
	CRUSADE				**ACTION**	
Quarter and Year	**Q1 06**	**Q2 06**	**Q3 06**	**Q4 06**	**Q1 07**	**Q2 07**
Number of patients	5505	5602	5333	4654	6563	6353
Patients undergoing PCI	43.4%	44.5%	45.4%	45.6%	45.7%	46.6%
Drug-eluting stent *	91.9%	90.4%	89.5%	81.6%	66.7%	63.3%
Bare-metal stent*	8.1%	9.6%	10.5%	18.4%	33.3%	36.7%
*Percentages calculated among those patients undergoing PCI						

2:00 p.m.

806-09 **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=.72 and validation C=.71), and scoring system (derivation C=0.70 and validation C=.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.



2:15 p.m.

806-10 **Questions and Answers**

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

3:00 p.m.

1024-41 **What is the Effect of Late Revascularization of a Totally Occluded Infarct-Related Artery?**

Andrew N. Rassi, Anthony A. Bavry, 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, 95% CI 0.72 to 1.41, p = 0.98), heart failure was 4.0% and 5.2% (RR = 0.59, 95% CI 0.29 to 1.22, p = 0.18), non-fatal myocardial infarction was 5.1% and 3.8% (RR = 1.36, 95% CI 0.95 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 = 0.26) while the incidence of persistent occlusion was 19.4% versus 74.0, 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.

3:00 p.m.

1024-42 **Improvements in Time to Reperfusion: Women Have an Advantage**

Veena S. Rao, Basmah Safdar, Veronica Lee, Janet Parkosewich, Gail D'Onofrio, JoAnne M. Foody, Yale University, New Haven, CT

Background: Several studies demonstrate that women have greater delays in primary percutaneous coronary intervention (PCI). To improve cardiovascular care for women, the Women's Heart Advantage (WHA) at Yale-New Haven Hospital (YNHH) developed patient and physician level interventions to improve early diagnosis and management of acute coronary syndrome (ACS) in women presenting to the emergency department.
Methods: We analyzed chart-abstracted data from all patients undergoing PCI for ST-elevation myocardial infarction (STEMI) at YNHH from January 2004-July 2007 and assessed quality of care for ACS in addition to trends in time to reperfusion. WHA and YNHH orchestrated several clinical initiatives as well as instituted hospital-wide systems to improve ACS care over these 31 months.
Results: Both men and women had declines in time to reperfusion (91 to 73 minutes and 120 to 74 minutes for men and women, respectively). Notably, improvements in time to reperfusion were more substantial in women; the greatest improvement was a reduction in the door-to-table time (50% decrease in women compared with 19% decrease in men [p<0.05]).
Conclusion: In this single-site study of men and women undergoing primary PCI at a large, urban teaching hospital, where ongoing interventions to increase both patient and physician awareness regarding heart disease in women were initiated, time to reperfusion for women improved to a greater degree than in men. These results are encouraging, showing that significant improvements in time to reperfusion can be made over a relatively short time frame. It is hoped that these reductions in time to reperfusion, particularly in women, are associated with improved outcomes; however, further studies are needed to verify this potential benefit.

3:00 p.m.

1024-43 **Efficacy and Safety of Early Clopidogrel Administration with or without Abciximab in Patients with ST-Segment Elevation Myocardial Infarction Transferred for Primary PCI. Results from the EUROTRANSFER Registry**

Jacek Legutko, Tomasz Rakowski, Zbigniew Siudak, Lukasz Rzeszutko, Magnus Janzon, Ralf Birkemeyer, Pawel Kleczynski, Dariusz Dudek, Jagiellonian University Medical College, Krakow, Poland

Background: Pre-treatment for primary PCI (pPCI) with 600 mg loading dose (LD) of clopidogrel is indicated by ESC guidelines. However, the efficacy and safety of early clopidogrel LD administration (before admission to cath lab) in patients with ST-segment elevation myocardial infarction (STEMI) remains unclear.
Methods: Consecutive data on 1,650 STEMI patients transferred for pPCI were gathered from 7 countries in Europe. We compared the rates of 30-day major adverse cardiac events (MACE) and bleedings in four groups of patients, according to early antiplatelet treatment: aspirin (Group 1, n=553), aspirin + clopidogrel LD (Group 2, n=370), aspirin + abciximab (Group 3, n=580), aspirin + clopidogrel LD + abciximab (Group 4, n=147).
Results: There was no difference between study groups according to baseline clinical characteristics. Rates of MACE are shown in table. Early administration of 600 mg LD of clopidogrel with aspirin and abciximab was an independent predictor of bleedings (Odds Ratio [OR], 4.62; 95% CI, 1.67-12.82; P=.003), including puncture site hematoma (OR, 3.57; 95% CI, 1.25-10.20; p=.017), and major bleedings requiring transfusion (OR, 11.34; 95% CI, 1.55-82.79; P=.017).
Conclusions: Early administration of clopidogrel LD in addition to aspirin and to aspirin + abciximab decreases the risk of 30-day MACE in STEMI patients transferred for primary PCI. However, early administration of 600 mg LD of clopidogrel with aspirin and abciximab significantly increases the risk of bleedings.

MACE from diagnosis to 30 days					
	Group 1	Group 2	Group 3	Group 4	P-value
Death, %	7.1	5.7	4.3	2.0	0.053
Death + ReMI, %	9.6	6.5	5.7	2.0	0.004
Death + ReMI + Revascularization, %	10.1	7.3	6.2	2.7	0.002

3:00 p.m.

1024-44 **Attenuated Soluble P-selectin Levels by Treatment with an Oral Direct Thrombin Inhibitor in Patients with Recent Myocardial Infarction**

Christina Christersson, Jonas Oldgren, Lars Wallentin, Agneta Siegbahn, Department of Medical Sciences, Uppsala, Sweden

Background: Acute myocardial infarction (MI) is a thrombotic complication with platelet and coagulation activity. Thrombin is a powerful platelet activator and we aimed to investigate whether treatment with an oral direct thrombin inhibitor will affect platelet

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

Treatment	Increase (%) in sP-selectin 1 week	Increase (%)in sP-selectin 6 months
Placebo n=179	15 (10-35)	16 (10-35)
Ximelagatran 24-36mg n=158	13 (10-32)	12 (9-31)
Ximelagatran 48-60mg n=174	7 (9-22)†	7 (9-26)
p*	0.002	0.02

* Mann Whitney U-test comparing the 40-60mg ximelagatran group and the placebo group. †p=0.01 comparing the two ximelagatran groups.
Conclusions: There is an increase in soluble P-selectin levels up to six months after an acute MI despite treatment with aspirin. This might indicate increased platelet activity after cessation of the acute antithrombotic treatment for the index MI. Long-term treatment with an oral direct thrombin inhibitor significantly attenuates platelet activity in a dose dependent manner.

3:00 p.m.

1024-45 The role of pre-procedural N-terminal pro B-type natriuretic peptide level in patients with acute ST-segment elevation myocardial infarction who underwent primary percutaneous coronary intervention

Youngkeun Ahn, Seo Na Hong, Nam Sik Yoon, Hyun Ju Yoon, Jae Yeon Moon, Kye Hun Kim, Young Joon Hong, Ju Han Kim, Hyung Wook Park, Myung Ho Jeong, Jeong Gwan Cho, Jong Chun Park, Chonnam National University Hospital, Gwangju, South Korea

Background: The aim of this study was to assess the relation between pre-procedural N-terminal pro-B-type natriuretic peptide (NT-proBNP) and angiographic no-reflow phenomenon and improvement of left ventricular (LV) systolic function in patients who underwent primary PCI.
Methods: We enrolled 163 patients (60.4±11.4 years, male 79.7 %) with LV systolic dysfunction [defined as an echocardiographic LV ejection fraction (EF) <45 %] who underwent primary PCI for acute STEMI. The level of NT-proBNP was measured on admission and before PCI. Angiographic no-reflow after PCI was defined as TIMI flow grade <3. All patients with no-reflow received intracoronary injection of nicorandil and adenosine after no-reflow. The follow-up LVEF was measured at 9.1±4.2 months after PCI.
Results: The baseline characteristics between the groups with no-reflow group (n=55) and normal reflow group (n=92) are similar. The level of NT-proBNP was significantly higher in the no-reflow group than that in the normal reflow group (2879.9±2198.2 vs. 1270.5± 1627.8 pg/mL, p=0.022). The LVEF was improved more significantly in normal reflow group (42.5 to 52.9 % vs. 43.8 to 47.9 %, p=0.017). In no-reflow group, the group was divided according to LVEF recovery at follow up: LVEF recovery group (n=30) and LVEF no-recovery group (n=25). The baseline LVEF was similar between the groups (42.6±2.2 vs. 40.1±3.1 %, p=0.558), but at follow-up LVEF was significantly higher in LVEF recovery group compared with that in LVEF no-recovery group (51.5±1.5 vs. 41.2±5.6 %, p=0.007). The baseline NT-proBNP level was significantly higher in LVEF no-recovery group than that in LVEF recovery group (3209.3±1946.6 vs. 1990.7±862.3 pg/mL, p=0.048). In multivariate analyses, baseline NT-proBNP level was the independent predictor for angiographic no-reflow phenomenone (odds ratio, 4.04; 95% CI 1.33 to 12.28, p=0.014) and no-recovery of LVEF in patients with no-reflow (odds ratio, 3.24; 95% CI 1.01 to 10.43, p=0.013).
Conclusions: Baseline NT-proBNP level is a strong predictor for development of no-reflow phenomenon and no-recovery of LVEF in acute STEMI patients who underwent primary PCI.

3:00 p.m.

1024-46 One Year Mortality of Patients with ST-Elevation Myocardial Infarction: Primary PCI versus Thrombolytic Therapy in the VIENNA-STEMI Registry

Karim Kalla, Guenter Christ, Ronald Karnik, Reinhard Malzer, Georg Norman, Herbert Prachar, Wolfgang Schreiber, Gerhard Unger, Helmut Glogar, Alfred Kaff, Anton Laggner, Gerald Maurer, Johannes Mlczoch, Joerg Slany, Heinrich Weber, Kurt Huber, 3.Dept. Med. Wilhelminenhospital, Vienna, Austria

Background and Aim: In several trials and large registries the impact of reperfusion strategy, either primary PCI (PPCI) or Thrombolytic Therapy (TT), and time to treatment in patients (pts) with acute STEMI on late clinical outcome have been discussed controversely. The aim of this study was to compare one-year mortality rates of pts treated either with PPCI or TT and the influence of time from onset of symptoms to treatment on late mortality.
Patients and Methods: All consecutive pts with an acute STEMI of < 12 hours (h) duration presenting at the participating PCI centers between March 2003 and December 2004 were included (n=1053). Impact of time to treatment (onset of pain to 1st balloon inflation or injection of the thrombolytic agent) on one-year mortality was investigated according to different time delays: < 2 h from onset of pain or > 2 h, respectively.
Results: Of the 1053 consecutive pts 18 were lost to long term follow up. Of the remaining 1035 pts (61,9±13,5 yrs; m/f=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 24,8% in this group. One-year mortality of patients treated within 2 hours after symptom onset was lower compared to mortality rates of patients treated later in both reperfusion groups. (PPCI ≤ 2 hours: 10% vs. > 2 hours 12.1%; TT ≤ 2 hours: 5.7% vs. > 2 hours: 18.2%;) with a trend in favour of TT over PPCI in the very early treatment period (p=0.236). 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.

1024-47 The Gender Gap in Door-to-Treatment Time and Outcomes in Acute ST Segment Myocardial Infarction

Elizabeth Z. Grey, Norma L. Thiessen, Timothy D. Henry, Denise Widenburg, Catherine A. Pastorius, Sue 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 asssess clinical variables in women and men who underwent 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 non-PCI capable community hospitals within 210 miles between 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 our center.
Results: Of the 1,665 patients, 28% (n=463) were women whose average age was 68.6+/-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-65%; men-52%, p<0.0001), fewer were current smokers (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 and 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.

1024-48 Predictors of Prehospital Delay Time in Acute ST-Elevation Myocardial Infarction

Carlos T. Aguiar, Jorge S. Ferreira, Investigators of the Portuguese Registry of AcuteCoronary 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 ST-elevation MI included in a nationwide registry and explored the relation between prehospital delay and age, gender, body mass index, hour (0-8h vs 8-24h) 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 (16.5%). 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, 1.14-1.81), 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 1.90; 95% CI, 1.55-2.33). Hospital mortality was 8.7% overall (245 deaths), and higher among Pts with a prehospital delay >2 hrs: 9.6% vs 6.7% when prehospital delay was ≤2 hrs (OR 1.49; 95% CI, 1.10-2.02).
Conclusions: Prehospital delay for ST-elevation MI is far from being optimal and is particularly long in the elderly, diabetics, and Pts with prior history of angina or for whom symptoms began during the night. Strategies aimed at improving prognosis of ST-

elevation MI should target these Pt subgroups in a more aggressive manner.

3:00 p.m.

1024-49 Systematic Bayesian Meta-Analysis Evaluating Cardiac Outcomes of Low Molecular Weight Heparin Versus Unfractionated Heparin Therapy in Patients With ST Elevation Acute Myocardial Infarction

Christopher Lang, Zafeer Baber, Mujtaba Ali, Phillip Tseng, Rohit R. Arora, Chicago Medical School, North Chicago, IL

Background: Several recent trials have compared the low molecular weight heparins (LMWHs) to unfractionated heparin (UFH) in patients with acute myocardial infarction (AMI). The results of these trials suggest a benefit conferred to LMWH versus UFH, yet the extent of this benefit is unclear. In order to elucidate the degree of this advantage, we conducted a systematic Bayesian meta-analysis with evaluation of the cardiovascular outcomes in post-AMI patients using LMWHs and UFHs.
Methods: A Bayesian meta-analysis of seven randomized trials totaling 27,604 patients was performed. The trials evaluated the efficacy of LMWHs or weight-based UFH in patients with ST-AMI who were treated with fibrinolytic therapy. The endpoints evaluated included mortality and reinfarction at both 7 and 30 days. Bayesian probabilities of benefit, and a sensitivity analysis of LMWH compared to UFH in ST-AMI were computed.
Results: The results of the Bayesian meta-analysis indicate that use of LMWH is associated with a greater than 90% likelihood of benefit compared to UFH for each of the endpoints. LMWH has a probability of benefit (Pb) of 0.944 for 7 day incidence of mortality, sensitivity analysis indicates a modest probability of a greater than 10% benefit (Pb (>10%) = 0.445). Similarly, the Pb for 30 day incidence of mortality is 0.945, while the Pb (>10%) is 0.39. Reinfarction at 7 days is associated with a Pb of 0.997 and a Pb (>50%) benefit equal to 0.954. At 30 days, incidence of reinfarction using LMWH is associated with a Pb of 0.997, and a Pb (>50%) benefit of 0.905.
Conclusions: The Bayesian meta-analysis we report confirms that patients with ST-AMI undergoing fibrinolytic therapy are more likely to benefit from using LMWH than UFH in terms of reduced incidence of mortality and reinfarction. However, the Bayesian meta-analysis indicates LMWH is unlikely to provide a clinically significant reduction in mortality. The analysis indicates the superiority of LWMH in the reduction of reinfarction compared to UFH. Thus, the Bayesian statistics generated suggest that LMWH can achieve a clinically important reduction in reinfarction in patients with acute ST-AMI, while providing a marginal benefit in reducing mortality.

3:00 p.m.

1024-50 Treatment of Spontaneous Coronary Dissection Presenting as Acute Myocardial Infarction

Charles X. Kim, Patricia J.M. Best, Mayo Clinic, Rochester, MN

Background: Spontaneous coronary artery dissection is a poorly understood phenomenon that often occurs outside the context of atherosclerotic coronary disease. The acute presentation can mimic signs and symptoms of traditional acute coronary syndrome, including biomarker elevation and electrocardiographic changes. It is unclear what the optimal therapeutic strategy entails. We sought to further characterize the initial presentation, comorbid conditions, angiographic anatomy, initial treatment strategy, and outcomes on follow-up.
Methods: The Mayo Clinic electronic medical record (1996-2007) was queried for the intersecting terms “spontaneous” and “coronary artery dissection.” All patients with detailed description of spontaneous coronary dissection were included. Follow-up data were obtained from the subsequent electronic medical record.
Results: 21 unique patients were identified. The median age was 44 years at presentation. 90% were female and 95% had chest pain / pressure as a presenting symptom with clinical evidence of myocardial infarction (ST-elevation or cardiac biomarker elevation). Patients received standard therapies for ACS, including aspirin and heparin. 33% of patients received thrombolytics and 11% received gpIIb/IIIa antagonists. On angiography, 81% involved a single vessel, with the LAD being involved 62% of the time. Nondissected arteries were largely free of coronary disease, with predominantly “normal” appearance. No female patients had stenosis >20% by diameter in uninvolved arteries. Treatment entailed coronary stent (38%), emergency CABG (14%), or medical therapy alone (52%). Subsequent dissection and myocardial infarction were uncommon after the index hospitalization. Only one patient died (non-coronary cause) in > 1000 months of follow-up (49 month average).
Conclusions: Spontaneous coronary dissection presenting as acute coronary syndrome with myocardial infarction is not associated with traditional coronary artery disease. However, treatment of the thrombotic complications with early revascularization and standard therapies for ACS can lead to durable outcomes and sustained survival free of repeat cardiovascular events.

3:00 p.m.

1024-51 Door-to-Balloon Times - Are We Meeting the AHA/ACC Guidelines? Results from an Australian Multicenter Registry

Christopher C. S. Lim, Andrew Teh, Louise Roberts, Nicholas Andrianopoulos, Christopher Reid, David Clark, Greg Szto, Andrew Ajani, Stephen Duffy, Box Hill Hospital, Box Hill, Australia, Melbourne Interventional Group, Melbourne, Australia

Background: Recent AHA/ACC guidelines recommend a door-to-balloon time (DTB) of 90 minutes or less. Previous studies have shown an association between longer DTB and mortality. The recent (National Registry of Myocardial Infarcts) NRMI-3 and NRMI-4 registries in the US showed that the majority of STEMI patients did not meet the guidelines target of DTB within 90 minutes. There has been no similar large registry data in an Australian setting.
Methods: Melbourne Interventional Group (MIG) is a voluntary collaborative of major hospitals with a primary PCI service in Melbourne, Australia. From April 2005 to January 2007, data was collected on primary PCI cases for the MIG registry. Door-to-balloon times and 30-day outcomes were analysed. Cardiogenic shock and rescue PCI cases were excluded.
Results: Median DTB was 105 minutes. Median DTB was longer in cases transferred from a non-PCI facility (146 minutes, n = 45) compared to cases presenting to a PCI facility (98 minutes, n = 252). Less than half (42%) of all cases met the guidelines target of DTB<90 minutes. Only 24% of transferred cases met the target of DTB<90 minutes, compared to 45% of non-transferred cases.

30-day outcomes	DTB<90 minutes n=126	DTB>90 minutes n=171	P-value
TVR	1.6% (2)	4.7% (8)	0.20
MI (CK > 3x ULN)	0.8% (1)	1.2% (2)	1.00
Mortality	1.6% (2)	4.7% (8)	0.20
MACE	3.9% (5)	10.5% (18)	0.047

Conclusions: This Australian registry shows the AHA/ACC guidelines are difficult to achieve. These real-world results are similar to that of the US NRMI-3 and NRMI-4 registries. Door-to-balloon times greater than 90 minutes resulted in increased MACE, confirming previous studies. Further ways to reduce DTB need to be examined.

3:00 p.m.

1024-52 Trends in Reperfusion Strategies, Door-to-Needle and Door-to-Balloon Times and In-Hospital Mortality among Patients with ST-Segment Elevation Myocardial Infarction Enrolled in the National Registry of Myocardial Infarction Database from 1990 to 2006

C. Michael Gibson, Yuri B. Pride, Paul D. Frederick, Charles V. Pollack, Jr., John G. Canto, Alan J. Tiefenbrunn, W. Douglas Weaver, Costas T. Lambrew, Eric D. Peterson, William J. Rogers, Beth Israel Deaconess Medical Center, Boston, MA, University of Alabama Medical Center, Birmingham, AL

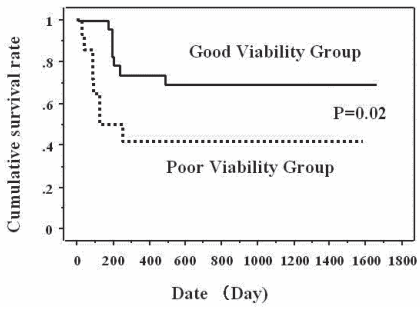
Background: Among patients with ST-segment elevation myocardial infarction (STEMI), rapid reperfusion of the infarct-related artery has been associated with improved mortality. As such, door-to-needle (DN) and door-to-balloon (DB) times have become two metrics of quality care and targets for intense quality improvement efforts.
Methods: The National Registry of Myocardial Infarction (NRMI) collected data regarding reperfusion therapy, its timing and in-hospital mortality among STEMI patients from 1990 through 2006.
Results: Since 1990, NRMI has enrolled 1,374,232 STEMI patients at 2,157 hospitals. Among those, 774,279 (56.3%) were eligible for reperfusion upon arrival to the first hospital. Since 1990, NRMI has enrolled 1,374,232 STEMI patients at 2,157 hospitals. Among those, 774,279 (56.3%) were eligible for reperfusion upon arrival to the first hospital. The proportion receiving fibrinolytic therapy fell from 52.5% in 1990 to 27.6% in 2006 (p<0.001), while the proportion undergoing primary percutaneous coronary intervention (pPCI) increased from 2.6% to 43.2%. Among those who received fibrinolytic therapy, there was a nearly linear decline in median DN time from 59 minutes in 1990 to 29 minutes in 2006 (p<0.001 for trend). This was accompanied by a significant decrease in hospital mortality from 7.0% in 1994 to 6.0% in 2006 among the fibrinolytic group (p<0.001). Among those undergoing pPCI, DB time among non-transfer patients also declined linearly from 111 minutes in 1994 to 79 minutes in 2006 (p<0.001) with a decline in mortality from 8.6% to 3.1% (p<0.001). The relative improvement in mortality attributable to improvements in DN and DB times were 16.5% and 7.7%, respectively.
Conclusions: Since 1990, there has been a progressive decline in both DN and DB time among reperfusion-eligible patients treated with fibrinolytic therapy and pPCI. These improvements have contributed, at least in part, to a progressive decline in mortality.

3:00 p.m.

1024-53 Myocardial Viability assesed by FDG-PET as a predictor of cardiac events in patients with Acute Myocardial Infarction

Masanori Tsurugida, Shuichi Hamasaki, Koichi Kihara, Ryo Arikawa, Shin Kawasoe, Chuwa Tei, Fujimoto Hayasuzu Hospital, Miyakonojyo, Japan, Kagoshima University, Kagoshima, Japan

Background: To predict cardiac events by myocardial viability has not been reported in patients with acute myocardial infarction (AMI).
Object: The purpose of this study was to examine whether myocardial viability assessed by FDG-PET in acute phase of AMI can be a predictor of cardiac events in patients with AMI.
Methods: A total of 37 patients with reperfused first anteroseptal AMI were studied. FDG-PET was perfomed 2 weeks after PCI. Myocardial viability was assessed by viability score (VS). VS is derived from the mean value of score of FDG-PET uptake for infarcted areas with 5-point score system (no uptake=0, best uptake=4). We divided the patients into 2 groups; good viability group: VS> 2 (n=23), and good viability group: VS<2 (n=14). We examined whether there was a difference in the appearance of subsequent cardiac events (death, heart failure, CABG, re-PCI and serious arrhythmia) by Kaplan Meier method as an end point of the duration from the onset of AMI to the day of cardiac events.
Results: The average observation period was 692 days. The event free survivial rate assessed by Kaplan-Meier method was significantly (P=0.02) reduced in good viability group.
Conclusion: The present study demonstrated that the preservation of good myocardial viability can predict subsequent cardiac events. Therefore, it is clarified that myocardial viability assessed by FDG-PET is useful for assessing clinical outcome in patients with AMI.



3:00 p.m.

1024-54 **Effects of Ranolazine on Disease-Specific Health Status and Quality of Life: Results From the MERLIN-TIMI 36 Randomized Trial**

Suzanne V. Arnold, David A. Morrow, Kaijun Wang, Yang Lei, Elizabeth M. Mahoney, Judith A. Kempf, Benjamin M. Scirica, David J. Cohen, Mid America Heart Institute, Kansas City, MO, TIMI Study Group, Brigham and Women's Hospital, Boston, MA

Background: Ranolazine (RAN) has been shown to reduce ischemia and symptom severity among selected pts with chronic angina. However, the effect of RAN on quality of life (QOL) and health status (HS) in a broad population of pts with CAD is unknown.
Methods: MERLIN-TIMI 36 was a randomized, double blind trial of RAN vs placebo in 6560 pts with non-ST elevation ACS. HS/QOL was evaluated at baseline and 4, 8 and 12 months after index hospitalization using the Seattle Angina Questionnaire (SAQ), London Dyspnea Questionnaire, SF-12 and EuroQol. Random effect growth curve models were used to examine changes in HS/QOL over time.
Results: All HS/QOL scores were similar at baseline and improved significantly at all follow-up time points for both treatment groups. RAN was associated with greater 12 month improvements in angina frequency, treatment satisfaction, and CAD-specific QOL (all p<0.05). Among pts with prior angina (n=3565), treatment with RAN was associated with substantial benefits across the full range of HS/QOL domains while there were no significant benefits among pts without prior angina (see Table). These benefits were independent of revascularization status and were observed despite the fact that RAN-treated pts received fewer other anti-anginal medications than those treated with placebo.
Conclusion: Among pts with a history of angina, treatment with RAN resulted in a significant and sustained improvement in HS and QOL over 12 months.

Mean Effect of Ranolazine vs. Placebo on CAD-Specific HS and QOL Over 12 Months

Outcome Measures*	History of Prior Angina		No History of Angina	
	Treatment Effect (95% CI)	P-Value	Treatment Effect (95% CI)	P-Value
SAQ Angina Frequency†	3.62 (1.99, 5.26)	<0.001	0.34 (-1.51, 2.18)	NS
SAQ Physical Limitations	1.85 (-0.01, 3.71)	NS	-1.16 (-3.22, 0.90)	NS
SAQ Quality of Life†	2.73 (1.25, 4.20)	0.003	0.72 (-0.85, 2.29)	NS
SAQ Treatment Satisfaction†	1.50 (0.50, 2.49)	0.003	-0.04 (-1.12, 1.04)	NS
Dyspnea Score	-0.13 (-0.22, -0.03)	0.012	0.03 (-0.08, 0.14)	NS
EuroQol Utility	0.016 (0.004, 0.028)	0.007	0.004 (-0.008, 0.017)	NS
SF-12 Physical Component	0.85 (0.08, 1.62)	0.030	0.35 (-0.46, 1.16)	NS
SF-12 Mental Component†	0.93 (0.19, 1.67)	0.014	-0.25 (-1.03, 0.53)	NS

* Higher scores indicate improved HS/QOL, except Dyspnea where lower scores indicate less severe symptoms

† Significant interaction between treatment effect and prior angina (p<0.05)

3:00 p.m.

1024-55 **Collateral Flow to the Occluded Infarct-related Artery is Associated with a Lower Rate of Heart Failure in the Occluded Artery Trial (OAT)**

Ph. Gabriel Steg, Arthur Kerner, Christopher E. Buller, Sandra A. Forman, Harvey D. White, Antonio C. Carvalho, Harmony R. Reynolds, Viliam Fridrich, Eric A. Cohen, G. B. John Mancini, Gervasio A. Lamas, Judith S. Hochman, Hôpital Bichat-Claude Bernard, Assistance Publique - Hôpitaux de Paris, Paris, France, New York University School of Medicine, New York, NY

Background: The OAT randomized trial (n=2201) found that percutaneous coronary intervention (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. 12.3 and 10.8% (NS) of the patients in the PCI and MED groups respectively had no angiographic collaterals to the infarct related artery. These patients were compared to those with grade I (71.6 and 70.9% respectively) or II (16.1 and 18.3% respectively) collaterals.
Results: Cumulative 60-month estimated event rates were as follows:

Outcome	Group	No collaterals N=251 (number of events) %	Any collaterals N=1922 (number of events) %	P value collaterals vs no collaterals	P value for interaction between treatment and collaterals (p<0.01 was prespecified for all OAT secondary analyses)
Primary outcome (Death, MI, class IV CHF)	All patients	22.7%	16.9%	0.014	
	PCI	(28)25.4%	(135)18.0%		0.89
	MED	(21)18.7%	(124)15.9%		
Death	All patients	15.4%	11.3%	0.16	
	PCI	(17)16.1%	(74)11.1%		0.44
	MED	(11)14.8%	(81)11.5%		
Fatal and non fatal recurrent MI	All patients	6.5%	6.1%	0.6	
	PCI	(8)6.9%	(52)7.1%		0.73
	MED	(6)6.0%	(39)5.1%		
Class III or IV CHF	All patients	11.6%	5.2%	<0.001	
	PCI	(9)7.5%	(48)5.6%		0.02
	MED	(18)16.3%	(42)4.8%		
Death or Class III or IV CHF	All patients	20.5%	14.1%	0.005	
	PCI	(23)20.8%	(108)14.2%		0.60
	MED	(22)19.4%	(111)14.1%		

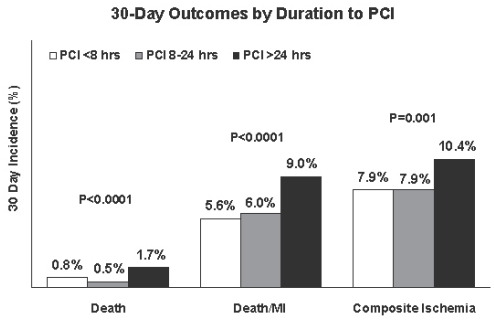
Presence of collaterals to the infarct related artery was associated with reduced risk of heart failure at 60 months in both treatment groups. There was a strong trend towards interaction between treatment assignment and collateral flow for heart failure, but not for the primary, or other secondary endpoints.
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.

3:00 p.m.

1024-56 **Increased Mortality in Patients with Acute Coronary Syndromes and Delay to Angioplasty of Greater than 24 Hours after Hospital Admission: An ACUITY Substudy**

Paul Sorajja, Bernard J. Gersh, Brent T. McLaurin, David C. Cox, Michael E. Bertrand, A. Michael Lincoff, Jeffrey W. Moses, Harvey D. White, Stuart J. Pocock, James H. Ware, Roxana Mehran, E. Magnus Ohman, Gregg W. Stone, Mayo Clinic College of Medicine, Rochester, MN, Columbia University Medical Center, New York, NY

Background: Although late reperfusion worsens survival in patients with ST-segment elevation myocardial infarction, there is a paucity of data on the potential harm from delay in early revascularization in patients with acute coronary syndromes due to unstable angina or non-ST segment elevation myocardial infarction (UA/NSTEMI).
Methods: 7,749 pts (median age, 63 yrs; 73% men) with UA/NSTEMI who underwent PCI as part of the ACUITY trial were examined. Patients were stratified according to revascularization by PCI at <8 hrs (n=2,197), 8-24 hrs (n=2,740), and >24 hrs (n=2,812) after hospital admission for analysis of outcomes.
Results: Delay in PCI >24 hrs after hospital admission was associated with increased 30-day mortality, death or myocardial infarction, and composite myocardial ischemia (Figure). The increase in mortality persisted at 1 yr (<8 hrs vs. 8-24 hrs vs. >24 hrs, 5.2% vs. 4.2%. vs. 7.5%; p=0.02). By multivariate analysis, delay to PCI >24 hrs was an independent predictor of mortality at 30 days (HR [95%CI] = 2.03 [1.29-3.19]; p=0.002) and 1 year (HR [95%CI] = 1.55 [1.19 - 2.02]; p=0.001). The differences in death attributable to PCI delay >24 hrs were greatest in high-risk patients.
Conclusions: In this large-scale study, delaying revascularization with PCI >24 hrs in patients with UA/NSTEMI was an independent predictor of one-year mortality. These findings suggest that urgent angiography and triage to revascularization should be a priority in acute coronary syndromes.

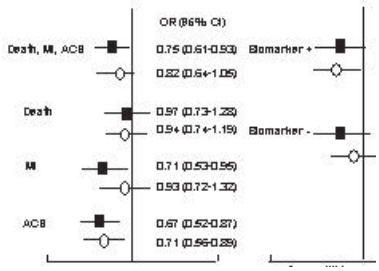


3:00 p.m.

1024-57 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'Donoghue, William E. Boden, Christopher P. Cannon, Tim C. Clayton, Robbert J. de Winter, Keith AA Fox, Bo Lagerqvist, Peter A. McCullough, Sabina A. Murphy, Rudolf Spacek, Eva Swahn, Lars Wallentin, Fons Windhausen, 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 0.75, 95% CI 0.61-0.93) and non-DM (OR 0.82, 95% CI 0.64-1.05, P int=0.59). 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 0.71, 95% CI 0.53-0.95), but had no significant effect in non-DM (OR 0.93, 95% CI 0.72-1.32, P int=0.22). 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 w/o (OR 0.92, 0.66-1.29, P int=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.



3:00 p.m.

1024-58 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=355,572) 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 per 100,000 (640 to 339 [47%] in men and 537 to 309 [42%] in women, in the 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 CHD death rates increased progressively during 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, of the 228 per 100,000 decrease in age-adjusted mortality, 280 deaths per 100,000 annually appear to have been truly prevented and 40 (17%) postponed to an older age. Contrary to fatal CHD, both the age-adjusted and the crude rates of hospital admission for nonfatal acute myocardial infarction did not decline appreciably in the 19-year period studied. The age-adjusted rate declined slightly from 853 to 844 per 100,000 (1% decrease) among men but increased from 488 to 559 (14% increase) among women. Median age, and the rate of comorbidities such as diabetes, hypertension, and renal disease also increased.
Conclusions: 1. The marked decrease in age-adjusted CHD mortality observed in the last 20 years is primarily due to true prevention while a significant minority is due postponement to an older age, especially among women (17%). 2. The increase in admissions for nonfatal acute myocardial infarction may be due to changes in case definition, increased co-morbidity, and decreasing in-hospital mortality.

3:00 p.m.

1024-59 Temporal Changes In The Use Of Early Invasive Management For Non-ST Elevation Acute Coronary Syndromes: Influence Of Age On Treatment Selection And Outcome

Alan J. Bagnall, Shaun G. Goodman, Thao Huynh, Asim N. Cheema, David H. Fitchett, Raymond T. Yan, Anatoly Langer, Andrew T. Yan, for the Canadian ACS Registry I and II Investigators, Canadian Heart Research Centre, Toronto, ON, Canada, Terrence Donnelly Heart Centre, St. Michael's Hospital, Toronto, ON, Canada

Background: Randomized clinical trials support early invasive management of high-risk non-ST elevation (NSTE) acute coronary syndromes (ACS). However, only limited data support this strategy in the elderly (65-74) and very elderly (≥75). We examined temporal changes in the relationship between age, in-hospital use of coronary angiography/revascularization and outcome.
Methods: The Canadian ACS registries were prospective observational studies of less selected (than clinical trial) patients with ACS. ACS I recruited 3279 NSTE ACS patients from 51 centres from Sept 99 to Jun 01; ACS II recruited 1956 patients from 36 centres from Oct 02 to Jan 04.
Results: Elderly and very elderly patients comprised 29.6% and 28.2% (in ACS I) and 27.8% and 27.5% (in ACS II), respectively. Rates of angiography, PCI and CABG increased significantly over time (all p<0.001).

	ACS I				ACS II			
	<65 (n=1386)	65-74 (n=969)	≥75 (n=924)	*p* for trend	<65 (n=873)	65-74 (n=544)	≥75 (n=537)	*p* for trend
Median GRACE score (inter-quartile range)	92 (79-108)	119 (105-139)	143 (124-168)	<0.001	99 (83-115)	124 (109-146)	151 (130-176)	<0.001
% In-hospital angiography	45.8	41.1	27.6	<0.001	75.6*	64.7*	45.3*	<0.001
% PCI	18.5	12.9	10.8	<0.001	40.2*	28.9*	17.9*	<0.001
% CABG	5.6	4.4	3.3	<0.01	11.5*	11.7*	8.6*	0.11
% any revascularization	23.9	17.2	14.0	<0.001	51.0*	40.4*	26.5*	<0.001
% In hospital death/re-MI	4.2	4.3	8.0	<0.001	6.6†	6.1	8.0	0.39
% 1 yr mortality	3.1	9.1	20.1	<0.001	2.9	5.1†	14.9†	<0.001

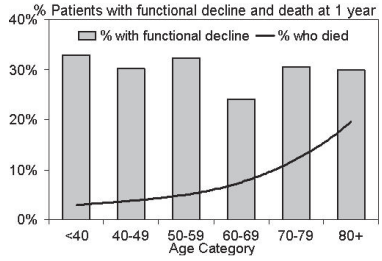
*p<0.001 †p<0.05 comparing within age groups between ACS I and II.
After adjusting for gender and other GRACE risk score prognosticators, older age remained independently associated with lower use of angiography (OR elderly=0.81, 95%CI 0.70-0.94 p=0.006; very elderly=0.45, 95%CI 0.39-0.53 p<0.001).
Conclusions: 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.

3:00 p.m.

1024-60 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.



3:00 p.m.

1024-61 **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, Yosef Kahn, Francisco J. Gonzalez, Akil Loli, Frank Cardello, Robert E. Halligan, Jr., Richard Gerkin, Kenneth B. Desser, 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 assessed the hypothesis 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. Follow-up occurred up to 5 years after initial presentation, with a mean of 1269 days.
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 all 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 as the strongest predictor. Strategies to increase HDL 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.

3:00 p.m.

1024-62 **Sex and Race Are Associated with the Finding of Non-Obstructive Coronary Artery Disease in Patients with Acute Coronary Syndromes**

Neel 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 (NOb-CAD) at angiography. The prevalence of this finding is variable in the literature. We examined the frequency of NOb-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 5/19/06 - 9/29/06 at one private (NYU Medical Center, N=613) and one public (Bellevue, N=522) urban academic medical center. Charts were reviewed for indication for and results of angiography and demographic data. ACS was defined as cardiac marker elevation and/or ST segment deviation with ischemic symptoms. Non-obstructive CAD (NOb-CAD) was defined as the absence of ≥50% stenosis in any major epicardial vessel.
Results: Overall, 32% of angiograms performed for varied indications showed NOb-CAD. The cohort included 547 pts with ACS, 52% of whom had confirmed MI by cardiac marker elevation. NOb-CAD was found at angiography in 20% of ACS pts overall and in 18% of pts with MI. Women were more likely to have NOb-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 NOb-CAD by race/ethnicity among 528 ACS pts for whom race/ethnicity was recorded.
Conclusion: The rate of NOb-CAD at angiography was high in this multi-ethnic sample of patients with ACS. NOb-CAD was particularly common among women and African-Americans.

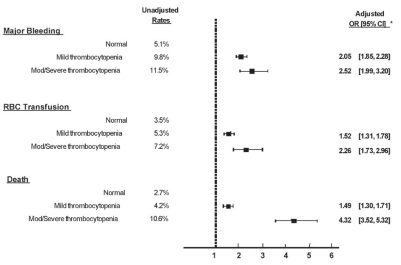
	All	Caucasian	Hispanic	African-American	Asian	p (by ANOVA)
	N=547	N=241	N=158	N=70	N=59	
NOb-CAD						
All pts % (N)	20% (108)	18% (44)	20% (31)	36% (25)	8% (5)	0.0002
Women	31% (55)	27% (17)	27% (17)	57% (16)	18% (3)	0.03
Men	14% (53)	15% (27)	15% (14)	21% (9)	5% (2)	0.29

3:00 p.m.

1024-63 **Incidence and Impact of Acquired Thrombocytopenia Among Patients With Acute Coronary Syndromes**

Tracy Y. Wang, Fang-Shu Ou, Matthew T. Roe, E. Magnus Ohman, W. 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 (>150x109/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 x109/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 mod/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.



3:00 p.m.

1024-64 **Trends in Presenting Characteristics and Hospital Mortality in Patients With ST-Elevation and Non-ST-Elevation Myocardial Infarction in the National Registry of Myocardial Infarction from 1990-2006**

William J. Rogers, Paul D. Frederick, Edna Stoehr, John G. Canto, Joseph P. Ornato, C. Michael Gibson, Charles V. Pollack, Jr., Joel M. Gore, Nisha Chandra-Strobos, Eric D. Peterson, William J. French, University of Alabama Medical Center, Birmingham, AL

Background: Although ST-elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction (AMI) have been the focus of intense, recent clinical investigation, limited information exists on characteristics and hospital mortality of patients not enrolled in clinical trials. Although previous large databases have reported declining mortality of patients with STEMI, substantial mortality change among those with NSTEMI has not previously been reported.
Methods: The National Registry of Myocardial Infarction enrolled 2,515,106 patients at 2,157 U.S. hospitals from 1990-2006. Of these, we evaluated 1,950,561patients with diagnoses reflecting acute myocardial ischemia on hospital admission.
Results: From 1990-2006, the proportion of NSTEMI increased from 14.2% to 59.1% (p<.0001), while the proportion of STEMI decreased. The mean age increased (from 64.1 to 66.4 years, p<.0001) as did the proportion of females (from 32.4% to 37.0%, p<.0001). On admission, patients were less likely to report prior angina, prior AMI or family history of coronary artery disease but were more likely to report history of diabetes, hypertension, current smoking, heart failure, prior revascularization, stroke and hyperlipidemia. From 1994-2006, hospital mortality fell among all non-transferred-out patients (10.4% to 6.3%), STEMI (11.5% to 8.0%), and NSTEMI (7.1% to 5.2%), (all p<.0001). After adjustment for baseline covariates, hospital mortality fell among all patients by 23.6% (odds ratio (OR) 0.764, 95% CI 0.744-0.785), STEMI by 24.2% (OR 0.758, 0.732-0.784), and NSTEMI by 22.6% (OR 0.774, 0.741-0.809), all p < 0.001.
Conclusions: This large, observational database from 1990-2006 shows a rising prevalence of NSTEMI, and, despite a higher risk profile on presentation, a falling risk-adjusted hospital mortality in patients with STEMI and, for the first time, in patients with NSTEMI as well.

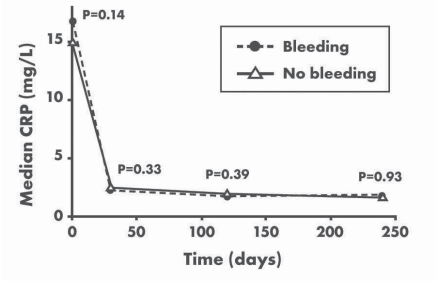
3:00 p.m.

1024-65 **Lack of Association Between Bleeding and Inflammation Among Patients With Acute Coronary Syndrome: Insights From the Aggrastat to Zocor (A to Z) Trial**

Tracy Y. Wang, Fang-Shu Ou, Michael A. Blazing, James A. De Lemos, Robert M. Califf, Eric D. Peterson, Duke Clinical Research Institute, Durham, NC, University of Texas Southwestern Medical Center, Dallas, TX

Background: In-hospital bleeding among patients with acute coronary syndromes (ACS) has been associated with worse long-term outcomes. One hypothesis is that inflammation, as a result of bleeding and transfusion, may contribute to long-term risk.
Methods: We studied C-reactive protein (CRP) levels as a marker of inflammation, collected at baseline, 1, 4 and 8 months after discharge among ACS patients enrolled in the A to Z trial. CRP trends over time were compared among patients with and without in-hospital bleeding or transfusion and by severity.
Results: Among 2322 ACS patients, 281 (12%) had an in-hospital bleeding event. Patients with bleeding tended to have higher baseline CRP levels (median CRP 20.1 mg/L among patients with severe bleeding v. 16.8 mg/L mild bleeding vs. 15.0 mg/L no

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.

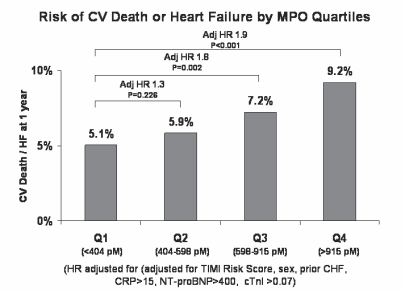


3:00 p.m.

1024-66 **Myeloperoxidase Levels Associated With Risk of Cardiovascular Death and Heart Failure After Non-ST Elevation Acute Coronary Syndrome**

Benjamin M. Scirica, 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, cTnI (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 followup 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 1.8, 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 cTnI (adjHR 1.9, p=0.001) or elevated cTnI (Adj HR 1.7, p=002). Elevated MPO was associated with CVD/MI at 30d (adjHR 1.6, p=0.016) with an attenuated relationship by 1-year (adjHR 1.3, p=0.06).
Conclusions: Elevated levels of MPO, a marker of leukocyte activation, are 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.



3:00 p.m.

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. Ajani, Nick Andrianopoulos, 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

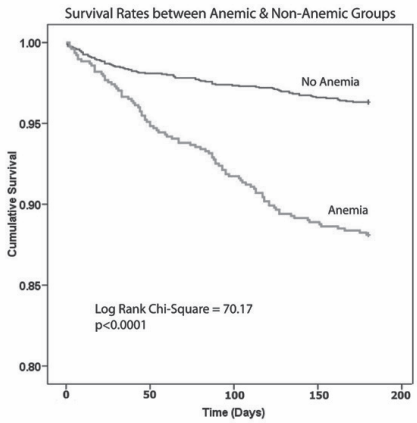
Background: The optimal duration of clopidogrel use for prevention of stent thrombosis with drug-eluting stent (DES) use is uncertain.
Methods: We analysed data from 2980 patients who underwent percutaneous coronary intervention (PCI) in a large registry who had 12-month follow-up; 1669 (56.0%) with 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 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.

3:00 p.m.

1024-68 **Impact of Anemia on Long-term Mortality in Patients with Acute Coronary Syndrome**

Umesh U. Tamhane, Irfan Hameed, Daniel Montgomery, Krishna Aragam, Garry Ng, Saagar Sanghvi, Eva Kline-Rogers, Kim A. Eagle, Hitinder S. Gurm, 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 six-month 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;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 Marcucci, Gian Franco Gensini, Rosanna Abbate, David Antoniucci, Careggi Hospital, Florence, Italy

Background The RECLOSE trial showed that non-responsiveness to clopidogrel is predictive of DES thrombosis and cardiac mortality at 6 months. No data exist about the predictive value of long-term adverse events in patients with DES and clopidogrel loading non-responsiveness.Our objective was to determine whether non-responsiveness to

clopidogrel, as revealed by high in vitro residual platelet reactivity after a 600 mg loading of the drug, is predictive of drug-eluting stent (DES) thrombosis and cardiac mortality at long-term follow-up.
Methods Prospective observational cohort study conducted from July 2005 to August 2007 in an academic hospital. A total of 804 patients who had successful sirolimus or paclitaxel-eluting stent implantation and who were compliant to clopidogrel treatment for at least 1 year, had the assessment of residual platelet reactivity after a loading dose of 600 mg of clopidogrel by light transmittance aggregometry (LTA). Long-term cardiac mortality was defined as death of cardiac or unexplained cause that occurred after 6 months from DES implantation. Very late definite/probable/possible DES thrombosis was defined according to the ARC definitions. Survival curves were generated using the Kaplan-Meier method, and the difference between curves was assessed by log-rank test.
Results The median follow-up time was 639 (IQ 555-756) days; follow-up was completed in 803 (99.9%) patients. After 6 months there were 11 late cardiac deaths, 4 in the nonresponder group (3.8%) and 7 in the responder group (1%). The overall long-term cardiac survival rates in non responder and responder patients were 89 ± 3%, and 97 ± 1%, respectively; p < 0.001. Very late definite/probable/possible DES thrombosis was higher in non responders than in responders patients, 2.8% and 0.3%, respectively; p=0.002
Conclusions High residual platelet reactivity after 600 mg loading dose of clopidogrel, as revealed by a single assessment with LTA, is a strong predictor of cardiac death and DES thrombosis.

3:00 p.m.

1024-70 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, BenoÃ®t Verret, Thao Huynh, Fernand Bertrand, Gilles R. Dagenais, James M. Brophy, Quebec Heart Institute/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: low plateau; high plateau; rising values; falling 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, 30% vascular 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.

CRP pattern of admission & discharge values (n)	OR (95% CI) for primary endpoint of patterns of admission & discharge CRP values	CRP pattern of admission, discharge, and 1 month values (n)	OR (95% CI) for primary endpoint of patterns of admission, discharge, and 1 month CRP values
Low Plateau (236)	1.0 (reference)	Low Plateau (129)	1.0 (reference)
High Plateau (193)	1.25 (0.64, 2.43)	High Plateau (97)	1.59 (0.52, 4.91)
Rising Values (425)	0.96 (0.53, 1.73)	Rising Values (110)	1.83 (0.63, 5.30)
Falling Values (141)	1.16 (0.55, 2.43)	Falling Values (105)	0.60 (0.15, 2.47)
No Pattern (193)	1.70 (0.91, 3.19)	No Pattern (733)	1.63 (0.69, 3.87)

Conclusion: Neither low or high plateaus nor rising or falling values predicted occurrence or non-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.

3:00 p.m.

1024-71 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, Chunxue Shi, Joshua Walczak, David A. Machon, Ronna H. Berezin, Roxana Mehran, E. Magnus 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 undergoing early invasive management, bivalirudin (BIV) monotherapy yields similar ischemic complication rates and less bleeding than regimens that include glycoprotein IIb/IIIa receptor inhibitors (GPI). The economic impact of this strategy is unknown.
Methods: We performed a prospective economic analysis of US pts enrolled in ACUITY (n=7851) who were randomized to receive heparin (UFH or LWMH) + 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 (see Table). 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 less major and minor bleeding (incremental cost = $8658 and $2282/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 heparin + GPI in pts with moderate-high risk ACS.

Table: 30-day Clinical Outcomes and Costs

	Heparin + Upstream GPI (n=1301)	Heparin + Cath Lab GPI (n=1308)	Bivalirudin Monotherapy (n=2615)	p-value
Death/MI/Urgent Revascularization	7.3%	8.1%	8.3%	0.60
Major Bleeding	5.5%	5.0%	3.2%	<0.001
Other Bleeding	29.1%	22.0%	14.2%	<0.001
Length of Stay (Days)	3.47	3.83	3.74	0.02
Costs				
Antithrombotic therapy	$896	$515	$976	<0.001
Index hospitalization	**$14,440**	**$14,028**	**$13,844**	**<0.001**
Follow-up	$767	$856	$917	0.66
Total 30 day costs	**$15,207**	**$14,884**	**$14,761**	**0.005**

GPI=Glycoprotein IIb/IIIa Receptor Inhibitor; Values in brackets represent medians

3:00 p.m.

1024-72 Coronary flow reserve is related to extension and trasmural entity of myocardial necrosis and predicts functional recovery after acute myocardial infarction. A study performed with contrast-enhanced magnetic resonance

Roberta Montisci, Massimo Ruscazio, Francesco Tona, Francesco Corbetti, Cristiano Sarais, Sara Pontarollo, Luisa Cacciavillani, Ramondo Angelo, Luigi Meloni, Sabino Iliceto, 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 clinical 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 transthoracic echocardiography 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), Troponin I peak (P=003), heart rate (P=0.03), NSI (P< 0.0001) and TSI (P=0.01) were related to CFR and that CFR (P< 0.0001), NSI (P= 0.01), TSI (P< 0.0001), microvascular obstruction at GE-MRI (P=0.01) and heart rate (P=0.03) are all related to functional recovery. Multivariable analysis revealed that TSI (P< 0.0001) was the only independent determinant of CFR and that CFR (P< 0.0001) was the only independent predictor of LV functional recovery.
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.

3:00 p.m.

1024-73 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. Steinhubl, Michele D. Voeltz, 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 Acute 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, intraocular, or retroperitoneal, access site with intervention, hematoma ≥5 cm, hemoglobin drop ≥3g/dL with source or ≥4g/dL without source or transfusion within 30 days. The impact of MB on 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, 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 hyperlipidemia (all p<0.05). MB was less frequent for BIV vs. H+GPI (3.0% vs. 5.7%, p<0.0001), and similar for BIV+GPI vs. H+GPI (p=ns). Mortality at one year was higher in patients with vs. without MB (14.4% vs. 3.3%, p<0.0001). 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 [2.24-3.72], 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.

3:00 p.m.

1024-74 **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 Feit, Sunil V. Rao, Steven R. Steinhubl, George D. Dangas, 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.

3:00 p.m.

1024-75 **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. Dangas, Michele D. Voeltz, Frederick Feit, 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 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. Anemia was defined using baseline hemoglobin values and the World Health Organization definition of hemoglobin <13.0 g/L in men and <12.0 g/dL in women. The association between anemia 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 13,039 patients with baseline hemoglobin data, 2,200 (16.9%) were anemic. Mean hemoglobin values were significantly lower in anemic vs. nonanemic patients (11.64 ± 0.99 mg/dl vs. 14.48 ± 1.22 mg/dl, p<0.0001). Anemic patients had higher composite ischemic event rates at one year vs. nonanemic patients (20.8% vs. 14.6%, p<0.0001). Similarly, unadjusted mortality rates at one year were higher in anemic vs. nonanemic patients (7.0% vs. 3.1%, p<0.0001). Anemia was an independent predictor of one-year mortality (hazard ratio [95% confidence interval] = 1.61 [1.32-1.98], p<0.0001).
Conclusion: Anemia is a common finding in patients with acute coronary syndromes and is associated with a significant increase in one-year mortality and ischemic event rates. Furthermore, anemia is an independent predictor of one-year mortality. Anemia should be recognized as a high-risk marker in patients with acute coronary syndromes.

3:00 p.m.

1024-76 **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. Henriques, Jan Baan, René J. van der Schaaf, Marije 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.

STR	Non-anterior MI			Anterior MI		
	HR	CI	p*	HR	CI	p*
≥ 70%	—			—		0.45
30% - 70%	3.0	1.5 - 6.1	0.043	—		
< 30%	4.9	2.4 - 9.8		2.0	1.2 - 3.3	

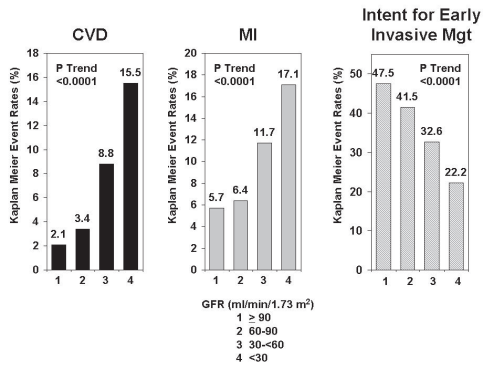
STR = ST segment deviation Resolution; HR = Hazard Ratio; CI = 95% Confidence Interval
* To test equality of HRs

3:00 p.m.

1024-77 **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 NSTE 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, htn, prior revasc, 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 y (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 GFR 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.

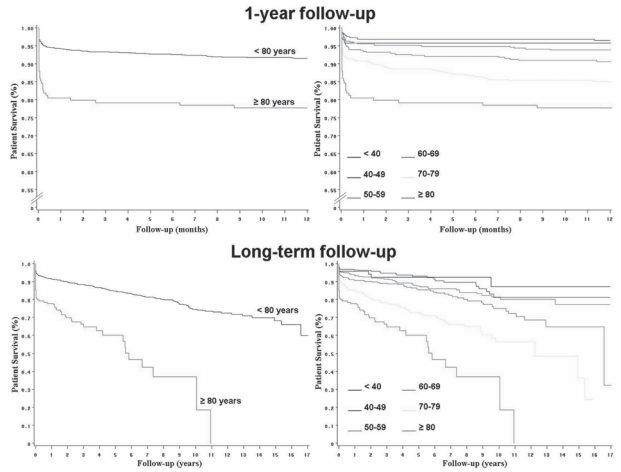


3:00 p.m.

1024-78 **Prognosis of Elderly Patients after Acute Myocardial Infarction and Coronary Revascularization Procedure**

NIcolas Mansencal, Rémy Pillière, Alain Beauchet, Thierry Joseph, Franck Digne, Pascal Lacombe, Olivier Dubourg, AP-HP, Hôpital universitaire Ambroise Paré, 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 compared data between group 1 (pts > 80 years of age (n=152; 83.9 ± 3.3 yo)) and group 2 (pts < 80 years (n=1535; 59.5 ± 11.6 yo)). Follow-up was established by phone contact with the pts, their families or their physicians.
Results: Global in-hospital mortality was 7%: 18% in pts ≥ 80 years versus 5.5% in pts of 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 month (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.



3:00 p.m.

1024-79 **Aspirin Resistance As A Predictor Of Adverse 1-Year Outcome In Patients With Non-ST Elevation Acute Coronary Syndromes**

Michael Zairis, Georgios Z. Tsiaousis, Stamatis Makrygiannis, Dionisios Xenos, Anastasios Theodosis-Georgilas, Konstantinos Kontos, Stilianos Karvounaris, ZInon Katidis, Stella Nini, Evdokia Adamopoulou, Ioannis Hatzissavas, Stephanos Foussas, Tzanio Hospital, Piraeus, Greece

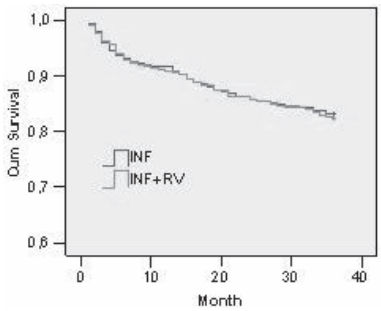
Background: There is scant data concerning the impact of aspirin resistance on long term outcome in patients (pts) with unstable coronary artery disease. We evaluated the predictive value of aspirin resistance for the incidence of 1-year composite of cardiovascular death and rehospitalization for non-fatal myocardial infarction in pts with non-ST elevation acute coronary syndromes (NSTE-ACS).
Methods: A total of 496 consecutive pts (age=69±9 yrs, 69% males) who hospitalized in the first 24 hrs following index pain, were included. Platelets response to aspirin therapy was measured by the platelet function analyzer (PFA-100) closure time (CT). CT was measured upon presentation or 6 hours after aspirin loading in pts with or without prior aspirin therapy respectively. Aspirin resistance was defined as a CT<193 sec based on the 90% central interval of normal.
Results: A total of 121 (24.4%) pts had a CT<193 sec (aspirin resistants). By 1-year 64 (10.7%) pts died and 42 (8.5%) were rehospitalized due to a non fatal myocardial infarction. Although there were not significantly differences between pts with or without aspirin resistance, the former were at significantly higher risk for the composite end point (37.2% vs. 16.3%; hazard ratio [HR]= 2.7; 95% CI=1.8-3.9; p<0.001). In particular aspirin resistants were at significantly higher risk for both cardiovascular death (23.1% vs. 9.6%; HR=2.6; 95% CI=1.6-4.3; p<0.001) and rehospitalization for non-fatal myocardial infarction than non aspirin resistants (14% vs. 6.7%; HR=2.2; 95% CI=1.2-4.1; p=0.01).
Conclusion: The present results show that aspirin resistance portends an increased risk for long term thrombosis related adverse outcome in pts with NSTE-ACS.

3:00 p.m.

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, Georgios Z. Tsiaousis, Dionisios Xenos, Anastasios Theodosis-Georgilas, Evridiki Gougourela, Petros Smilakos, Joseph Papadopoulos, Konstantinos Garefallakis, Nikolaos Tellis, Konstantinos Katsaros, 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.

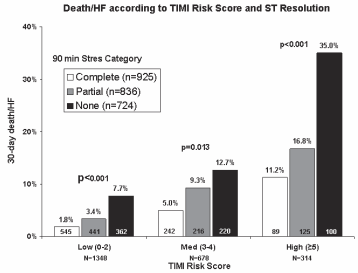


3:00 p.m.

1024-83 **Extent of ST Segment Resolution After Fibrinolysis Adds Dynamic Risk Stratification to the TIMI Risk Score for STEMI**

James R. Harkness, Benjamin M. Scirica, Marc S. Sabatine, David A. Morrow, Sarah Sloan, Stephen D. Wiviott, Robert P. Giugliano, Christopher P. Cannon, Eugene Braunwald, TIMI Study Group, Boston, MA, Brigham and Women's Hospital, Boston, MA

Background: The TIMI risk score (TRS) for STEMI is a validated risk score for predicting mortality. Though not part of the TRS, ST segment resolution (STRes) may provide a dynamic method of risk stratification based on response to reperfusion and therefore improve on the risk stratification of the TRS alone. **Methods:** CLARITY-TIMI 28 randomized 3491 pts with STEMI receiving fibrinolysis to clopidogrel v. placebo. 2347 pts had ECGs valid to calculate STRes at 90min, which was defined as complete(>70%), partial(30-70%), or no resolution(30%). TRS was defined as low(0-2), medium(3-4) and high(≥5). Pts were followed for 30 days. **Results:** In a multivariable analysis, both TRS and STRes were strongly associated with death (high TRS [adjOR 10.2, p<0.01], mod TRS [adjOR 3.1, p<0.01], no STRes [adjOR 5.2, p<0.01] and partial STRes [adjOR 3.1, p<0.01]) and death/HF (high TRS [adjOR 6.2, p<0.01], mod TRS [adjOR 2.2, p<0.01], no STRes [adjOR 3.7, p<0.001], and partial STRes [adjOR 1.8, p=0.01]). Furthermore, STRes status provided a consistent gradient of risk across all TRS categories (Figure). The area under the receiver-operating characteristic curves for death/HF increased from 0.72 with TRS alone to 0.76 when STRes was added (p<0.01), with a similar relationship with mortality alone. **Conclusion**: The extent of STRes is an independent and additive predictor of death and HF when used with the TRS. STRes may be used together with the TIMI risk score to better risk stratify pts following fibrinolysis.



3:00 p.m.

1024-84 **Does Continuous ST-Segment Monitoring Add Prognostic Information to the TIMI, PURSUIT, and GRACE Risk Scores?**

Pedro L. Carmo, Jorge S. Ferreira, Carlos T. Aguiar, Pedro A. Goncalves, Luis F. Raposo, Antonio M. Ferreira, Jose M. Aniceto Silva, Hospital Santa Cruz, Carnaxide, Portugal

Background: Recurrent ischemia is frequent in patients (pts) with non-ST-elevation acute coronary syndromes (NSTE-ACS), and portends a worse prognosis. Continuous ST-segment monitoring (CSTM) adequately reflects the dynamic nature of myocardial ischemia and allows the detection of silent ischemic episodes. The aim of this study is to investigate whether CSTM adds prognostic information to the risk scores currently used in clinical practice.
Methods: We studied 234 pts with NSTE-ACS in whom CSTM was performed in the first 24 hours after admission. An ST episode was defined as a transient ST-segment deviation in ≥1 lead of ≥0.1 mV, and persisting ≥1 min. Three risk scores were calculated for each pt: TIMI (for NSTE-ACS), PURSUIT (death/MI model), and GRACE. The endpoint was defined as death or nonfatal myocardial infarction (MI), whichever occurred first by 1 year follow-up.
Results: ST episodes were detected in 54 pts (23.1%) and associated with worse 1-year outcome: 25.9% endpoint rate vs 12.2% for pts without ST episodes (OR = 2.51; 95% CI, 1.18-5,35; P = 0.026). All 3 risk scores predicted 1-year outcome, but the GRACE risk score (c-statistic = 0.755; 95% CI, 0.695-0.809) was superior to both TIMI risk score (c-statistic = 0.632; 95% CI, 0.567-0.694) and PURSUIT risk score (c-statistic = 0.644; 95% CI, 0.579-0.706). A GRACE risk score >124 showed the highest accuracy for predicting the study endpoint. The presence of ST episodes added independent prognostic information to the TIMI risk score (HR = 2.23; 95% CI, 1.13-4.38) and to the PURSUIT risk score (HR = 2.03; 95% CI, 1.03-3.98), but not to the GRACE risk score.
Conclusions: CSTM provides incremental prognostic information beyond the TIMI and PURSUIT risk scores, but not the GRACE risk score. Hence, the GRACE risk score should be the preferred stratification model in daily clinical practice.

3:00 p.m.

1024-85 **Chromogranin A Levels in the Acute Phase Independently Predicts Mortality and Heart Failure Hospitalizations During Follow-up in Patients With Non-ST Elevation Acute Coronary Syndromes**

Helge Rosjo, Anna M. Jansson, Alan Flyvbjerg, Anita Persson, Thomas Karlsson, Marianne Hartford, Torbjorn Omland, Kenneth Caidahl, Akershus University Hospital, Lorenskog, Norway, Karolinska University Hospital, Stockholm/ Solna, Sweden

Introduction: The neurohumoral marker chromogranin A (CgA) has in small studies been shown to predict mortality and heart failure hospitalizations after ST-elevation myocardial infarction. We hypothesized that CgA also would predict mortality and heart failure hospitalizations during follow-up in patients with non-ST elevation acute coronary syndromes (NST-ACS), and that CgA would provide additional information to echocardiographic findings and contemporary cardiovascular biomarkers.
Methods: CgA, cardiac troponin I, C-reactive protein (CRP) and B-type natriuretic peptide (BNP) were measured within 24 hrs of admission in 477 patients with NST-ACS (mean age 65 years, 32 % female). Echocardiographically determined left ventricular ejection fraction (LVEF) was obtained within day 5 of admission (n=357).
Results: During a median follow-up of 44 months, 85 patients (18%) died and 50 (10%) were hospitalized for heart failure. By Cox proportional hazards regression model (hazard ratio per 1 SD increase in log transformed CgA), baseline CgA concentration was strongly associated with the primary outcome mortality or heart failure hospitalizations (HR 1.61 [1.39-1.86], p<0.0001). After adjusting for contemporary cardiovascular biomarkers and conventional risk markers (age, gender, smoking status, prior myocardial infarction, diabetes, hypertension, congestive heart failure, heart rate, Killip class (>I) on admission, creatinine clearance, and peak CKMB), CgA still predicted outcome (HR 1.33 [1.07-1.66]; p=0.01). Further adjustment for LVEF attenuated the association, but baseline CgA concentrations were still predictive of mortality or heart failure hospitalizations (HR 1.33 [1.03-1.73], p=0.03).
Conclusions: CgA is a powerful predictor of mortality and heart failure in NST-ACS and provides incremental prognostic information to cardiac Troponin I, CRP, BNP, and LVEF.

3:00 p.m.

1024-86 **Effect of Enhanced External Counterpulsation on Symptoms, Quality of Life, 6-Minute Walking Distance, and Left Ventricular Systolic and Diastolic Function After 35 Days of Treatment and at 1-Year Follow-Up in 47 Patients With Chronic Refractory Angina**

Anil Kumar, Wilbert S. Aronow, Aniket Vadnerkar, Puneet Sidhu, Sanjay Mittal, Ravi R. Kasliwal, Naresh Trehan, Soundshore Medical Center/New York Medical College, New Rochelle, NY, ESCORTS Heart Institute and Research Center, New Delhi, India

Background: Enhanced external counterpulsation (EECP) improves symptoms and exercise duration in patients with refractory angina pectoris. The effect of EECP on left ventricular (LV) systolic and diastolic function needs to be investigated.
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 dimensions, LV end-diastolic and end-systolic volumes, E/A ratio, isovolumic relaxation time, and 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 with 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.

3:00 p.m.

1024-87 **Do Different Healthcare Systems Impact Major Outcomes In Stable Coronary Disease Patients Enrolled In COURAGE?**

Bernard R. Chaitman, Pamela M. Hartigan, David C. Booth, Koon K. Teo, John Mancini, William J. Kostuk, John A. Spertus, David J. Maron, Marcin Dada, Robert A. O'Rourke, William S. Weintraub, William E. Boden; for the COURAGE Investigators, Daniel S. Berman, Leslee J. Shaw, Saint Louis University School of Medicine, St. Louis, MO

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 yr follow-up. Patients were enrolled from US Veteran Affairs (VA) (n=968), US non-VA (US) (n=385) and Canadian (CDN) (n=931) 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.
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 yrs 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 was not significant for the endpoint of death (p=0.25) or the composite endpoint of death/MI (p=0.24). Similar results 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.

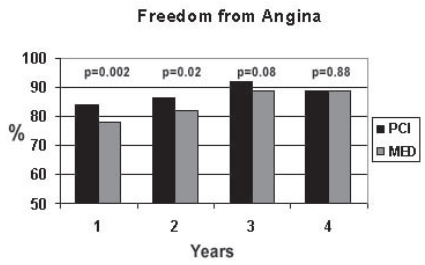
	OMT	PCI	P	OMT	PCI	P
	Death	Death		Death/MI	Death/MI	
VA	58 (12.1)	42 (8.6)	0.07	104 (21.7)	107 (21.9)	0.94
US	15 (7.9)	15 (7.7)	0.94	38 (19.9)	30 (15.3)	0.24
CDN	22 (4.7)	28 (6)	0.37	60 (12.8)	74 (16)	0.17
Total	95 (8.3)	85 (7.4)	0.38	202 (17.8)	211 (18.4)	0.62

3:00 p.m.

1024-88 **Routine PCI Improves Short but not Long term Angina Status in Patients with an Occluded Infarct Artery: Results from the Occluded 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, Paulo Caramori, George Sopko, Eduardo Balcells, Jonathan Leor, Bruce A. Barton, Judith S. Hochman, Waikato Hospital, Hamilton, New Zealand, New York University School of Medicine, New York, NY

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-protocol 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 3 yrs (p=.08). Use of anti-anginal therapy was similar in the 2 groups. At 5 yrs, revasc was more frequent in MED (22% vs. 19% for PCI, p=.03). However, in pts with follow-up angina (n=764), revasc rates were not different between groups (17% PCI vs. 19% MED, p=.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=.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 angina status that was lost by 3 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.



ACC.ORAL CONTRIBUTIONS

813

Issues in Revascularization and Concomittant Therapy

Tuesday, April 01, 2008, 8:00 a.m.-9:30 a.m.
McCormick Place, Room E352

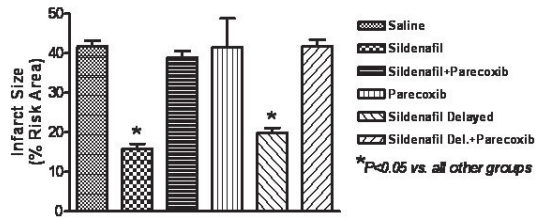
8:00 a.m.

813-4 COX-2 Inhibition with Parecoxib Abrogates Acute and Delayed Cardioprotective Effects of Sildenafil against Ischemia/reperfusion Injury

Fadi N. Salloum, Evan D. Ownby, Rakesh C. Kukreja, Virginia Commonwealth University Medical Center, Richmond, VA

Background: Phosphodiesterase-5 (PDE-5) inhibitor sildenafil (Viagra) induces protective effect against ischemia/reperfusion injury (I/R) in the intact heart and cardiomyocytes through generation of nitric oxide (NO). Since cyclooxygenase-2 (COX-2) is activated by NO, we tested the hypothesis if sildenafil-induced acute and delayed cardioprotective effect is also dependent on COX-2.
Methods: Adult male ICR mice were anesthetized and subjected to ischemia by coronary artery occlusion for 30 min followed by 24 hr reperfusion. Six groups were studied. 1- Controls; 2- Sildenafil (0.71 mg/kg; ip) given 1 hr before I/R; 3- Sildenafil (as in group 2) + Parecoxib (COX-2 inhibitor; 0.75 mg/kg; ip) given 30 min before I/R; 4- Parecoxib given as in group 3; 5- Sildenafil given 24 hr before I/R and 6- Sildenafil given as in group 5 + Parecoxib as in group 3. At the end of reperfusion, IS was measured by computer morphometry of triphenyl tetrazolium chloride stained heart sections.
Results: IS (mean ± SEM) was significantly reduced with acute and delayed sildenafil treatment compared to saline controls (Fig. 1). The risk area was not different between the groups. Interestingly, administration of parecoxib following either acute (30 min) or delayed (24.5 hrs) after sildenafil treatment completely abolished the protective effects of sildenafil. Parecoxib alone had no effect on IS.
Conclusions: For the first time, this study identifies COX-2 as a novel mediator of cardioprotection induced by a PDE-5 inhibitor.

Figure 1.



8:15 a.m.

813-5 Aspirin is Insufficient in Inhibition of Platelet Aggregation and Thromboxane Formation Early after Coronary Artery Bypass Surgery

Frantisek Bednar, Pavel Osmancik, Vera Jedlickova, Jan Hlavicka, Zoltan Paluch, Tomas Vanek, Cardiocenter, Kralovske Vinohrady University Hospital, Clinic of Cardiac Surgery, Prague, Czech Republic

Background: Aspirin administered early after coronary artery bypass grafting surgery (CABG) improves graft patency and patients survival. However, the antiplatelet effect of aspirin seems to be variable and aspirin resistance is currently still being discussed. The aim of the study was to asses aspirin efficacy in the early postoperative period.
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 withdraval) 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%,26%],p<0.05). On day 2, despite the aspirin administration, platelet aggregability increase above the values from day 1 (32%; 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 95ng/mL;95% CI [67,122]. On day 1, there was increase in concentration (181ng/mL;95% CI [104,258], p<0.05) and on day2, the concentration remained almost similar in comparing with the preoperative values (85ng/mL; 95% CI[49,120], p=N.S.). Only on day 5, significant decrease in concentration of thromboxane metabolite was achieved (63ng/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.

8:30 a.m.

813-6 Relative Contribution of Patient Characteristics and Clinical Site Characteristics to Saphenous Vein Graft Stenosis and Adverse Cardiac Events Following Coronary Artery Bypass Graft Surgery: A PREVENT-IV Analysis

Jacqueline L. Buros, Yuri B. Pride, John H. Alexander, Nicholas T. Kouchoukos, Eric D. Peterson, T. Bruce Ferguson, C. Michael Gibson, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, Duke University Medical Center, Durham, NC

Background: The goal of this analysis was to evaluate the relative contribution of patient characteristics and surgical clinical site characteristics on saphenous vein graft (SVG) stenoses at routine follow-up angiography as well as major adverse clinical events (MACE) during clinical follow-up in the PREVENT-IV study.
Methods: PREVENT-IV randomized 3,014 patients undergoing CABG at 105 sites to either edifoligide or placebo. Of those, 1,293 patients underwent routine follow-up angiography to evaluate the patency of saphenous vein grafts from 12-18 months following surgery. Percent diameter stenosis was measured by quantitative coronary analysis (QCA) at an angiographic core laboratory. MACE were defined as the composite of all-cause mortality, myocardial infarction, or repeat revascularization procedure with graft failure.
Results: Twenty percent of the variance in SVG percent diameter stenosis by QCA at follow-up was attributable to patient characteristics (i.e. the intra-class correlation (ICC) was 0.20, p<0.001). Independent of the contribution of patient characteristics, 3% of the variance in SVG stenoses was explained by characteristics of the clinical center enrolling the patient (ICC=0.03, p=0.02). 15% of the variance in MACE was attributable to the clinical center (theta=0.15, p<0.001).
Conclusions: While 20% of the variance in SVG stenoses is explained by patient characteristics, up to 15% of the variance in MACE outcomes are attributable to the clinical site characteristics. Future CABG trials should consider adjusting for clustering of events within enrolling centers. Further research in cardiovascular trials is warranted to understand the processes of care, techniques or decisions that contribute to the role of clinical sites in adverse outcomes.

8:45 a.m.

813-7 Clopidogrel and CABG-related Bleeding: Not as Important as Currently Believed?

John H-J Kim, L. Kristin Newby, Robert Clare, Linda K. Shaw, Andrew Lodge, Peter Smith, Marc E. Jolicoeur, Daniel B. Mark, Christopher B. Granger, Duke University Medical Center, Durham, NC, Stanford University, Palo Alto, CA

Background: Acute clopidogrel in ACS patients reduces ischemic events, but concerns of coronary artery bypass surgery (CABG)-related bleeding and delays to CABG limit early use.
Methods: Using 4794 consecutive CABGs in the Duke Databank for Cardiovascular Disease (Dec 1999 to Jun 2003), we created multivariable logistic regression models of CABG-related bleeding (reoperation for bleeding [re-op], red cell transfusion [transfusion], and a composite of re-op/transfusion/hematocrit drop >15%) relative to clopidogrel use <5 d pre-CABG. Models were adjusted for baseline covariates and propensity for clopidogrel <5 d.
Results: Of 4794 patients, 332 (6.9%) had clopidogrel <5 d pre-CABG; 65, >5 d prior and 4397, never. Bleeding rates for clopidogrel <5 d vs no clopidogrel <5 d were: re-op, 3.3 vs 2.6%; transfusion, 70.2 vs 68.2%; and composite, 94.3 vs 91.3%. Of those with clopidogrel <5 d, re-op was higher with clopidogrel stopped nearer CABG: 1 d (5.6%) or 2 d (7.5%) vs 3 d (1.9%) or 4 d (2.6%). There was no temporal pattern by day for transfusion or composite. After adjustment, neither re-op (OR 1.24 [0.64-2.41]) nor composite (OR 1.23 [0.72-2.10]) were significantly different between groups. Clopidogrel <5 d pre-CABG was modestly associated with transfusion, OR 1.40 (1.04-1.89) and number of PRBC units, but much more weakly than other factors (Table).
Conclusion: While bleeding risks were modestly higher with clopidogrel use <5 days pre-CABG, surgeon-based variations and GP 2b/3a use appear much more important.

Independent Variables Predicting Transfusion		
Surgeon (10 degrees of freedom)	Wald Chi Square 95.1	P Value <0.0001
Female	54.5	<0.0001
Hematocrit	54.5	<0.0001
Creatinine Clearance	54.0	<0.0001
Cardiopulmonary Bypass	26.1	<0.0001
Number of Diseased Vessels	25.4	<0.0001
Age	20.6	<0.0001
Use of GP 2b/3a During Hospitalization	17.0	<0.0001
Urgent Surgery	12.8	0.0003
Clopidogrel ≤5 days	4.9	0.03

9:00 a.m.

813-8 Frequency And Clinical Outcome of Patients Undergoing Non-Cardiac Surgery in the Year After Drug Eluting Stent Placement: Results from the EVENT Registry

Peter B. Berger, Neal S. Kleiman, Wen-hua Hsieh, Michael Pencina, Steven R. Steinhubl, Allan Jeremias, Ali Sonel, Kevin F. Browne, Greg Barseness, David J. Cohen, Geisinger Clinic, Danville, PA

Background: Little is known about the risk associated with non-cardiac surgery after drug-eluting stent (DES) implantation.
Methods: In the EVENT Registry, consecutive patients (pts) who underwent attempted stent placement at 42 hospitals in the USA between 7/04 and 9/05 were enrolled and followed for 1 year. We analyzed all pts who received >1 DES to determine the frequency of non-cardiac surgery and subsequent adverse events. The main outcome measure was a composite of death, MI or stent thrombosis in the week after non-cardiac surgery.
Results: Among 4,637 DES recipients in the first 2 waves of recruitment, 206 pts (4.4%) underwent major non-cardiac surgery in the year after their index PCI (median time to surgery 179 days). Overall, stent use averaged 1.5/pt; 53% of pts received a Taxus, 51% a Cypher, and 7% a BMS. The operations were orthopedic (36%), abdominal (31%), vascular (20%), ENT (4%), thoracic (3%), urologic (1%), intracranial (1%), and other (4%). Compared with pts who did not undergo surgery, those who did were older (67 vs 64 yrs, p<0.001), more likely to be female (39 vs 31%, p=0.016) and have had a prior stroke (13 vs 8%, p=0.021); the frequency of prior MI (39 vs 37%), prior CABG (25 vs 20%), and diabetes (36 vs 34%) were similar, as were LVEF and the indication for PCI. In the first 7 days after surgery, 4 pts died, had an MI, or suffered stent thrombosis (1.9%). Moreover, pts who underwent non-cardiac surgery were less likely to remain on dual antiplatelet therapy at 1 year (54 vs 64%, p=0.001). By time-dependent proportional hazards analysis, the risk of the composite ischemic outcome was increased 27-fold in the week following non-cardiac surgery (hazard ratio (HR) 27.3 [95 % CI, 10.1, 74.2], p<0.001) and remained similar in risk-adjusted analyses (HR 27.1 [95% CI, 9.9, 74.1], p<0.001).
Conclusions: The frequency of major non-cardiac surgery in the year after DES placement is >4%. Although the overall risk of adverse outcomes appears to be less than previously reported, it is significantly increased in the week after major non-cardiac surgery.

9:15 a.m.

813-9 Validation of a Risk Score for a New Target Vessel Revascularization After Coronary Stent Implantation

Alexandre S. Quadros, Fabiane Diemer, Carlos AM Gottschall, Institute of Cardiology of Rio Grande do Sul / FUC, Porto Alegre, Brazil

Background: Coronary drug-eluting stent implantation is associated with low rates of target vessel revascularization (TVR), but recent evidence has questioned its long-term safety. A selective approach of bare-metal stent (BMS) implantation in patiens at low risk for restenosis could be a reasonable alternative to this problem. The objective of this research was to validate a risk score for a new TVR after BMS implantation.
Methods: The risk score was developed in a consecutive cohort of patients treated with BMS implantation at our institution, as previously reported (J Invasive Cardiol. 2006; 18:22). This risk score ranges from 0 to 5 points, according to the presence of diabetes mellitus (1 point), the reference vessel diameter (>3.5 mm=0 points; 3-3.5mm=1; <3 mm=2) and the lesion length (10mm or less=0 points; 10-20mm=1; greater than 20 mm=2).Patients included in the validation cohort were treated between January and December 2005, and those with cardiogenic shock, intrastent restenosis or unsuccessful procedures were excluded. Patient characteristics and one-year clinical follow-up were prospectively recorded into a dedicated database. A new angiographic study in the follow-up period was done only when recurrent ischemia was suspected.
Results: In the study period, 491 patients were included, with a mean age of 61 ± 10.5 years, and 35% of women. Diabetes mellitus was present in 22%, a previous percutaneous coronary intervention in 12% and previous myocardial infarction in 35%. The mean reference vessel diameter was 2.80±0.56 mm and the mean lesion length was 12.45±6.3 mm. Clinical follow-up was complete in 88% of the patients, and the overall TVR rate was 13.9%. One-year TVR rates increased with each score level: Score=0, TVR=0%; Score 1=5.3%; Score 2=12%; Score 3=14%; and Score 4/5=25%; (p=0,008; chi-square test for trend). The c-statistic of the risk score was 0.60 (Confidence interval=0.51-0.67); p=0.02.
Conclusions: The risk score was significantly associated with a new TVR after BMS implantation. This score can be used as a tool to aid in the clinical decision making process of the type of stent to be implanted, since it is simple and based on variables obtained before stent implantation.

ACC.POSTER CONTRIBUTIONS

1031

Stable Ischemic Syndrome; Cardiopulmonary Resuscitation; Coronary Artery Bypass Surgery

Tuesday, April 01, 2008, 9:00 a.m.-12:30 p.m.
McCormick Place, South Hall

11:00 a.m.

1031-41 Prognostic Value and Therapeutic Implications of the Ischemic Cascade Using Dipyridamole Stress CMR in Patients With Known or Suspected Coronary Disease

Vicente Bodi, Juan Sanchis, Julio Nunez, Luis Mainar, Oliver Husser, Maria P. Lopez-Lereu, 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%, 3.4 [0.9-12.5], 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 and for making decisions in patients with ischemic chest pain. The presence of ischemia in stress perfusion CMR associates 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.

11:00 a.m.

1031-42 Effect of Amlodipine, Atorvastatin and the Combination on Transient Myocardial Ischemia in Coronary Artery Disease from the DUAAL Study

John Deanfield, Jan Bultas, Philippe Sellier, Erik Thaulow, 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) 5->10 mg, 2) Atorvastatin (AT) 10->80 mg, 3) Combination (AM/AT) 5/10mg->10/80 mg; in 311 patients (78% men, mean age 62 yrs) with stable angina (≥2 attacks /week), CAD history, ≥3 TMI 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 TMI free in all 3 groups. This was accompanied by comparable marked reduction in angina and nitroglycerin consumption. AT was as effective as AM in relief of TMI. CRP fell by 40% in patients receiving AT with no change for AM. Adverse events were comparable in all groups.
Conclusions: AT was as potent an anti ischemic agent as AM. The mechanism for benefit is likely to be different. TMI decrease was so great with monotherapy that no additional benefit was shown for the combination. The complementary mechanisms of AT and AM may be advantageous in the management of patients with CAD and TMI.

Key Efficacy Results at Week 26					
		Amlodipine	Atorvastatin	Combination	P value between groups
TMI (median)	baseline change	5.0 -4	5.0 -4	5.0 -4	0.922
angina attacks/ wk (mean)	baseline change	5.2 -4.11	4.6 -3.68	4.9 -3.89	0.150
NTG tablets/wk (mean)	baseline change	3.9 -2.60	2.7 -1.93	2.5 -2.45	0.014
CRP (mg/dL) (median)	baseline change	2 0.2	1.9 -0.8	2 -0.4	<0.001

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. Steckman, Peter J. Hynes, Nitasha Sarswat, Paul A. Tunick, Bernardo D. Vargas, Raj M. Khandwalla, Itzhak 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 ≥50% 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.

	Mean CCA IMT ≥ 0.9 mm	**Plaque**	**Plaque or mean CCA IMT ≥ 0.9 mm**
Ischemic Cardiomyopathy	p*=0.011	p=0.0002	p<0.0001
Sensitivity (%)	62.5	90.9	97.0
Specificity (%)	64.5	45.1	40.3
Negative Predictive Value (%)	76.9	90.3	96.2
Positive Predictive Value (%)	47.6	46.9	46.4
"Significant" CAD	p=0.018	p=0.0008	p=0.0002
Sensitivity (%)	61.7	83.3	89.6
Specificity (%)	70.2	48.9	44.9
Negative Predictive Value (%)	64.7	74.2	80.8
Positive Predictive Value (%)	67.4	62.5	44.7
			*all p by Fisher's exact test

11:00 a.m.

1031-44 Risk of Contrast-Induced Nephropathy in Diabetic Patients With and Without Dipstick Proteinuria Referred for Cardiac Catheterization

Reyan A. Ghany, Erik Bernstein, Julio Chirinos, 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 fluid voulme prior to cardiac catheterization.
None of the 37 patients without proteinuria developed CIN (95% CI for proportion = 0-9.5%), whereas 4 out 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.

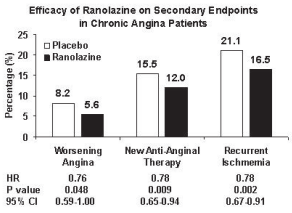
	No proteinuria (N=37)		**Proteinuria (N=56)**		***P* value**
	Mean	SD	Mean	SD	
Age in Years	58.1	10.0	60.3	8.6	0.25
Brachial Systolic Blood Pressure, mmHg	144.6	15.5	145.8	15.7	0.69
Brachial Diastolic Blood Pressure, mmHg	86.6	10.2	82.7	11.1	0.09
Brachial Pulse Pressure, mmHg	58.0	14.5	63.1	12.3	0.05
Hemoglobin at baseline, g/dL	13.8	1.2	13.6	1.3	0.46
Body Mass Index, kg/m2	26.5	1.8	25.6	1.5	0.03
Left ventricular Ejection Fraction, %	51.4	7.0	51.0	7.2	0.9
Pre-Catheterization IV Fluids, mL	335.9	234.1	463.8	284.7	0.03
Contrast Volume, mL	121.0	43.6	118.8	51.9	0.28
	N	%	N	%	
Male Gender	25	67.6	44	78.6	0.23
LDL Cholesterol > 130 mg/dL	19	51.4	26	46.4	0.64
Smoking	11	29.7	14	25	0.61
ACE Inhibitor Use	23	62.2	21	37.5	0.02
ARB Use	4	10.8	6	10.8	1
	Mean	**SD**	**Mean**	**SD**	***P* value**
Baseline Serum Creatinine, mg/dL	1.0	0.2	1.1	0.2	0.59
Serum Creatinine at 48 hours, mg/dL	1.1	0.2	1.2	0.2	0.35
Serum Creatinine at 7 Days, mg/dL	1.1	0.1	1.1	0.1	0.75

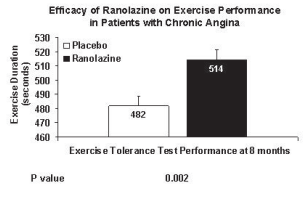
11:00 a.m.

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. Scirica, Sabina A. Murphy, Jacqueline L. Buros, 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 positive 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 1° 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.

1031-46 Sustained Increase Of Platelet Activation Indices Following Sirolimus-Eluting Stent Implantation

Maria Marketou, George Kochiadakis, Katerina Sfiridaki, Aikaterini Giaouzaki, Dimitris Arfanakis, Emmanouel Skalidis, Ermioni Kantidaki, Panos Vardas, Heraklion University Hospital, Heraklion, Greece, Venizelio Hospital, Heraklion, Greece

Background: Despite the proven superiority of sirolimus-eluting 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, 62Â±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 cCD40L and sP-selectin levels 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 treated 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 1

	SES			BMS		
	before	48 hours	1 month	before	48 hours	1 month
sCD40L (pg/ml)	140 ± 85	195 ± 78*	192 ± 75*	152 ± 72	142 ± 64	164 ± 88
sP-selectin (ng/ml)	45 ± 16	47 ± 22	60 ± 35*	55 ± 37	59 ± 27	58 ± 39

11:00 a.m.

1031-47 Vascular endothelial growth factor protein levels and gene expression in peripheral monocytes after stenting: A randomized comparative study of sirolimus-eluting and bare metal stents

Maria Marketou, George Kochiadakis, Dimitrios Panutsopulos, Dimitrios Arfanakis, Emmanuel Skalidis, Nikolaos Igoumenidis, Michael Hamilos, George Sourvinos, Demetrios Spandidos, Panos Vardas, 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 monocytes 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-vessel 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 mRNAs were estimated by real-time quantitative reverse transcriptase-PCR (TaqMan). VEGF serum levels were determined each time by ELISA.
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=0.002). 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 relationship 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.

1031-48 Prognostic Impact of Various Platelet Function Assays and Definitions of Non-responsiveness to Clopidogrel 600 mg on Early Outcome After Elective PCI

Dietmar Trenk, Willibald Hochholzer, Christian Stratz, Christian M. Valina, Hans-Peter Bestehorn, Heinz Joachim Buettner, Franz-Josef Neumann, Herz-Zentrum Bad Krozingen, Bad Krozingen, Germany

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). We assessed the prognostic impact of alternate platelet function assays and currently used non-responder definitions as alternate approach.
Methods The prognostic impact of the expression of the platelet surface proteins activated GP IIb/IIIa (PAC-1) and P-selectin was determined in the EXCELSIOR cohort (802 patients). In addition, we tested the impact of RPA after stimulation with ADP 20µM and two currently used definitions of non-responsiveness to clopidogrel. Non-responsiveness was defined either as ≤10% change in RPA or as <20% inhibition of RPA using ADP 20µM as stimulant. Parameters were obtained from blood samples drawn immediately before PCI
Results Odds ratios with 95% confidence intervals for the different parameters characterizing antiplatelet response to the 600-mg bolus dose of clopidogrel are provided in the table.

Parameter	Odds ratio	95% CI	p-value
RPA ADP 5µM above median	6.71	1.52 - 29.41	0.003
Activated GPIIb/IIIa above median	1.42	0.38 - 5.71	0.76
P-Selectin above median	1.04	0.28 - 3.94	0.85
Non-responsiveness [≤10% change]	1.51	0.34 - 13.88	0.89
Non-responsiveness [<20% inhibition]	1.58	0.42 - 5.15	0.57

In contrast to RPA after stimulation with ADP 5µM neither the expression of PAC-1 or P-selectin nor currently used non-responder definitions to clopidogrel showed a significant prognostic impact on MACE within 30 days after PCI.
Conclusion RPA after stimulation with ADP 5 µM provides superior prognostic impact regarding 30-days clinical outcome after elective PCI.

11:00 a.m.

1031-49 Demographic and Clinical Factors Predicting the Antiplatelet Effect of a Loading Dose of Clopidogrel 600 mg in Patients Undergoing Cardiac Catheterization With and Without PCI

Dietmar Trenk, Willibald Hochholzer, Christian Stratz, Christian M. Valina, Hans-Peter Bestehorn, Heinz Joachim Buettner, Franz-Josef Neumann, Herz-Zentrum Bad Krozingen, Bad Krozingen, Germany

Background The EXCELSIOR-study showed the impact of variability in antiplatelet response to a 600-mg clopidogrel bolus on 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%; 1.1-2.9%; 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:1.6-9.8%; P=0.007; n=71) and diabetics with sulfonyl urea drugs (+6.6%; 95% CI:3.1-10.2%; P<0.001; n=94) had an increased RPA at angiography.

	Δ RPA (%) [95% CI]	P-Value
Age per 10 years	2.2 [1.2-3.1]	p<0.001
Body weight per 10 kg	1.1 [0.5-1.7]	p=0.001
Diabetes mellitus	3.5 [1.3-5.7]	p=0.002
Coronary heart disease	2.2 [0.3-4.1]	p=0.023
Angiography <2h after clopidogrel 600 mg	10.5 [8.8-12.2]	p<0.001

Conclusion Antiplatelet effect of 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.

1031-50 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 Kolm, 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, ultimately, 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 A1c, systolic blood pressure (BP) and diastolic BP, use of angiotensin converting enzyme (ACE) inhibitors, lipid-lowering therapies, beta-blockers and angiotensin II receptors 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=0.545). 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 1.068 95% CI 1.033-1.105; p<0.001), use of ACE inhibitors (OR 1.04 95% CI 1.004-1.077; 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 yrs 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.

11:00 a.m.

1031-51 Healthcare Resource Utilization in Patients With Refractory Angina

Alex R. Campbell, Daniel Satran, Richard Birkett, Ross Garberich, Daniel Hayward, Rachel E. Olson, Charlene R. Boisjolie, 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 OPTions 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.

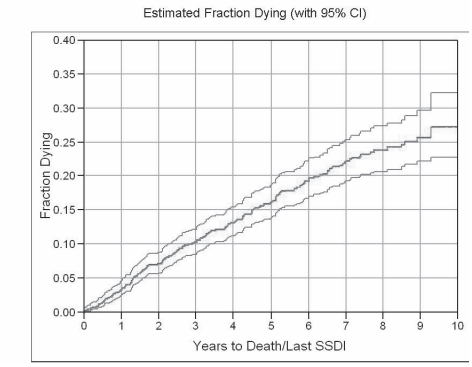
Healthcare Resource Utilization in Patients with Refractory Angina			
Lifetime (n=200)	Percentage of Population	Mean per Patient	Range
Coronary Angiograms	100	6.2	0-38
PCI	81	2.6	0-30
CABG	74	1	0-4
One Year Period (n=200)			
Coronary Angiograms	32	0.4	0-4
Revascularization	17	0.19	0-5
Echocardiograms	46	0.64	0-6
SPECT Imaging	30	0.33	0-2

11:00 a.m.

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

Timothy D. Henry, Daniel Satran, Alex R. Campbell, Randall J. Johnson, Anil K. Poulose, James Hodges, Bradley A. Bart, Rachel E. Olson, Karen L. Harvey, Patricia A. Mitchell, Theresa L. Arndt, 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 OPtions 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. Death status and cause of death were determined using the Social Security Death Index, clinical data and death certificates. Time to event analysis was performed using time from determination of no traditional revascularization options.
Results: For 1135 patients average age was 63 yrs (77% male) with 72% prior CABG, 74% prior PCI, 32% CHF, and 36% DM. Median follow up was 4.7 yrs (range 0-16 yrs, 10% over 9 yrs). 197 patients died (17.4%). From Kaplan Meier analysis, mortality was 3.3% (95% CI 2.3-4.3) at 1 yr and 25.8% (95% CI 22-29) at 9 yrs. There were 126 (64%) cardiovascular deaths (37 CHF, 29 sudden death, 26 MI, 34 unclear). 18 pts (9%) suffered periprocedural death. Predictors of all cause mortality were: age, DM, CHF, moderate/severe valve disease, kidney disease (all p<0.0001), cerebrovascular disease (p=0.001), prior MI (p=0.0006).
Conclusions: Patients with refractory angina actually have low long-term mortality. Therapeutic options for this growing population should focus on chest pain relief and improved quality of life.



11:00 a.m.

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 (Ala)(26±7.7 vs 19±7.0%, P<0.001) and reflected wave amplitude (14±7.2 vs 8.2±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 2901±1784 dyne-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.

11:00 a.m.

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 Faletra, 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 atherosclerotic coronary plaques in comparison with catheter-based angiography (QCA) and intravascular ultrasound (IVUS). Methods: After 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 understimate 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			
	MSCT vs QCA	**MSCT vs IVUS**	**IVUS vs QCA**
Lumen Area Stenosis (%)	71,5±13,8 vs 59,1±13,0 r =0,177 P<0,001	71,5±13,8 vs 70,4±6,7 r =0,822 P=0,426	70,4±6,7 vs 59,1±13,0 r =0,206 P<0,001
Lumen Cross-Sectional (mm2)	5,5±3,0 vs 4,2±1,2 r =0,729 P<0,001	5,5±3,0 vs 4,8±1,7 r =0,854 P=0,012	4,8±1,7 vs 4,2±1,2 r =0,730 P<0,001
External Elastic Membrane Cross-Sectional Area (mm2)		18,0 ± 5,0 vs 17,1 ± 4,4 r =0,847 P=0,031	
Plaque Cross-Sectional Area (mm2)		12,2±3,5 vs 11,7±3,2 r =0,788 P=0,118	

11:00 a.m.

1031-55 Postconditioning Protects the Human Heart After Flow Restoration in Patients With Subtotal or Significant Coronary Lesions

Efstathios K. Iliodromitis, Ioannis A. Paraskevaidis, Dimitrios Farmakis, Ioanna Andreadou, Aikaterini Fountoulaki, Ignatios Ikonomidis, Aias Antoniadis, Dimitrios 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 five patients with coronary artery disease and target lesions causing stenoses 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 with 6 cycles of 10sec ischemia/ 10sec reperfusion (postC group, N=29) or it was withdrawn with no additional intervention (control group, N=26). Blood samples were taken at baseline, immediately after the end of the last deflation and 15min later. Malondialdehyde (MDA) and nitrotyrosine (NT) were assessed as indexes of oxidative stress and nitrosative stress, respectively. Echocardiographic assessment of EF and WMS was performed at 24 hours and 10 days after the intervention.
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 vs all he 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 vs 6.44 ± 1.1 nmol/l). Both wall motion score and EF improved significantly in the postC group, from 1.17±0.18 to 1.08±0.11 (p=0.009) and from 64±8 to 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.

11:00 a.m.

1031-56 Key Role of Postchallenge Hyperglycemia for the Presence and Extent of Coronary Atherosclerosis: An Angiographic Study

Christoph H. Saely, Heinz Drexel, Harald Sourij, Stefan Aczel, Heidrun Jahnel, Robert Zweiker, Peter Langer, Thomas Marte, Guenter Hoefle, Werner Benzer, 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 artery disease (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, 394 had normal glucose tolerance (NGT), 190 impaired glucose tolerance (IGT), 90 isolated postchallenge diabetes (postchallenge glucose ≥200 mg/dl), and 366 type 2 diabetes previously established 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%, 95.6%, 89.1% vs. 80.7%; p = 0.030, 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 (77.8%; p = 0.001) or conventional diabetes (68.0%; 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.

11:00 a.m.

1031-57 Long-Term Clinical Prognosis of Patients With Cardiac Syndrome X

Gregory A. Sgueglia, Antonella Spinelli, Pasquale Santangeli, Priscilla Lamendola, Antonio Di Monaco, Giancarla Scalone, Fabio Infusino, Leonardo Marinaccio, Alfonso Sestito, Gaetano A. Lanza, Filippo Crea, Catholic University of Sacred Heart, Rome, Italy

Background: Classical follow-up studies of patients with angina and normal coronary arteries at angiography consistently reported an excellent prognosis of these patients. However, some recent series questioned the excellent prognosis of CSX patients, suggesting an increased risk of cardiac events in those with evidence of endothelial dysfunction.
Methods: We performed clinical follow-up of 154 patients (mean age 58.9±10 years, 39 men) diagnosed to have CSX at our Institute between 1991 and 2004, according to the following criteria: 1) typical effort angina; 2) evidence of myocardial ischemia based on ECG exercise stress test and/or ECG Holter monitoring and/or myocardial scinrigriphic stress tests; 3) totally normal epicardial arteries at coronary angiography. All patients were administered a detailed questionnaire about their angina history and clinical outcome during the years of follow-up.
Results: At a mean follow-up of 137±78 months (range 24-372) from the onset of symptoms, no patient died from cardiovascular causes, whereas 4 deaths (2.6%) occurred for non cardiac causes (3 cancers, 1 acute pancreatitis). Furthermore, no patient developed an acute myocardial infarction during follow-up. Despite the lack of major cardiac events, at least 1 hospital readmission because of acute chest pain at rest or worsening effort angina occurred in 89 patients (57.8%), 33 of whom (21% of total) underwent at least one further coronary angiographic study, with two of them showing flow-limiting coronary stenoses in at least one epicardial vessel (6% of patients who repeated angiography; 1.3% of all patients). Compared to the basal evaluation, angina symptoms were improved in 82 patients (53%), unchanged in 51 (33%) and worsened significantly, despite treatment, in 21 (14%) patients.
Conclusions: Our study, which involves the largest cohort of CSX pts until now followed-up, show the substantial absence of major cardiac events at long term follow-up (average >10 years) in CSX patients. Our data, however, show the persistence or worsening of symptoms, which may significantly impair quality of life, in a significant proportion of these patients.

11:00 a.m.

1031-58 Effects of Rosuvastatin And Ezetimibe on Flow Mediated Dilation in Patients With Congestive Heart Failure: A Double-Blind, Cross-Over Trial

Penny Gounari, Dimitris Tousoulis, Charalambos Antoniades, Nikos Papageorgiou, Georgia Roulia, George Latsios, Alexios Antonopoulos, Gerasimos Siasos, George Hatzis, Anna-Maria Kampoli, Christodoulos Stefanadis, 1st Cardiology Department, Hippokration Hospital, Athens Medical School, Athens, Greece

Background: Congestive heart failure is characterised by increased proinflammatory stimulation and impaired endothelial function. Although statin treatment exerts a beneficial effect on endothelial function, reflected in an improvement of clinical outcome in patients with heart failure, it is still unclear whether this effect is due to lipid-lowering or their pleiotropic effects. We compared the effect of short-term treatment with rosuvastatin or ezetimibe on endothelial function in patients with congestive heart failure.
Methods: In this double-blind, placebo controlled, cross-over trial, 13 patients with congestive heart failure (ejection fraction 31.9±1.5%, age 59.7±3.3 years old) were randomised to receive ezetimibe 10mg/d or rosuvastatin 10mg/d for 4 weeks, with 4 weeks wash-out period between the two interventions. Endothelial function was evaluated by flow mediated dilation (FMD) in the brachial artery at the beginning and at the end of each treatment period.
Results: There was no change in the baseline brachial diameter after treatment with either ezetimibe (from 47±1.8mm to 48±2.3 mm, p=NS) or rosuvastatin (from 48±2mm to 48±1.3mm, p=NS). However, there was a significant improvement of FMD in the rosuvastatin group (from 4.23±1.7% to 9.88±2.29%, p<0.05) but not in the ezetimibe group (from 3.1±2.1% to 5.3±2.2%, p=NS). The change in lipid levels were similar between groups (p=NS). The change in FMD was not significantly correlated with the decrease of serum LDL in either the ezetimibe (r=-0.104, p=0.747) or rosuvastatin (r=-0.364, p=0.271) treated groups.
Conclusions: Rosuvastatin improves endothelial function in patients with congestive heart failure, by mechanisms independent of lipid-lowering. On the contrary, lipid-lowering treatment achieved by ezetimibe is unable to affect endothelial function in these patients. These findings indicate a direct beneficial effect of statins in patients with congestive heart failure, further to lipid-lowering.

11:00 a.m.

1031-59 The Ala379Val Polymorphism of Lipoprotein-Associated Phospholipase A2 Affects the Risk for Arterial Hypertension and Modifies Platelets Activation

Despina Kardara, Dimitris Tousoulis, Charalambos Antoniades, Nikolas Koumallos, Alexios Antonopoulos, Nikos Papageorgiou, Costas Tsioufis, Charalambos Vlachopoulos, Elli Stefanadi, Carmen Vasiliadou, Christodoulos Stefanadis, 1st Cardiology Department, Hippokration Hospital, Athens Medical School, Athens, Greece

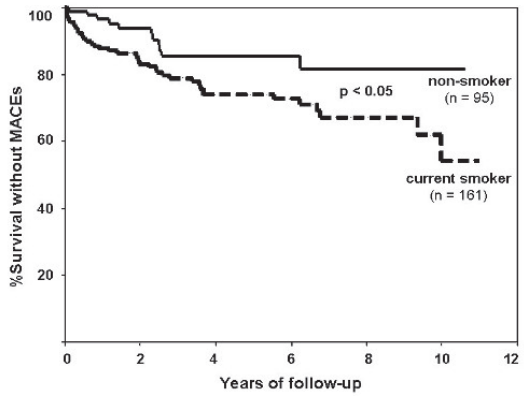
Background: Lipoprotein-associated phospholipase A2 (Lp-PLA2) activity has been identified as a risk factor for atherosclerosis. Lp-PLA2 has proinflammatory properties and it hydrolyses platelet activating factor. Genetic polymorphism Ala379Val has been associated with Lp-PLA2 activity, but its effect 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 sCD40L, P-selectin oxidized LDL (ox-LDL) were measured by ELISA.
Results: The genotype distribution was: Val/Val: 9 (3.8%), Ala/Val:69(29.4%) and Ala/Ala: 157(66.8%) in hypertensives, and Val/Val: 9 (3.6%), Ala/Val:98(38.7%) and Ala/Ala: 146(57.7%) in controls. The carriers of the Val allele had significantly lower risk for arterial hypertension (OR[95%CI]:0.678[0.469-0.980], 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±2.7U/L) compared to Ala homozygotes (71.3±2.4U/L, p<0.05). Val homozygotes also had lower levels of P-selectin (20.0±6.4 ng/ml) and sCD40L (3.5±0.8ng/ml) compared to Ala homozygotes (38.0±1.8 ng/ml and 5.7±0.3ng/ml 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 lower levels of sCD40L and P-selectin, suggesting lower platelets activation. These findings suggest that this polymorphism may be implicated in the pathogenesis of hypertension and platelets activation.

11:00 a.m.

1031-60 **Long-Term Outcome of Korean Patients With Vasospastic Angina**

Sang-Yong Yoo, 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.



11:00 a.m.

1031-61 **Comparison Between Three-Dimensional Angiographic Reconstruction and Intravascular Ultrasound Imaging for the Measurement of Intracoronary Cross-Sectional Luminal Dimensions**

Tim A. Fischell, Edmund Bermudez, Borgess Heart Institute, Kalamazoo, MI

Background: Given its greater spatial resolution over traditional two-dimensional angiography, intravascular ultrasound has enabled the measurement of minimal luminal area of coronary stenoses, of which, an area of less than 4.0 mm^2 has been shown to correlate with hemodynamically significant stenoses. Angiographic three-dimensional reconstruction of luminal dimensions can provide similar measurements without further invasive study. **Methods:** We prospectively enrolled consecutive patients undergoing invasive coronary angiography and intravascular ultrasound for the assessment of angiographically intermediate coronary lesions (50-70%) at a high volume tertiary care hospital between July 1, 2006 and June 1, 2007. Intravascular Ultrasound using motorized pullback was performed on all lesions with offline measurements of minimal luminal dimension and area. Using a commercially available three-dimensional angiographic reconstruction software package (CardiOP-B, Paieon Inc., Israel), two orthogonal angiographic views were obtained to reconstruct and calculate lesion dimensions. **Results:** A total of 31 patients were enrolled with 32 lesions assessed in 31 vessels. Lesions were assessed in the left anterior descending artery, left circumflex artery, and right coronary artery in 42% (n=13), 26% (n=8), and 32% (n=10), respectively. Overall mean minimal luminal area was 3.5 mm^2 ± 1.6mm and minimal luminal dimension 1.87 mm ± 0.58 mm. Three-dimension reconstruction measurements of cross-sectional minimal luminal area highly correlated in a linear fashion with measurements by intravascular ultrasound (r=0.88, p<0.0001). Similarly, minimal luminal dimensions correlated in a statistically significant fashion between both methods (r=0.78, p<0.0001). The sensitivity of angiographic reconstruction to detect a hemodynamically significant lesion (minimal luminal area <4.0 mm^2) was 89%, with a specificity of 46% and overall accuracy of 72%. **Conclusions:** Three-dimensional angiographic measurements of intracoronary stenoses highly correlate with measurements by intravascular ultrasound and provide a sensitive method of detecting cross-sectional areas of less than 4.0 mm^2.

11:00 a.m.

1031-62 **Gender Differences in Risk Factors Including C-Reactive Protein in a Large Consecutive Patient Cohort Undergoing Elective Coronary Angiography**

Alois Suessenbacher, Maria Wanitschek, Suzanne De Waha, Jakob Doerler, Matthias Frick, Otmar Pachinger, Hannes F. Alber, Division of Cardiology, Innsbruck, Austria

Background: Little information is available about gender differences concerning the presence and influence of cardiovascular risk factors including C-reactive protein (CRP) in consecutive patients undergoing coronary angiography (CA) for the evaluation of coronary artery disease (CAD).
Methods: 5641 consecutive patients (33.1% women) undergoing elective CA were analysed. Cardiovascular risk factors were assessed by standardised questionnaire and routine blood chemistry. CAD was graded by visual estimation of lumen diameter stenosis. Significant stenoses were defined as lumen diameter reduction ≥70% in at least one major coronary artery. Coronary angiograms were graded as non-significant CAD, as 1-, 2- or 3-vessel disease or as non-CAD.
Results: Women were older than men (65.2±11.0 vs. 63.1±11.0 years, p<0.001)and had more often a positive family history for premature CAD (30.2 vs. 24.5%, p<0.001). The number of risk factors was higher in men (2.4±1 vs. 2.3±1, p=0.01) and smoking was more common in men (55.9 vs. 35.0%, p<0.001). In addition, CRP levels were higher in men (0.82 vs. 0.97mg/dl, p=0.02). The prevalence of hypertension (76.1 vs. 77.5%, p=0.25), hypercholesterolemia (68.5 vs. 69.4%, p=0.47) and diabetes (17.6 vs. 17.4%, p=0.86) was not different between gender. CAD was more often found in men (80.0 vs. 59.1%, p<0.001). In multinomial logistic regression analyses including age, total cholesterol, HDL-cholesterol, CRP, diabetes, hypertension and prior statin use in men all variables except hypertension were independent predictors of CAD. In women total cholesterol and hypertension were not independently associated with CAD. According to Wald statistics, CRP was a much stronger independent predictor of CAD in men than in women.
Conclusion: In this large consecutive patient cohort women and men have almost similar risk factor profiles when referred for CA. The influence of traditional risk factors on the prevalence of CAD is similar between gender, but CRP is a stronger independent predictor of CAD in men.

11:00 a.m.

1031-63 **Prevalence and Predictors of Suboptimal Response to Aspirin in Patients with Coronary Artery Disease**

Roland Youssef Kassab, Mirna Germanos, Georges Badaoui, Miche Fahed, Youssef Massaad, Zeina Kadri-Maalouf, Elie Salame, Rabih R. Azar, Hotel Dieu de France Hospital, Beirut, Lebanon

Background: Patients with coronary artery disease (CAD) who are resistant to aspirin (ASA) are at increased risk for recurrent cardiac events. However, the prevalence and predictors of a suboptimal response to ASA remain insufficiently defined. **Methods:** We measured platelet aggregation in response to 125 µg of arachidonic acid using the Plateletworks test (Helena Laboratories). With this test, patients who are not exposed to ASA have an inhibtion of platelet aggregation < 40%. Based on this, we defined a suboptimal response in patients taking ASA by an inhibition < 40%. We enrolled patients with stable CAD who have been on ASA for > 1 month. Patients with acute coronary syndrome and those on other anti-platelet drugs were excluded. **Results:** 352 patients were enrolled: 37% with prior MI, 32% with prior PCI and 45% with prior CABG. Mean inhibition of platelet aggregation was 48 ± 17% in the whole group. One hundred thirteen patients (32%) were poor responder to ASA and had a mean platelet inhibition of 29 ± 8% compared to 57 ± 12% in patients with good response (p < 0.001). ASA dose was similar between the 2 groups (104 ± 40 vs. 100 ± 29 mg/day). Increased age, lower body mass index, male gender and a history of prior MI were associated with a suboptimal ASA response (table) while traditional risk factors and medications other than aspirin were not. **Conclusion:** The prevalence of a suboptimal response to ASA is as high as 32% and should be especially considered in elderly male patients with low body mass index and a history of prior MI.

Predictors of Suboptimal Response to ASA		
	Relative Risk (95% CI)	**P Value**
Male gender	2.2 (1.3-3.6)	< 0.001
Age	1.03 (1.01-1.05)	0.007
Body Mass Index	0.9 (0.84-0.97)	0.008
Prior MI	1.3 (1.01-1.85)	0.04

11:00 a.m.

1031-64 **Comparison of Stress CMR with Stress SPECT for the Diagnosis of Coronary Artery Disease**

Ijaz Ahmad, John Heitner, Igor Klem, Frederick Meine, Michele Parker, Robert Judd, Michael W. Hanson, Salvatore Borges-Neto, Raymond J. Kim, New York Methodist Hospital, Brooklyn, NY, Duke University Medical Center, Durham, NC

Background: Single positron emission scintigraphy (SPECT) imaging is one of the most utilized outpatient procedures. The diagnostic accuracy of SPECT can be limited by soft tissue attenuation and low resolution. Cardiac magnetic resonance imaging (CMR) assesses myocardial perfusion with higher spatial resolution and without susceptibility to soft tissue attenuation.
Objectives: To compare stress CMR to stress SPECT in the diagnosis of coronary artery disease (CAD) in patients who present with chest pain.
Methods: We prospectively enrolled 65 patients with chest pain who were at intermediate

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 either 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 a negative CMR and SPECT, there were no clinical events on follow up (mean 2 ½ years).

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

Baseline Characteristics			
Characteristics	Entire Group (n=63)	CAD (n=13)	No CAD (n=50)
Age(years)	58.1	58.5	58
Males	41(65%)	11 (85%)	30(60%)
Diabetes	12 (19%)	5(38%)	7(14%)
Hypertension	38(60%)	10 (77%)	28(56%)
Hypercholesterolemia	32(51%)	8(61%)	24(48%)
Statins	28 (44%)	8 (61%)	20(40%)
Beta Blocker	18 (29%)	6 (46%)	12(24%)
Aspirin	30 (48%)	9 (69%)	21(42%)
C-reactive Protein	0.4	0.58	0.36

11:00 a.m.

1031-65 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. Sedlis, 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 ≥ age 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 OMT + PCI, 1,381 patients (60%) were < age 65 years (mean age: 56 ± 6 years) and 904 patients (40%) were ≥ age 65 years (mean age: 72 ± 5 years). Rates of death, MI, stroke, and ACS stratified by treatment arm and age dichotomized at 65 years are shown (Table).

CV Outcomes	Age	PCI + OMT	OMT	P value
Death	< 65	28 (4 %)	41 (6 %)	0.12
	≥ 65	57 (12 %)	54 (12 %)	0.92
MI	< 65	83 (12 %)	76 (11 %)	0.52
	≥ 65	60 (13 %)	52 (12 %)	0.54
Death or MI	< 65	107 (16 %)	109 (16 %)	0.93
	≥ 65	104 (23 %)	93 (21 %)	0.54
Death, MI, stroke	< 65	113 (16 %)	114 (16 %)	0.99
	≥ 65	109 (24 %)	99 (22 %)	0.62
ACS	< 65	87 (13%)	85 (12%)	0.83
	≥ 65	60 (13%)	52 (12%)	0.47
Death, MI, stroke, ACS	< 65	172(25%)	175 (25%)	0.91
	≥ 65	141 (31%)	130 (29%)	0.65

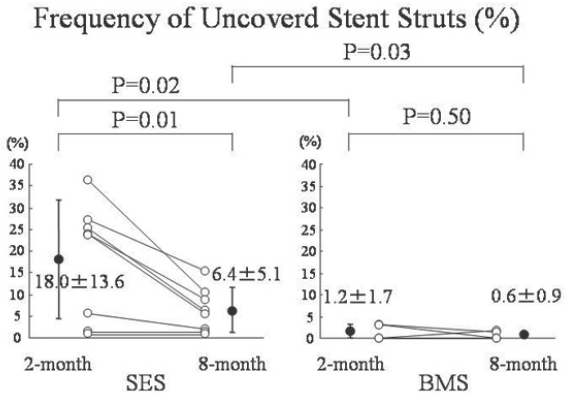
Conclusions: Patients ≥ age 65 years had more deaths than younger patients, but not more nonfatal MIs. The addition of PCI to OMT did not reduce CV events; thus, it appears difficult to justify PCI as an initial strategy in older stable CAD patients, and it is unlikely to be cost-effective as well. These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

11:00 a.m.

1031-66 Serial Analysis of Neointimal Coverage Following Sirolimus-eluting Stent Implantation Using Optical Coherence Tomography: Comparison with Bare-metal Stent

Tatsuya Ito, Mitsuyasu Terashima, Yoshihiro Takeda, Jean-François Surmely, Osamu Katoh, Tetsuo Matsubara, Takahiko Suzuki, Toyohashi Heart Center, Toyohashi, Japan

Background: Late stent thrombosis (LST) in sirolimus-eluting stents (SES) after discontinuation of antiplatelet 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 inplanted stent segment were analyzed at intervals of 1mm. Eight SES including 1270 struts and 5 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 1.2 ± 1.7%, 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 0.6 ± 0.9%, p=0.03). **Conclusions:** The window of thrombotic risk for SES extends far beyond that for BMS.



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 Harbuzariu, Laurel S. Kleppe, Robert D. Simari, Gregory W. Barsness, Mayo Clinic, Rochester, MN

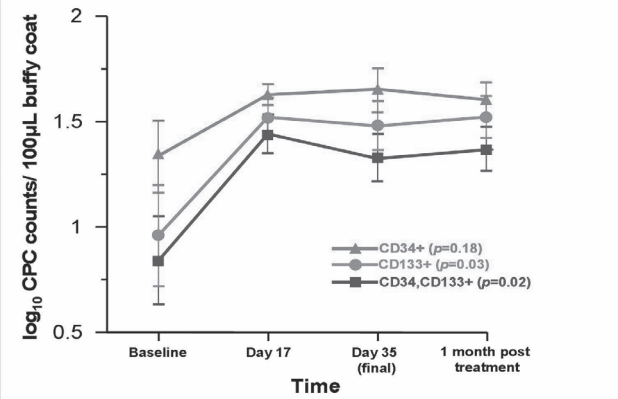
Background: The mechanism underlying the benefits of Enhanced External Counterpulsation (EECP) is not clear. We hypothesized that this could be associated with an increase in circulating bone-marrow derived progenitor cells (CPCs) and increased erythropoietin (Epo) levels, as studies have demonstrated 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 MU/ml at baseline to 22±3 MU/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 Enhanced External Counterpulsation Improves One Year Mortality in Angina Patients With End Stage Coronary Disease

William E. Lawson, John CK Hui, Elizabeth D. Kennard, Marc A. Silver, Oslem Soran, Sheryl F. Kelsey, Gregory Barsness, 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. Multivariable analysis of pts alive at 60 days after EECP was begun was used to determine independent predictors of one year mortality.
Results: Records of 4,597 pts were analyzed; 3,962 pts (86%) completed (C) the usual course of therapy, 14% did not (IC). Cardiac events (death, MI, CABG, PCI) accounted for 12% of the IC. Baseline demographics and history of IC and C cohorts were comparable: 89% prior CABG or PCI, 70% prior MI, 91.5% Class III or IV angina, and only 15% considered candidates for CABG or PCI. Post EECP angina class improved significantly, 85% versus 25% improving ≥1 CCS, in the C(mean 36±4 hours) versus the IC cohort (mean 13±8 hours). At 1 year there was a significant difference in mortality rates favoring the C group (4.1% versus14.1%; p<0.001), and decreased rates of myocardial infarction (4.1% versus 7.7%), CABG (2.5% versus 6%), and PCI (6.3% versus 11.3%)(all p<0.001). Predictors of 1 year mortality in pts alive at 60 days included: LVEF ≤ 35%, HR=2.70 (p<0.001); completion of EECP, HR=2.00 (p<0.001); CHF, HR=1.65 (p<0.001); Diabetes, HR=1.47 (p=0.012); Age (per year), HR=1.05 (p<0.001).
Conclusions: EECP therapy completion improves CCS angina class and 1 year survival in end stage CAD pts. Predictors of mortality are similar to those having prognostic value in coronary disease pts, including: heart failure and left ventricular dysfunction, diabetes, male gender, age.

11:00 a.m.

1031-69 Is Cardiac Magnetic Resonance Imaging a Useful Test in the Diagnosis of Women with Microvascular Angina?

Melissa H. Slivka, Chrisandra Shufelt, Yuching C. Yang, Louise E. Thomson, Saibal Kar, Leslee Shaw, Daniel S. Berman, Bina Ahmed, Kirsten Tolstrup, C. Noel Bairey Merz, Cedars Sinai Medical Center, Los Angeles, CA

Background: Women with microvascular angina (open coronary arteries but myocardial ischemia) have an adverse prognosis comparable to that of obstructive coronary disease as shown in prior research. Coronary reactivity testing (CRT) is useful in this diagnosis as traditional imaging tests are unable to detect subendocardial ischemia. Cardiac magnetic resonance imaging (CMR) may be useful to detect subendocardial ischemia due to abnormalities in coronary vascular function. We tested the sensitivity of CMR in women with angina and open coronary arteries for the diagnosis of microvascular angina using CRT as gold standard.
Methods: Forty women with clinical evidence of ischemia and non-obstructed coronary disease were referred for CRT and CMR. Women with myocardial bridging (n=1), left ventricular hypertrophy (n=1), obstructive coronary disease (n=2) and anomalous coronary (n=1) were excluded. CRT included intra-coronary artery adenosine coronary flow reserve (CFR) (non-endothelial microvascular function), changes in coronary blood flow and vessel diameter following intra-coronary acetylcholine (endothelial dependent macro and microvascular function) and vasodilatation following intra-coronary nitroglycerine (non-endothelial dependent macrovascular function). CMR included adenosine stress and rest perfusion using a 17 segment myocardial model with visual interpretation by two observers blinded t the CRT and angiography findings.
Results: The mean age of women was 54 ± 9.3 years, 19% were non-white, 48% dyslipidemic, 34% hypertensive, 46% had history of smoking. An abnormal CRT was found in 91%, and 68% had abnormalities in CMR subendocardial stress perfusion with normal delayed enhancement and ventricular function. The sensitivity of CMR to CRT defined vascular dysfunction was 69% with a positive predictive value (PPV) of 92%. For the quantitative read, scoring the % ischemic myocardium of ≥10% by CMR resulted in a sensitivity of 68% and PPV of 88%.
Conclusions: Women with ischemia and open coronary arteries have a high rate of CRT and CMR abnormalities. CMR appears to have a fair sensitivity and good PPV for microvascular angina. Further study is indicated.

11:00 a.m.

1031-70 Effect of Enhanced External Counterpulsation on Ejection Fraction in Patients with Ischemic Heart Disease

William E. Lawson, Himanshu Padh, Subramanian Ramasamy, John CK Hui, Samarpan Heart Hospital and Research Center, Jamnagar, India, The People's College of Medical Sciences, Jamnagar, India

Background: Enhanced External Counterpulsation (EECP) has been shown to decrease symptoms of myocardial ischemia, improve perfusion, endovascular function, and exercise capacity. There are no large studies evaluating the effect of EECP on ejection fraction (EF) in patients with ischemic heart disease.
Methods: Two-dimensional transthoracic echocardiography was performed on 505 patients with ischemic heart disease 1 week before their 35 hours (1 hour daily) of EECP treatment and repeated within 1 week after completion of treatment. Patients were divided into two groups, one with baseline EF>35% (N=360) and the other with EF≤35% (N=145). Pre- and post echo parameters were compared in both groups using a 2-tailed paired t-test with significance at p<0.05.
Results: The EF>35% group was slightly younger than EF≤35% group (58.1 versus 61.3 years), predominately male (86 versus 88%), with similar percentage with diabetes (55 versus 50%), hypertension (75 versus 72%), hypercholesterolemia (64 versus 61%), MI (48 versus 49%), CABG (21 versus 31%) and PCI (13% versus 8%). In the EF≤35% group, the EF and stroke volume (SV) increased significantly from a baseline of 29.3±6.3% and 67.7±8.4 ml to 45.1±7.9% and 75.0±9.2 ml (p< 0.001), with no significant change in heart rate (78±13 to 77± 13 beats/min). Surprisingly, the mean EF and SV of the >35% group also increased from 48.1±7.4% and 78.4±8.2 ml at baseline to 56.3±5.5% and 85.6±9.3 ml post-EECP (p<0.001). The improvement in EF and SV was mainly from a significant reduction of end systolic volume from 59.3±10.4 to 53.6±8.4 ml (p<0.001) in the EF≤35% group and from 54.6±7.6 ml to 50.4±6.0 ml in the EF>35% group, without significant change in end diastolic volumes (127.0±10.8 to 128.6 ±10.9ml and 133.8±11.8 to 136.0±10.4 ml respectively).
Conclusions: EECP treatment significantly increased ejection fraction and stroke volume, mainly due to a decrease in end systolic volume. Potential underlying mechanisms include improvement in left ventricular contractility due to improved myocardial perfusion and/or afterload reduction secondary to normalization of endovascular tone and function.

11:00 a.m.

1031-71 Cardiac Magnetic Resonance Imaging and Coronary Reactivity Testing: A Useful Noninvasive Tool

Chrisandra L. Shufelt, Saibal Kar, Melissa Slivka, Louise Thomson, Yuching Yang, Daniel Berman, Donna Polk, Kristen Tolstrup, C. Noel Bairey Merz, Cedars-Sinai Medical Center, Los Angeles, CA

Background: Coronary reactivity testing (CRT) is used in the diagnosis of microvascular dysfunction based on endothelial and non-endothelial dependent markers. Adenosine stress cardiac magnetic resonance imaging (CMR) may be a useful non-invasive method to detect subendocardial ischemia. We sought to determine the relationship between CRT and CMR abnormalities in a selected population of women.
Methods: Thirty-five 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 micro- and macrovascular function, respectively) 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.
Results: 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, resp). 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=0.09, 0.07, resp).
Conclusions: 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 CFR and study in a larger group including normal controls is needed.

11:00 a.m.

1031-72 Accurate Detection of Coronary Artery Disease without use of Radiation using Non-Stress Magnetocardiography

Indraneil Ray, 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. Currently 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 unshielded 9 channel MCG in a general clinical setting. Scan time was 6 minutes. The MCG data were processed 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 ECG (79%) 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

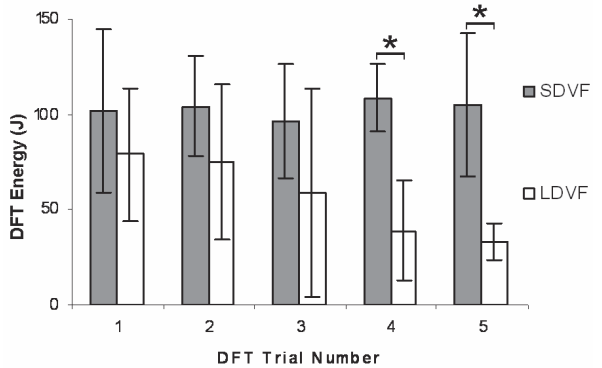
73% and 92%, respectively. In comparison, the sensitivity, specificity, PPV and NPV of stress SPECT was 90%, 68%, 68% and 90%, respectively.
Conclusion: MCG is a rapid risk free method for detection of coronary artery disease without the use of radiation, contrast or stress testing.

11:00 a.m.

1031-73 Defibrillation Threshold Decreases With Repeated Episodes of Long Duration Fibrillation

Derek J. Dosdall, 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.



* Significantly different with paired t-test, p<0.01 with Bonferroni correction.

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.

11:00 a.m.

1031-74 Clinical Relevance of Hemolysis During Circulatory Support With Percutaneously Implantable Axial Flow Pumps

Markus Ferrari, Markus Schlosser, 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 intermediate 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 LP2.5, or AMED LVAD 16F). 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 male, duration of circulatory support was 27.3 +/- 38.36 hours (10 - 140 hours). The fHb increased from 2.9 +/- 2.13 µmol/l to a maximum of 27.9 +/- 30.84 µmol/l within 4 hours of pump support. The serum level of fHb decreased to 13.9 +/- 12.10 µmol/l after 8 hours, and remained on this level until removal of the pAFP. Afterwards, we observed a normalization of fHb within 48 hours. Blood transfusions were necessary in 6 patients (42.9 %). All patients were successfully weaned from pAFP. The 1-month survival rate was 78.6% (11 pts.).
Conclusions: The initial maximum of hemolysis within the first 4 hours of pAFP support is partly reversible. However, no further increase in hemolysis should be expected afterwards. Signs of hemolysis should not result in termination of circulatory support. The benefit of hemodynamic improvement overweighs the need for blood transfusion as observed in less than half of the patients.

11:00 a.m.

1031-75 Resuscitated Cardiac Arrest is Associated with Reduced In-Hospital, but not Long-term Survival in Acute Coronary Syndrome

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

Introduction: Acute Coronary Syndrome (ACS) complicated by pre-hospital Cardiac Arrest (CA) is commonly associated with poor clinical outcomes. Data regarding longer term prognosis and the effects of contemporary therapies are lacking in this cohort. We sought to assess the impact of successfully resuscitated Cardiac Arrest on ACS outcomes in routine clinical practice.
Methods: The Australian Collaborative Acute Coronary Syndromes 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, involving 39 Australian metropolitan and rural sites. ACS patients presenting following successfully resuscitated cardiac arrest were the focus of this investigation. Patient characteristics, management and clinical outcomes were assessed.
Results: In the seventy-nine patients assessed, successfully resuscitated, pre-hospital CA strongly predicted in-hospital mortality (HR 17.2, 95% CI 8.9-33.1, p<0.0001). Admission glomerular filtration rate (eGFR) <60mL/minute was strongly associated with increased in-hospital mortality following CA (HR 4.7, 2.5-8.8, p<0.0001), but an invasive management strategy was associated with a marked reduction in in-hospital mortality (HR 0.42, 0.23-0.79, p=0.007) despite multivariate adjustment and exclusion of patients dying within 24-hours of hospital presentation. Notwithstanding a poor short-term prognosis, no incremental hazard was seen at 12-month follow-up in ACS patients surviving to hospital discharge following CA (HR 1.2, 0.29-4.9, p=0.79).
Conclusions: Resuscitated CA prior to hospitalisation strongly predicted in-hospital mortality, but not post-discharge survival. The substantial in-hospital survival advantage conferred by early invasive therapy lends further support to the routine invasive management of such high-risk ACS patients.

11:00 a.m.

1031-76 Loss of Heart Rate and Blood Pressure Variability in Murine Sepsis

Anupam Gupta, Bryan Foley, Josh Weinstock, Karine Hageboutros, Jad Skaf, Joseph E. Parrillo, Sergio Zanotti, Steven M. Hollenberg, Cooper University Hospital, Camden, NJ

Background: Nonlinear analysis of beta-to-beat heart rate and blood pressure variability may provide insights into disease pathophysiology not available from standard linear measures. Calculation of volatility (standard deviation (SD) variability) is a means of assessing variability that may minimize artifact-induced error. We compared heart rate and blood pressure volatility in a murine model of resuscitated sepsis.
Methods: Radiotelemeters for noninvasive measurement of blood pressure were implanted into the ascending aorta of C57Bl/6 mice (8-12 weeks, n=23). After 5 to 7 days of recovery post-implantation, baseline data were collected for 24 hours. The mice were then made septic by cecal ligation and puncture and resuscitated with fluids and antibiotics every 6 hours; controls underwent sham ligation. Heart rate and blood pressure SDs were calculated for 1 minute and 5 minute intervals. For each animal, the SD cutoff of both heart rate and blood pressure that represented the lowest 5% was determined, and the % of low SDs (low volatility) in the entire experimental period was defined by this cutoff. The % of low volatility periods was calculated over 1-hour and 4-hour intervals to generate time courses.
Results: Intervals with low heart rate and blood pressure volatility were increased in septic animals compared to controls (heart rate, 45.5±32% vs 4.7±4%, blood pressure 39.2±19% vs 11.7±5%, both p<0.05). Heart rate volatility decreased early in sepsis, and remained low in both septic survivors and non-survivors. Blood pressure volatility decreased early, but returned to control values in survivors and remained low in non-survivors.
Conclusion: Analysis of volatility is less susceptible to artifact than other nonlinear analytic measurements. These techniques show dramatic differences between septic and control animals. Heart rate volatility is a sensitive leading indicator of hemodynamic decompensation, while blood pressure volatility measures something distinct and may be a marker for failure to resolve organ dysfunction. Extrapolation of this methodology to the bedside has the potential to provide novel markers of hemodynamic decompensation in critically ill patients.

11:00 a.m.

1031-77 Resuscitation with Intraosseous Infusion of Liposome-Encapsulated Hemoglobin (Artificial Oxygen Carrier Named TRM645) from Lethal Hemorrhagic Shock

Bonpei Takase, Satoshi Shono, Manabu Kinoshita, Yashiro 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. Intraosseous blood infusion (IOI), 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 16 mice (C57BL/6). Eight mice were gradually exchanged blood with 5% Albumin (Alb group) through superior vena cava while 8 mice exchanged with TRM645 (TRM645

group). Study 2: Total 70% hemorrhagic shock was induced by femoral vein bleeding. Immediately after bleeding, 17 mice were resuscitated with tibial bone IOI of 5% Albumin (5% Albumin), 18 mice resuscitated with mouse-washed RBC (wash RBC) and 14 mice resuscitated with TRM645 (TRM-645). Survival rates were compared.
Results: Study 1: All mice died in Alb group whereas all survived in TRM645 group. Study 2: All mice survived 48 h after IOI of TRM645 whereas only 47% and 45% mice survived in 5% Albumin and wash RBC, respectively (Fig. 1).The changes in RBC levels after IOI were not different among 3 groups (Fig. 2).
Conclusions: TRM645 has a salutary anti-shock effect in both i.v. and IOI. Especially, TRM645 is more effective than wash RBC in IOI probably due to smaller size. IOI of TRM645 could be useful in disaster medicine.

Figure 1 The survival rate after IOI

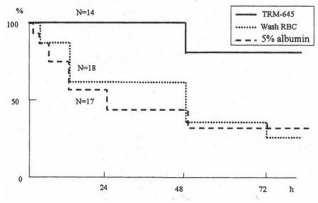
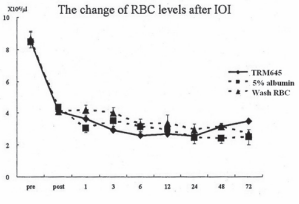


Figure 2 The change of RBC levels after IOI



11:00 a.m.

1031-78 **A Systematic Review and Meta-analysis of the Value of Intra Aortic Balloon Pump Therapy in ST-elevation Myocardial Infarction Patients. Should we change the Guidelines?**

Krischan D. Sjauw, Annemarie E. Engström, Jan G.P. Tijssen, Jan J. Piek, José P.S. Henriques, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

Background: Intra-aortic counterpulsation (IABP) in STEMI complicated by cardiogenic shock (CS) is listed in the ACC/AHA guidelines as a class IB recommendation. We performed meta-analysis in order to analyse the evidence in favour of concomitant IABP versus no support in high risk STEMI and in STEMI with CS.
Methods: Medical literature databases were scrutinized to identify randomized controlled trials (RCTs) of IABP therapy in acute high risk STEMI. Additionally, in the absence of RCTs, observational studies in STEMI with CS were identified. Two separate meta-analysis were performed respectively. Random-effect absolute risk differences (ARD) were computed.
Results: Meta-analysis 1, which included 7 RCTs investigating IABP therapy in high risk STEMI patients (n=1009), showed no mortality difference (ARD 0.01 CI [-0.03, 0.04]; p=0.75). However, the rates of major bleeding and stroke were significantly higher in IABP treated patients.
Meta-analysis 2, which included 9 observational studies in STEMI patients with CS (n=10329) showed a survival benefit of IABP therapy (ARD -0.11 CI [-0.13, -0.09]; p<0.0001). However, significant heterogeneity existed. Subsequent, subgroup analysis revealed a mortality benefit in patients who received IABP adjunctive to thrombolysis (ARD -0.19 CI [-0.21, -0.16]; p<0.0001). However, amongst others, higher rates of rescue PCI and CABG in patients receiving IABP in this subgroup, were identified as important confounders. In the subgroup of patients treated by primary PCI, IABP was associated with a higher mortality (ARD 0.06 CI [0.06, 0.10]; p<0.0001).
Conclusion: There is no evidence for routine IABP therapy in patients with high risk STEMI. Although IABP therapy may be beneficial as an adjunct to thrombolysis in STEMI patients with CS, this is only supported by observational data which importantly seems affected by confounders. The observational data did not support IABP adjunctive to primary PCI in STEMI patients with CS. However, meta-analysis of observational data should be seen as hypothesis generating. There is no scientific evidence supporting a class 1 recommendation for IABP therapy in STEMI with or without CS. This study will impact on current guidelines.

11:00 a.m.

1031-79 **Epidemiology of Cardiogenic Shock Requiring Intensive Care Admission in Olmsted County, Minnesota**

Amir H. Shoja, Rodrigo Cartin-Ceba, Mohammed Ahmed, Jaise Poulose, Girish Mour, Javier Cabello-Garza, Harpreet Suri, Ognjen Gajic, Daryl Kor, Mayo Epidemiology and Translational Research in Intensive Care (M.E.T.R.I.C.), Mayo Clinic College of Medicine, Rochester, MN

Background: While the incidence of Cardiogenic Shock (CS) following an acute coronary syndrome has been described, the epidemiology of all-cause CS requiring an Intensive Care Unit (ICU) admission is not, to our knowledge, known. The purpose of this study was to evaluate the epidemiology of CS in residents of Olmsted county, MN.
Methods: This was a retrospective cohort study of all Olmsted County residents admitted to the ICU's of Mayo Clinic, Rochester, MN. This is the only center capable of providing continuous ICU services for patient's in this demographic. A random quarter sample of the population was selected for analysis. We excluded patients who denied research authorization, were less than 18 years of age and who needed vasoactive support in the immediate post-cardiopulmonary bypass period. Those with prior withdrawal of care orders or a "mixed" distributive and CS picture were also excluded.
CS was defined as a patient having 1. A shock index >1 or Systolic Blood Pressue (SBP) persistently <90 mmHg or need for vasoactive infusions to maintain a SBP >90 mmHg, 2. Evidence of end organ hypoperfusion and 3. Evidence of elevated filling pressures.
Results: The adult population of Olmsted County in 2006 was 100,716. During this one year evaluation, 88 patients developed 100 episodes of CS.
Median age of the patients with CS was 76 (IQR 63.5-81) of which 64% were females. The median BMI was 25.2 (IQR 22.7-34.1). The all cause in-hospital mortality following CS was 45% (95%CI 35-65).
CS was caused by NSTEMI in 40%, STEMI in 20% and other causes (arrhythmias, valvular disease, decompensated heart failure) in the remaining 40%.
The cumulative incidence of CS was 99 episodes (95%CI 68-147) per 100000 person-years at risk. This translates to one episode of CS for every 1007 patient years. For a national life expectancy of 77.9 years, approximately one in 13 patients would develop CS in the course of his or her life in Olmsted county.
Conclusions: 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.

1031-80 **Clinical Profiles of Patients Undergoing Coronary Artery Bypass Surgery or Percutaneous Coronary Intervention in California: A Comparative Analysis of Over 60,000 Patients**

Zhongmin Li, Khung-Keong Yeo, Richard White, Geeta Mahendra, Ezra Amsterdam, University of California, Davis Medical Center, Sacramento, CA

Background: The clinical characteristics and peri-procedural outcomes among patients undergoing either 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 preoperative 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, mitral insufficiency 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 MI/cardiac surgery/PCI (all p<0.001). On peri-procedural outcomes, CABG patients had lower odds of procedure-related MI (OR: 0.57, 95%CI: 0.53-0.62) or follow-up CABG (OR: 0.11, 95% CI: 0.08-0.15) but did have 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.
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Clinical characteristics, outcomes and multivariate analyses in patients undergoing PCI vs. CABG in California, 2004

Variable	PCI (N=42,232)	CABG (N=19,409)	p-value	Adjusted Odds Ratio (Control=PCI)	95% CI	
Age, yrs (mean)	66.6	67.5	0.000	1.003	1.001	1.005
Female	33.1%	28.3%	<.0001	0.699	0.672	0.727
Non-white	28.7%	32.0%	<.0001	1.194	1.149	1.241
Non-scheduled	61.1%	51.1%	<.0001	0.642	0.620	0.665
'Do not resuscitate'	0.8%	0.9%	0.971	0.996	0.824	1.205
Hypertension	72.8%	76.3%	<.0001	1.152	1.104	1.201
Diabetes	35.1%	41.0%	<.0001	1.193	1.149	1.239
Peripheral arterial disease	11.2%	14.4%	0.007	1.079	1.021	1.140
Cerebrovascular disease	8.1%	12.3%	<.0001	1.407	1.326	1.492
Heart failure	18.8%	26.3%	<.0001	1.283	1.224	1.345
Heart block	7.8%	7.2%	<.0001	0.745	0.695	0.798
Dysrhythmia	14.2%	19.1%	<.0001	1.289	1.228	1.353
Chronic lung disease	13.5%	18.9%	<.0001	1.321	1.258	1.387
Prior myocardial infarction	21.2%	20.6%	<.0001	0.819	0.784	0.856
Dialysis	2.4%	2.5%	0.001	0.798	0.700	0.909
Renal failure	4.6%	5.7%	0.519	0.971	0.886	1.063
Obesity	1.6%	3.0%	<.0001	1.867	1.664	2.094
Hepatic failure	0.8%	1.1%	<.0001	1.447	1.211	1.728
Mitral insufficiency	6.8%	14.6%	<.0001	2.131	2.009	2.260
Operative outcomes:						
1) Post-operation AMI, %	7.61	4.52	<.0001	0.57	0.53	0.62
2) Re-Admission for CABG, %	2.07	0.23	<.0001	0.11	0.08	0.15
3) Operative Deaths, %	1.15	2.88	<.0001	2.55	2.25	2.88
1) or 2) or 3)	8.62	7.31	<.0001	0.84	0.78	0.89

11:00 a.m.

1031-83 **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**

Jinghua He, Almut G. Winterstein, Thomas M. Beaver, Department of Pharmacy Health Care Administration, College of Pharmacy, University of Florida, Gainesville, FL, Division of Thoracic and Cardiovascular Surgery, College of Medicine, University of Florida, Gainesville, FL

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: I. 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 analysis. 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 (IDR: -2.90%, -5.10%, -0.70%; IMR -2.10%, -3.70%, -0.51%). The improvement was more pronounced in the stratum with pre-operative renal dysfunction ($P < 0.05$) (IDR: -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 significant in scenario I and II ($P < 0.05$), but reversed in scenario III (IDR: -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.

11:00 a.m.

1031-84 **Chronic Olive Oil Consumption Is Associated With Better Short-Term Prognosis of Patients After Open Heart Surgery**

Melina Sifakaki, Akrivi Lysikatou, Demosthenes B. Panagiotakos, Athanassios Manginas, George Stavrides, Maria Kotiou, Peter Alivizatos, Panagiotis Kariofillis, Dennis V. Cokkinos, Onassis Cardiac Surgery Center, Athens, Greece, Harokopio University, Athens, Greece

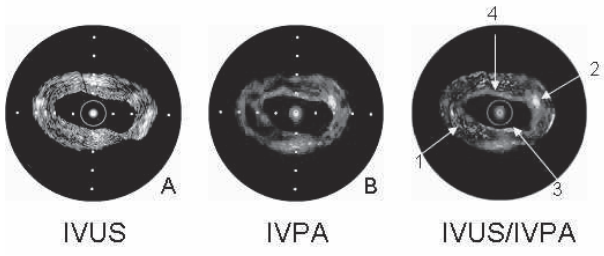
Background: Although the role of olive oil in the primary prevention of cardiovascular disease (CVD) has been studied and seems to be protective, research concerning its role in secondary prevention is rather limited. The aim of this work was to evaluate the association between olive oil intake and CVD risk after open heart surgery.
Methods: We enrolled 216 consecutive patients undergoing scheduled open-heart surgery; There were 163 men (62±12 years) and 53 women (65±10 years). Consumption of olive oil, vegetable seed oils, butter and margarines was assessed, by asking the patients about consumption in daily cooking. Quantification of olive oil intake was determined as: a) low (<1spoon per use), b) moderate (2-3spoons per use), c) large (>3spoons per use). Patients were categorized as a) only olive oil consumers, b) olive oil plus other oils consumers, c) non- olive oil consumers. Clinical and biological characteristics were also measured. Multiple logistic regression models were used to evaluate the association between olive oil intake and the 30 day outcome (death or re-hospitalization due to CVD), after adjusting for various potential confounders.
Results: The 30 day CVD event rate following surgery was 13.4 per 100 patients (gender-specific event rate: 14.7% in males vs. 9.2% in females, p=0.23). Only 4 cases were fatal (1.9%). Exclusive olive oil consumers were less likely to experience an adverse cardiac event within 30-days following surgery (p=0.02). Moreover, patients who reported plentiful olive oil consumption were almost 4 times less likely to have an adverse event during the follow-up period (p=0.001).
These findings were independent of sociodemographic, clinical and other lifestyle characteristics, including the Euroscore.
Conclusion: Our findings support the protective role of daily olive oil consumption in the short term prognosis of patients who had had open heart surgery. The wide range of antiatherogenic effects associated with olive oil consumption could explain its beneficial effects in secondary prevention.

11:00 a.m.

1031-85 **Intravascular Imaging Using Combined Intravascular Ultrasound and Photoacoustic Catheters in a Rabbit Atherosclerotic Model**

Cezar A. Iliescu, Shriram Sethuraman, James Amirian, Silvio H. Litovsky, Bo Wang, Salavat Aglyamov, Andrew Hamilton, Stanislav Y. Emelianov, Richard W. Smalling, The University of Texas Health Science Center, Houston, TX

Background: Adverse clinical cardiovascular are frequently caused by rupture of plaques considered insignificant on coronary angiography. An integrated IVUS and intravascular photoacoustic (IVPA) imaging system improves visualization of both structural and functional properties of the atherosclerotic plaque.
Methods: A total of 12 New Zealand rabbits were fed a low cholesterol diet (0.1%) over 6-12 months, high cholesterol diet (0.8%) over 3-4 months and created atherosclerotic lesions. IVUS (40 MHz) pullback was recorded in the descending thoracic aorta. The combined IVUS/IVPA imaging with spatially co-registered and temporally adjacent ultrasonic and photoacoustic beams acquired to generate one complete image was then performed ex vivo sample. The specimens were processed for H&E, collagen (picrosirius red) and macrophage activity (RAM11) histological staining.
Results: The combination of IVUS and IVPA imaging was technically possible and photoacoustic imaging complemented the structural data obtained with IVUS which correlated with tissue histology. The IVPA image demarcates the presence of lipids (lipid pool-1), fibrous collagen (2), macrophages (3) and normal collagen (4).
Conclusions: IVUS/IVPA imaging can detect lipid filled vulnerable plaque and plaque containing macrophage foam cells, suggesting that IVUS/IVPA imaging system may provide a superior clinical tool in cardiovascular medicine.



11:00 a.m.

1031-86 **Emergent Coronary Bypass Surgery Following Percutaneous Coronary Intervention: Incidence, Predictors and Outcomes**

Probal Roy, Teruo Okabe, Tina L. Pinto Slottow, Saquib Samee, Daniel H. Steinberg, Kimberly Smith, Zhenyi Xue, Lowell F. Satler, Kenneth M. Kent, William O. Suddath, Augusto D. Pichard, Ron Waksman, Washington Hospital Center, Washington, DC

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 unselected 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.1.1% 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.

	Odds ratio	Confidence intervals	P
Prior PCI	1.77	1.13-2.79	0.01
Number of diseased vessels	1.62	1.28-2.04	<0.001
Left anterior descending artery	1.62	1.12-2.36	0.01
Type C lesion	2.52	1.74-3.66	<0.001

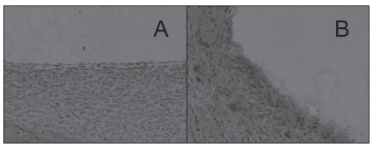
11:00 a.m.

1031-87 **Magnetically Targeted Cell Delivery Improves 30-day Endothelialization of Synthetic Vascular Grafts**

Adriana Harbuzariu, Danny Vo, Tyra Witt, Manju Kalra, David R. Holmes, Jr., Robert D. Simari, Gurpreet S. Sandhu, Mayo Clinic, Rochester, MN

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. These were labeled with 0.9u Bangs Labs SPIO (500 particles/cell) for 16h. TUNEL and BrdU assays confirmed viability. A magnetic sheet was annealed circumferentially around 5mm grafts. Cells (106/ml) were placed within the grafts (n=3) for 10 min prior to surgical interposition in porcine carotids. Non-magnetic graft segments (n=3) were treated similarly.
Results: Magnetic and non-magnetic grafts had circumferential neointima (~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.