Conclusion: In women with chest pain, mild renal insufficiency is an independent predictor of significant angiographic CAD. Impaired creatinine clearance may be a marker for unmeasured pro-atherogenic factors.

1003-115 Randomized Comparison of Fenoldopam and N-Acetylcysteine to Saline in the Prevention of Radio-Contrast Induced Nephropathy

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Introduction: 5% of patients undergoing cardiac angiography experience radio-contrast induced nephropathy (RIN). This risk triples in patients with renal insufficiency. The currently accepted prophylaxis is intravenous hydration (IVF) with 0.45 NS. Emerging evidence suggest N-acetylcysteine (NAC) and fenoldopam (FEN) may also have a protective role.

Methods: Patients with creatinine (Cr) > 1.5 mg/dL who had a cardiac angiogram were randomized to one of three treatment groups: 1) IVF with 0.45 NS at 1 cc/kg/hr pre and post procedure, 2) IVF as above plus 600-mg BID of NAC the day prior to and on the day of procedure, 3) IVF as above plus FEN at 0.1 mcg/kg/min starting 30 min prior to and continuing for 4 hrs post procedure. Cr levels were drawn prior to the angiogram and at 5-7 days after the procedure. The primary end-point of the study was an increase in Cr of 0.5 mg/dL or a 25% increase from baseline. **Results:** 68 patients with a mean age 67±10 (24% females, 76% males) and a mean Cr level of 1.92±0.34 mg/dL were randomized into the three treatment groups of IVF only, NAC, and FEN. Baseline characteristics for the groups were similar. A statistically greater number of patients in the NAC group had an increase in baseline Cr > 25% as compared to the other two treatment groups (see Table 1). **Conclusion:** In patients with renal insufficiency, hydration with 0.45NS alone is as effective as FEN plus hydration in preventing RIN. The combination of NAC and IVF was the least effective regimen.

Table 1: Patients with an increase in Cr at 5-7 days.

	Hydration (n=23)	NAC (n=24)	Fenoldopam (n=21)	p-value
Increase in Cr > 0.5 mg/dL	3	6	1	0.155
Increase in Cr > 25%	2	8	2	0.043

1003-116 A Simple Clinical Score Is an Accurate Prognostic Indicator in a Community-Based Population

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Introduction: Clinical scoring systems have been developed for initial assessment of patients with coronary artery disease (CAD) but are not widely applied due to their complexity and lack of validation. The purpose of this study was to validate a simple clinical prognostic score, originally developed in a cohort of patients referred to our nuclear cardiology laboratory, in a "less-selected" community-based population.

Methods: The score was designed specifically to use a limited number of clinical variables and an integer system to simplify calculation and recall: 1 point each for male gender, typical angina, diabetes, insulin use, history of myocardial infarction (MI), and 1 point for each decade of age beginning at age 40 (40-49=1, 50-59=2, etc) (range of score 0 to 9). The score was applied to all residents of Olmsted County, MN undergoing an initial exercise test between January 1987 and December 1990 (n=3566).

Results: Clinical characteristics included: age 50±15, male 64%, typical angina 8%, diabetes 5%, insulin use 3%, history of MI 10%. Follow-up was 7.6±2.7 yrs. Annual event rates were strongly associated with the score: overall mortality χ^2=525, p<0.001; cardiac death χ^2=192, p<0.001; cardiac death or MI χ^2=274, p<0.001 (see table).

Conclusion: This simple prognostic score was highly accurate for risk-stratifying this community population, supporting a more wide-spread application of this score in patients with CAD.

Score	Patients	Overall Mortality	Cardiac Death	Cardiac Death/MI
≤ 4	3076 (86%)	0.6%	0.2%	1.0%
5	275 (8%)	2.4%	0.8%	2.0%
≥ 6	215 (6%)	6.2%	2.8%	4.2%

POSTER SESSION

1004 Innovative Experimental Surgical Revascularization Methods

Sunday, March 30, 2003, 9:00 a.m.-11:00 a.m.
McCormick Place, Hall A
Presentation Hour: 9:00 a.m.-10:00 a.m.

1004-92 Paclitaxel Reduces Neointimal Formation In Vitro and in a Porcine Model of Saphenous Vein Interposition Grafting

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Background: Following early thrombosis, 10-15% of coronary vein grafts fail over the next 5 years due to intimal thickening. Paclitaxel is a potent inhibitor of cell proliferation by inducing a sustained block of mitosis at the metaphase/anaphase boundary. The aim of this study was to investigate the effect of paclitaxel pre-treatment in a porcine model of Saphenous vein to carotid artery interposition grafting. **Methods:** In-vitro evaluation of the effect of short-term paclitaxel exposure on neointimal proliferation involved saphenous vein pre-treatment, by suspension in Paclitaxel (10 μmol/L) or vehicle control, for 1 hour, prior to plating and 14 day culture. Samples were histologically analysed. Subsequently, ten Large White pigs (25-33.5 kg) underwent bilateral saphenous vein to carotid artery interposition grafting. Each animal received a Paclitaxel treated and a vehicle control graft. Animals were sacrificed at 29 days, vein grafts were harvested and pressure fixed prior to histological/morphometric analysis. **Results:** In-vitro Paclitaxel exposure resulted in a significant reduction in neointimal thickness, compared with vehicle control; 77.80+/-48.80μm vs 148.35+/-82.73μm (p=0.008). Only patent grafts were included in the in-vivo analysis (see table).

Parameter	Control (n=8)	Treated (n=8)	P value
Luminal Area (mm^2)	32.08±15.45	25.26±15.53	0.017
Neointimal Area (mm^2)	2.43±1.35	1.59±0.95	0.0004
Medial Area (mm^2)	6.83±2.57	6.18±5.84	0.25
Neointimal/Medial Ratio	0.37±0.18	0.299±0.16	0.029

Conclusion: Our data demonstrates that Paclitaxel pre-treatment reduces neointima formation, in-vitro and in-vivo. Paclitaxel may be a highly attractive candidate for prevention of late vein graft failure.

1004-94 Functional Myocardial Angiogenesis Resulting From Persistent Systolic Perfusion

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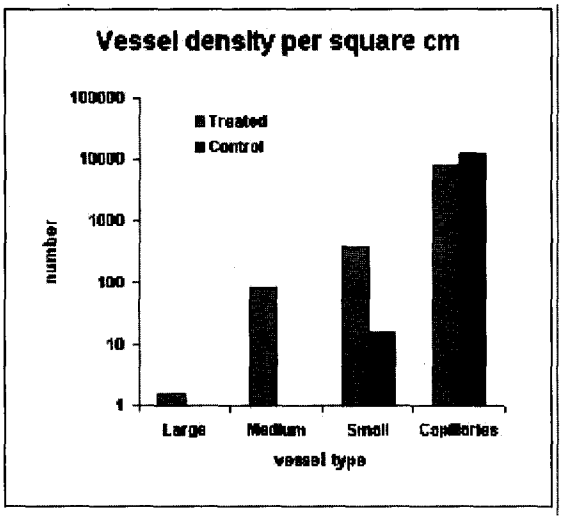
Background: The effects of systolic perfusion on distal coronary bed myocardium were studied by using a device that creates a permanent transmyocardial flow channel between the left ventricle and a coronary artery (Ventriculocoronary Artery Bypass (VCAB) procedure). **Methods:** The stent-like direct revascularization device (DRD), an L-shaped titanium tube with a meshed distal tip, was implanted between the left ventricular cavity and the mid left anterior descending coronary artery (LAD) in 15 juvenile domestic pigs using a beating heart approach. The LAD was ligated proximal to the device. Patency was assessed via retrograde angiography at explant for surviving animals at 12 weeks (n=12). Morphometry of blood vessels (150 fields total) was assessed in the subendocardium using PAX-It™ software. Hearts retrieved acutely from pigs were used as controls.

Results: 3/15 animals died within 24 hours related to procedural complications. At 12 weeks, patency was achieved in 11/12 pigs. Morphometric assessment of the target myocardium showed a significant increase in number of small (25-200 μm), medium (200-400μm) and large (>400μm) arterioles compared to the control in the subendocardial region (see graph). **Conclusions:** This study demonstrates persistent patency of a

large myocardial region subtended by a DRD for 12 weeks. Histopathologic analysis of the subendocardium indicates a significant angiogenesis effect resulting from systolic perfusion.



1004-95 Extracellular Nucleotide Contractions in Human Coronary Bypass Vessels

Tomas Gudbjartsson, Catharina Borna, Lingwei Wang, Lena Karlsson, Sverker Jern, Malin Malmsjö, David Erlinge, Lund University Hospital, Lund, Sweden, Sahlgrenska University Hospital, Östra, Sweden

Background: Long term patency is worse for saphenous vein (SV) grafts compared to internal mammary artery (IMA) when used as conduits for CABG surgery (50% *vs.* 90% occlusion rate after 10 years). The reason for this difference is not known but P2 cell surface receptors could play a role. When activated by extracellular nucleotides (ATP, ADP, UTP and UDP) P2 receptors mediate both contraction and growth stimulatory effects on vascular smooth muscle cells (VSMC). This study was designed to evaluate the relative contribution of different contractile P2 receptors in endothelium-denuded human SV and IMA obtained during CABG surgery. **Methods:** Isolated vessel segments from 16 patients were stimulated with selective agonists *in vitro* and the isometric tension recorded, expressed as percentage of K^+ concentration. P2 receptor mRNA expression was quantified by realtime PCR. **Results:** The $P2X_1$ receptor agonist, αβ-MeATP, was the most potent vasoconstrictor with more efficacious contractions in the SV (K_{25} = 5.19, C_{max} = 76 ± 10) than in the IMA (K_{25} = 4.15, C_{max} =24 ± 13, $p < 0.05$). The selective $P2Y_6$ receptor agonist, UDPβS, was also more efficacious in the SV than IMA (K_{25} =4.99, C_{max} =80 ± 30 *vs.* K_{25} = 4.28, C_{max} =42 ± 14, $p < 0.05$). Furthermore, UDPβS induced longlasting contractions for more than 2 hours, explained by the low desensitization rate of the $P2Y_6$ receptor. The ATP-induced vasoconstriction could not be abolished by desensitization of $P2X_1$ receptors, with αβ-MeATP, or $P2Y_{2/4}$ receptors, with UDPβS, indicating the presence of yet another contractile ATP receptor. Based on quantification with realtime PCR, the $P2Y_{11}$, receptor could be responsible for this ATP contraction. **Conclusions:** $P2Y_6$ and $P2X_1$ receptors elicit more prominent contractions in the SV as compared to the IMA. Because $P2Y_6$ receptors also mediate growth stimulatory effects in VMSC they could contribute to increased restenosis in the SV. These results may present one explanation for the differences in SV and IMA graft properties. Selective antagonists of $P2X_1$ and $P2Y_6$ receptors could potentially be used to prevent vasospasm and restenosis in the SV during and after CABG surgery.

1004-96 Adaptive Coronary Vessel Remodeling Following Surgical Coronary Artery-to-Left Ventricle Stent (VSTENT) Implantation

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Background: A left ventricle (LV)-to-left anterior descending (LAD) artery conduit (VSTENT™) has been developed as a novel approach to myocardial revascularization. Initial experiments demonstrated that upon VSTENT™ implantation distal to a total proximal LAD occlusion, significant forward flow was provided to the distal LAD, which preserved regional myocardial function. In this study, covered stent conduits were placed in the mid-LAD in the absence of proximal LAD occlusion, to evaluate the chronic response of the LAD to the flow patterns produced in the presence of the VSTENT™.

Methods: Eight pigs (40-60 kg) were implanted via left thoracotomy with an ePTFE-covered, balloon-expandable stent (VSTENT™). This was placed through the posterior wall of the mid-LAD artery, thus creating flow between the LAD and the LV. The LAD was not occluded proximal to the placement site. Coronary angiography was performed before VSTENT™ placement, immediately after implantation, and at 28 days post-implant. The mean diameter of proximal LAD and left circumflex (LCX) artery was measured by QCA.

Results: VSTENT™ was successfully implanted in all 8 pigs. A bi-directional flow pattern was seen in the LAD immediately proximal to the conduit, with retrograde systolic flow from the LV to the LAD and antegrade diastolic flow from the proximal LAD to the LV and distal LAD. Prior to the open surgical procedure, the baseline LAD diameter was 3.17±0.09 mm, and LAD/LCX diameter ratio was 1.04± 0.02 (mean±SEM, no unit). Follow-up angiograms confirmed VSTENT patency at 28 days post-implant. Quantitative evaluation then revealed an LAD diameter of 5.32±0.21 mm, and LAD/LCX diameter ratio was significantly increased to 1.43±0.05 ($p<0.0001$). **Conclusion:** Adaptive structural coronary remodeling occurs in the LAD in the presence of the LV-to-LAD conduit at 28 days post-implantation. Further studies will address the time course and persistence of this remodeling, as well as its occurrence in hte context of vessel disease.

1004-97 Diazoxide and Controlled Reperfusion Improve Sodium Homeostasis in Severe Ischemia-Reperfusion Injury

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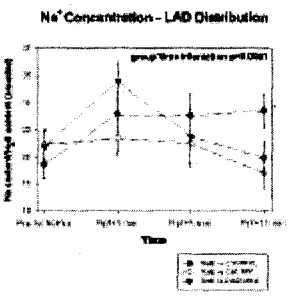
Background: Intra-myocyte Na^+ accumulation due to ischemia-reperfusion (IR) injury results in Ca^{++} influx and myocyte damage. This study determines whether controlled reperfusion (RPF) (initial RPF with warm blood cardioplegia (CP)) and pharmacologic preconditioning with diazoxide (DZX) (a mitochondrial K^+_{ATP} channel opener) improve intra-myocyte Na^+ homeostasis using a porcine model of severe IR injury in cardiac surgery.

Methods: Three groups (N=10 pigs/group) had 75 mins of LAD occlusion (including 30 min during 1 hour of CP arrest). Group 1 had no treatment, group 2 had controlled RPF (warm CP followed by normal blood), and group 3 had DZX (50 umol/L infused for 10 minutes prior to LAD occlusion). Transmural biopsies were taken from the LAD region prior to ischemia or DZX, and at 3, 5, and 10 mins post RPF. Intra-myocyte Na^+ and water contents were measured using atomic absorption spectroscopy.

Results: (see graph) By 10 mins of reperfusion intra-myocte [Na^+] in group 2 had decreased, and groups 2 and 3 were less than group 1 ($p=0.04$ and 0.01, respectively). Intra-myocyte [Na^+] during reperfusion was significantly different for group 1 vs. groups 2 and 3 due to persistence of increased [Na] concentration in group 1 (group*time effect $p=0.0001$). Conclusion: DZX and controlled RPF improve intra-myocyte Na^+ homeostasis in this model of severe IR injury during cardiac surgery. Our current studies will determine if improved ion homeostasis benefits contractile recovery and reduces infarct size.



1004-98 Surgical Implantation of Bone Marrow Cells May Reverse Perfusion and Wall Motion Abnormalities in Patients With Previous Myocardial Infarction and Dominance of Scar

Massimo Mariani, Ugo Limbruno, Claudio Favre, Paolo Marzullo, Gianmario Sambuceti, Vitoantonio Di Bello, Davide Giorgi, Rossella Di Stefano, Carmela Nardi, Anna S. Petronio, Rita Dell'Anna, Jean Grandjean, Mario Mariani, University of Pisa, Pisa, Italy

Background: Autologus bone marrow stem cells (SC) implantation has been suggested as a new treatment to improve blood flow distribution and regional function in infarcted myocardium.

Methods: To this purpose, 4 male patients (59 ± 3 yrs) underwent autologous SC intramyocardial injection in dysfunctioning myocardium concomitant with off-pump coronary artery bypass grafting. In each patient, 600 ml of bone marrow were harvested and 5 to $14x10^8$ cells obtained from the mononuclear fraction were delivered through 10 to 23 intramyocardial 0,1 ml spots. SC delivery area was chosen according to ungraftability, dominance of scar and hypo/akinesis at gated SPECT. Myocardial perfusion and function in the SC treated area were characterized by tetrofosmin gated SPECT scintigraphy and quantitative myocardial contrast echo (QMCE) performed before and 10 weeks after treatment. At gated SPECT, scar and perfusion were quantified as percent of segmental hypoperfusion (extension) and number of standard deviations below matched normals (severity) in a 20-segment model. At QMCE, myocardial perfusion was evaluated by the product slope*plateau of the filling curve of contrast-echo in the treated area. Regional