14:55 - 15:45 EC1 - Basic Science Hall H

Chairs: **L. Gepstein**
J. George

14:55 **Elevation of Cell FreeE DNA During CABG Operations**
D. Mozalbat , A. Douvdevani , G. Sahar , M. Matsa
Beer Sheva

15:04 **Synergistic Effect of Hyperglycemia and Ox-LDL in Type 2 Diabetes**
S. Hamed , B. Brenner , Z. Abassi , A. Aharon , D. Daoud , A. Roguin
Haifa

15:13 **Novel Stent Surface Coating Inhibits Thrombus Formation in a Baboon Ex-Vivo Model**
R. Jabara [1,2] , K. Robinson [2] , G. Radhika [2] , P. Lakshmana [2] , N. Chronos [2] , H. Stephen [3]
[1] Jerusalem, [2] Atlanta, GA, [3] Portland, Oregon

15:22 **In Vivo Feasibility of Catheter Based Selective Profound Cerebral Hypothermia**
D. Meerkin [1] , S. Lownie [2] , C. Prestigiacomo [3] , R. Solar [4]
[1] Jerusalem, [2] London, Ontario, [3] Newark, NJ, [4] San Diego, CA

15:31 **Novel Bioabsorbable Salicylate-Based Polymer as a Drug-Eluting Stent Coating**
R. Jabara [1,2] , N. Chronos [2] , K. Robinson [2]
[1] Jerusalem, [2] Atlanta, GA

Elevation of Cell FreeE DNA During CABG Operations

David Mozalbat [1], Amos Douvdevani [2], Gideon Sahar [1], Menachem Matsa [1]

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Background: Increased levels of plasma cell free DNA (CFD) have been reported in numerous conditions of tissue injury including cancer, strokes, myocardial infarction, trauma and sepsis. The objective of this paper was to follow the changes in CFD levels during standard coronary artery bypass grafting procedure during its several stages.

Patients and methods: In 10 patients who underwent a CABG operation (mean 3-5 grafts) CFD concentrations were measured during five stages of this procedure: before skin incision, before going on cardiopulmonary bypass (CPB), during CPB, at wound closure and one hour after. CFD was measured by a novel fluorometric assay developed at our laboratory. This assay is accurate, quick and inexpensive and is applicable to various body fluids.

Results: The CFD concentration before operation was 496±282 ng/ml (mean ± SD), mild elevation of CFD concentration 869±380 ng/ml before CPB, and following the connection of the patient to CPB machine a remarkable increase was noticed 2571±767 ng/ml ($p<0.001$ compared to basal levels). CFD levels decreased significantly upon removal of CBP machine (817±413 ng/ml) and remained at similar levels at one hour after operation (1348±1361 ng/ml).

Conclusion: Our results indicate that the most traumatic and stressful stage in an uneventful CABG procedure is during the performance of the cardiopulmonary bypass. CFD levels can be a possible objective indicator of operative tissue injury that may influence the patient's clinical outcome.

Synergistic Effect of Hyperglycemia and Ox-LDL in Type 2 Diabetes

Saher Hamed [1,2,5], Benjamin Brenner [2,5], Zaid Abassi [4,5], Anat Aharon [4,5], Deeb Daoud [3], Ariel Roguin [1,5]

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Background: Previous studies suggested negative effect of either hyperglycemia or oxidized low-density lipoprotein (OxLDL) on the functional activity of endothelial progenitor cells (EPCs). The present study was conducted to examine the effect of both factors simultaneously on EPCs.

Methods: EPC number and activity were studied in 55 patients divided into three groups: patients with type 2 diabetes (DM), patients with coronary artery disease (CAD), patients with DM/CAD, and 15 control subjects. All measurements were correlated with subject's serum OxLDL. EPCs from DM patients were incubated with OxLDL, and EPCs from CAD patients were incubated with high glucose (HG). EPCs incubated with combination of HG and OxLDL in the presence or absence of sodium nitroprusside (SNP). After incubation, EPC adherence to human umbilical vein endothelial cells (HUVECs) and NO bioavailability were evaluated. Western blot was performed to assess nitric oxide synthase (NOS) and Akt activity.

Results: EPC number, colonies and NO bioavailability were significantly reduced in DM and DM/CAD patients compared with controls ($p<0.01$). These parameters were inversely correlated with serum OxLDL ($r=-0.43$, $p=0.004$, $r=-0.63$, $p<0.001$, and $r=-0.65$, $p<0.001$; respectively). Incubations of DM-EPCs with OxLDL or CAD-EPCs with HG as well as incubation of controls-EPCs simultaneously with HG and OxLDL were associated with the most significant reduction in EPC adherence to HUVECs and NO bioavailability. These alterations were ameliorated by the presence of SNP.

Conclusions: Our findings suggest that combination of HG and OxLDL exerts a synergistic adverse effect on EPC functional activity through NO system modification. Avoiding this interaction in the future may provide a clinical approach to minimize vascular injury in diabetic patients.

Novel Stent Surface Coating Inhibits Thrombus Formation in a Baboon Ex-Vivo Model

Refat Jabara [1,2], Keith Robinson [2], Gadesam Radhika [2], Pendyala Lakshmana [2], Nicolas Chronos [2], Hanson Stephen [3]

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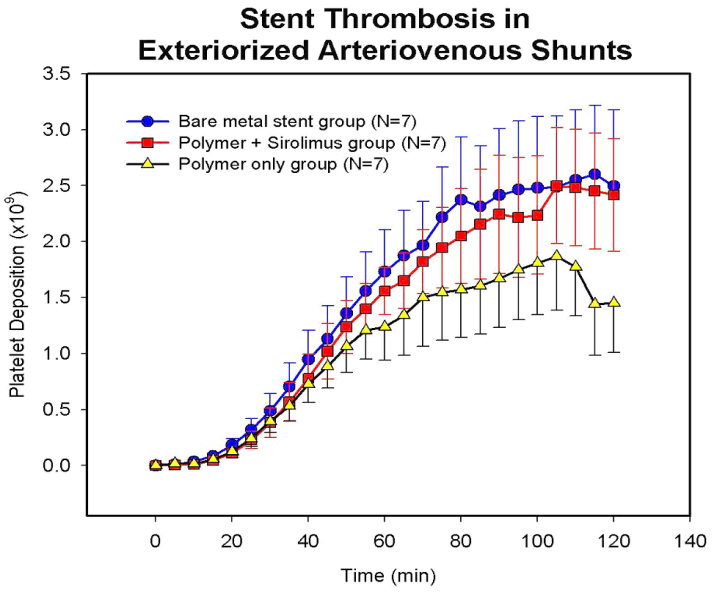
Background: Thrombogenicity of permanent polymers used on existing drug-eluting stents (DES) is implicated in late stent thrombosis; novel polymers that are thromboresistant may be advantageous. The non-human primate *ex-vivo* arteriovenous shunt is a valid, reliable, and relevant model to assess stent thrombogenicity.

Objectives: To compare thrombogenicity of stents coated with a novel bioabsorbable salicylate-based polymer without (polymer-only) or with sirolimus (polymer+sirolimus), to that of bare metal stents (BMS).

Methods: Stents (n=21, 7 of each type) were assessed for accumulation of ^{111}In-oxine labeled platelets and ^{125}I labeled fibrinogen during a 2hr exposure to 100ml/min flowing blood in *ex vivo* shunts of conscious, non-anticoagulated baboons. Subsequently stents were examined macroscopically and by scanning electron microscopy (SEM).

Results: Polymer-only coated stents accumulated fewer platelets (graph) during the 2hr shunt exposure than either BMS (P=0.017) or polymer+sirolimus (P=0.025). There was also a trend for polymer+sirolimus to have reduced platelet thrombus compared to BMS (P=0.05). Fibrin deposition was similar among stent types. Thrombus accumulation was notable for all stent types by macroscopy and SEM, but somewhat more pronounced in BMS. No marked differences in thrombic components between groups were revealed by SEM.

Conclusions: Salicylate polymer coating reduces thrombogenicity of metal stents in arterial blood flow conditions, even when the drug sirolimus is included. This novel, fully bioabsorbable salicylate-based polymer may be advantageous for reducing DES thrombotic complications.



In Vivo Feasibility of Catheter Based Selective Profound Cerebral Hypothermia

David Meerkin [1], Steven Lownie [2], Charles Prestigiacomo [3], Ronald Solar [4]

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Background: Mild hypothermia has been shown to improve outcome in comatose survivors after resuscitation from out-of-hospital cardiac arrest. It has been suggested that induction of deep hypothermia before reperfusion may further improve outcome. Current techniques involve total body cooling, with the limitations of rapidity and depth of cooling due to systemic adverse effects. We studied a novel catheter-based system designed to rapidly and selectively cool the brain while maintaining systemic temperature within normal range. The unique design incorporates a counter current flow to insulate the normothermic systemic blood from the cooled blood perfusing the brain. **Methods**: A transfemoral approach was employed in 12 swine (65-72kg). Using standard radiological techniques, the multilumen catheter was positioned to isolate the common carotid artery. Blood was withdrawn from the aorta via one lumen, cooled extra corporeally, and reperfused through a second lumen into the carotid artery. Outflow blood was cooled to 5-20°C, and reperfused at rates of 80-250 ml/min for 30-180 minutes. Temperature was measured in bilateral frontal lobes, nasopharynx, ear, esophagus and descending aorta.
Results: Unilateral hemicranial and hemicerebral cooling to 15°C was achieved. Only limited associated systemic cooling was noted. Initial cooling rates of 1.8°C/min were attained, and were dependant on inflow rate and temperature. No adverse events occurred. Contralateral hemispheric cerebral temperature closely followed systemic temperature. Passive rewarming did not result in rebound hyperthermia.
Conclusion: This new catheter-based system demonstrated feasibility in providing rapid, selective deep cerebral hypothermia, and may offer an improved method for neuroprotection during cardiac arrest and other ischemic injury.

Novel Bioabsorbable Salicylate-Based Polymer as a Drug-Eluting Stent Coating

Refat Jabara [1,2], Nicolas Chronos [2], Keith Robinson [2]

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Background: Permanent polymers used in current DES can trigger chronic inflammation and hypersensitivity reactions which may contribute to increased risk of late thrombosis and rebound restenosis. Therefore, optimal polymer selection and the use of completely absorbable but biocompatible polymers are expected to minimize these risks.
Objectives: We sought to evaluate a novel, potentially innately anti-inflammatory, bioabsorbable salicylate-based polymer as a drug-eluting stent coating, in a clinically relevant animal model.
Methods: Four types of stents were implanted in pig coronary arteries using QCA to optimize stent apposition: bare metal stents (BMS); salicylic acid/adipic acid bioabsorbable polymer-only coated metal stents (SA/AA); biostable polymeric sirolimus-eluting stents (Cypher); and metal stents coated with salicylic acid/adipic acid bioabsorbable polymer containing sirolimus (SA/AA + S). The dose density of sirolimus was 8.3 μg/mm of stent length (similar to Cypher) with *in-vitro* studies demonstrating elution over 30 days and complete polymer degradation in 37 days. Animals underwent angiographic restudy and were terminated at 1 month for complete histopathologic and histomorphometric analyses.
Results: Both SA/AA + S and Cypher stents had significantly lower angiographic % stenosis compared to BMS and SA/AA polymer-only groups (6±4% and 5±4% vs. 15±7% and 16±5%, respectively, $P<0.001$). Intimal thickness was lower for SA/AA + S and Cypher, than for BMS (0.14±0.06mm and 0.13±0.04mm vs. 0.23±0.05mm, respectively, $P<0.001$). Histologic % area stenosis was also lower for SA/AA + S and Cypher, compared to BMS (22±7% and 23±6% vs. 33±5%, respectively, $P<0.001$). There was a strong trend towards reduced inflammatory response in the SA/AA and SA/AA + S compared to BMS and Cypher groups ($P=0.072$).
Conclusions: This study shows favorable vascular compatibility and efficacy for a novel bioabsorbable salicylate-based polymer as a DES coating, and supports further research and development of this unique class of polymer materials for applications in cardiovascular devices.