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Development of a Novel Calcified Chronic Total Occlusion In a Rabbit Femoral Artery

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Background: Percutaneous revascularization of chronic total occlusions (CTO) is limited by failure of guidewire crossing. Calcification in the CTO increases with age of occlusion and counted as one of the most important obstacles to guidewire crossing. The aim of the current study was to develop an animal model of CTO that will contain significant amount of amorphous calcified mineral as well as bone.

Methods and results: CTO (n= 15) were created in the femoral arteries of New Zealand White rabbits using the thrombin injection model. Different concentration of bone morphogenetic protein (BMP-2; 0.5,1,2, 6 µg), dipotassium phosphate and calcium chloride (0,100,200 mM) were tested and injected to the site of femoral occlusion. 3 animals received high cholesterol diet 0.5%, calcium carbonate 75mg/d and vitamin D 50,000 units/d. In 8, the calcium carbonate/vitamin D was given every other day, 4 rabbits were on 0.25% cholesterol only. Animals were sacrificed at 2, 6 and12 weeks post treatment and arterial samples were excised for micro CT imaging (µCT) and histology analysis. At the side of BMP and calcium phosphate injection-µCT imaging showed significant calcification at 6 weeks and 12 weeks. On histology-amorphous calcium crystals were found in the medial layer and throughout the occluded lumen of the CTO, these were mostly diet dependant. Active formation and resorption of cartilaginous or bone like structures by osteoblasts and osteoclasts respectively were seen in the occluded CTO lumen, the fragments size was correlated with age of occlusion and BMP-2 dose.

Conclusions: This calcified model simulates occlusions found in humans CTO and will serve as a basic model for learning the pathophysiology of CTO calcification and development of treatments modalities that will enhance guidewire crossing.

<IMAGE02>,<IMAGE04>,<IMAGE06>

Imposed Vs. Spontaneous Caloric Restriction Reduces Cardiac Ischemic Injury through Distinct Pathways

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Imposed caloric restriction (CR) extends longevity in mammals and attenuates age-related diseases including ischemia-induced cardiac injury. Adiponectin, an adipokine that increases under starvation and senses the cellular energy status, has been implicated in CR-induced cardioprotection. Transgenic αMUPA mice fed ad libitum spontaneously consume less food (~25%) compared to wild-type (WT) control mice (FVB/N). αMUPA mice share many similarities with CR animals including improved health and increased life span. Here we investigated the response of αMUPA mice to ischemic stress in vivo compared to control mice both under ad libitum feeding. We also studied the response of C57Bl mice fed 65% of their spontaneous food consumption for two weeks compared to ad libitum fed C57Bl mice. Mice were tested after ligation of left anterior descending (LAD) coronary artery for 24 hours. Both αMUPA and CR C57Bl mice showed better contractile functions, weaker inflammatory responses and smaller infarct sizes ($p<0.05$). CR C57Bl, but not αMUPA mice, also demonstrated significantly reduced numbers of apoptotic cells. Moreover, CR C57Bl mice showed increased adiponectin levels (~45%) in the serum and reduced levels of leptin (~60%), an adipokine associated with satiety and energy status. Conversely, αMUPA exhibited increased levels of leptin (60%) with no changes in adiponectin. Furthermore, the aforementioned improvement in cardiac parameters after LAD ligation was abrogated by treating αMUPA mice with antibodies for leptin, or with AG490 and Wartmannin that interfere with leptin signaling. In addition, both

Myocardial Pre-Conditioning-The Role of Inflammatory Regulation in Myocardial Protection

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Background: Preinfraction angina has been shown to reduce infract size in experimental models and lead to a more favorable clinical outcome in post-MI patients. The mechanism of protection conferred by preinfarction angina is unknown. We explored the potential role of inflammatory regulation pathways in preinfraction angina-induced myocardial protection in patients who develop acute MI.
Objectives: To investigate the hypothesis that circulating regulatory T (Treg) cells are involved in ischemic preconditioning in AMI patients with angina pectoris occuring during three months prior to the cardiac event.
Methods: Our study consisted of patients enrolled in the TAPAS registry trial who had Acute MI and underwent cardiac catheterization in the 'Tel aviv Sourasky' medical center. ECG characteristics upon administration (ST-segment, Q-leades), CPK peak levels, LV dilatation and segmental analysis, LVEF in day 1 and day 30 (by echocardiogram evaluation) were used as a measure of myocardial damage and infract extent. Treg-cell levels were evaluated by flow cytometry (Treg cells identified as CD4+CD25highCD127low) and mRNA expression of FoxP3.
Results: No difference was observed in Treg-cell levels comparing preconditioned versus non-preconditioned patients in a pilot study (n=26) which included 8 patients in the IPC group and 18 control patients.
Conclusion: Based on our preliminary data, Treg levels do not seem to be involved in ischemic preconditioning in the model described, however, additional patients are required to reach a final conclusion (patients recruitment is ongoing).

AMI (n-22047, 1990-2010) in Context with the Paradigm - Month of Birth and Longevity

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Time and environmental physical activity are involved in timing of many medical events. In a recent study published by the National Academy of Science , USA it was shown that month of birth is related to longevity .The aim of this study was to check the month of birth distribution in a great group of AMI patients of both gender,one of the great killers in the developed countries, to check the mentioned paradigm of month of birth and longevity.

Methods & Patients: Patients admitted to Cardiology Departments of a tertiary University Hospital in Kaunas, Lithuania with AMI at years 1990-2010 (n-22047) were studied. Month of birth of these patients, total and both gender were checked. Monthly, quarterly and trimestrial comparition were done. Statistical differences established using t-Student test and percentual distribution of the yearly months of birth.

Results: It was a significant difference in the month of birth of the studied AMI population. January and first quarter and trimester born patients were more often in the studied AMI patients group. The higher morbidity by Cardiovascular diseases can be a significant ingredient in the structure of population longevity. Possible mechanisms explaining our findings are discussed.

Conclusion: In the AMI population people born in January, first quarter or trimester of the year are dominating in total and both gender groups. The results of this study can be an additional confirmation of the paradigm about links between month of birth and longevity.