a semiquantitative scale after the following stainings: hematoxylin eosin (for assessment of intra- and extracellular lipids and for assessment of thrombus formation), Elastica van Gieson, anti-CD31 for assessment of vessel density, anti-CD68, anti-CD3 and anti-CD15 for analysis of local inflammation, anti-SMC actin to stain smooth muscle cells, anti-CD61 for platelet depositions, TUNEL staining for apoptotic cells.
Results: Lipid and foam cell content was most pronounced in aortic lesions (P=0.02, P=0.04), calcification and SMC actin in femoral lesions (P=0.001, P=0.001), CD3+ cells in carotid lesions (P=0.004) and TUNEL+ apoptotic cells in coronary lesions (P=0.01). Thrombus was most prevalent in carotid and aortic lesions (P=0.02). Neutrophil (CD15+) and monocyte (CD68+) cell infiltrations as well as vessel density were most pronounced in carotid and femoral lesions (P=0.04, P=0.02, P=0.005). No significant changes were observed in vessel hemorrhage or platelet content. These results suggest more inflammatory lesions in carotid and femoral arteries with an increase in calcification and SMC content in femoral lesions as compared to more lipid rich lesions within the aorta and an increase in apoptotic cells within coronary lesions. Additionally, gene expression of atherosclerosis related genes in carotid and femoral endaterectomy specimen was measured. An overall increased metabolism was found in femoral plaques, especially genes concerning inflammatory response, response to stress, apoptosis, adhesion, whereas in carotid lesions, we detected overexpression of genes related to lipid/cholesterol transport and metabolism and negative transcription regulators.
Conclusions: Different arterial territories are differently affected by atherosclerosis: Our results suggest more inflammatory lesions in carotid and femoral arteries with an increase in calcification and SMC content in femoral lesions as compared to more lipid rich lesions within the aorta and an increase in apoptotic cells within coronary lesions. Concerning PAD, gene expression in atherosclerotic lesions shows significant differences. Understanding of the local differences of atherosclerosis may aid to improve prevention and lead to targeted treatment of atherosclerosis and its complications

TCT-819

Healing of a Combination Sirolimus-Eluting, Endothelial Progenitor Cell Capture Stent Compared to an Everolimus-Eluting Stent in an Atherosclerotic Rabbit Model

Fumiyuki Otsuka[1], Erica Pacheco[1], Kenichi Sakakura[1], Kazuyuki Yahagi[1], Ed Acampado[1], Frank D. Kolodgie[1], Renu Virmani[1]
[1]CVPath Institute, Inc., Gaithersburg, MD

Background: The Combo Dual Therapy stent (OrbusNeich Medical, Ft. Lauderdale, FL) combines anti-proliferative abluminal sirolimus elution from a bioresorbable matrix with luminal CD34 antibody endothelial progenitor cell capture. This study compares the healing of the Combo stent to an everolimus-eluting stent [EES] (Xience Prime; Abbott Vascular, Santa Clara, CA), along with the Genous stent (OrbusNeich) as control.
Methods: 31 atherosclerotic rabbits were implanted with bilateral iliac stents and survived for 28 days or 45 days. Select animals underwent assessment by OCT after stent implant and again prior to sacrifice. To assess cellular proliferation, animals were given BrdU before sacrifice. The stented arterial segments were designated for either light microscopy evaluation or en face assessment by both SEM for endothelial coverage and immuno confocal microscopy for expression of endothelial markers CD31/PECAM and eNOS.
Results: At 28 days, morphometric comparison of areas measurements showed statistically comparable EEL, IEL, lumen, stent, media, and plaque areas and thicknesses between groups. Uncovered struts were seen in all groups with the highest and statistically significant frequency in EES > Combo > Genous. At 45 days, morphometric values remained relatively similar to day 28 with a slight increase of stenosis seen with Genous. Endothelial coverage at 28 days above struts by SEM was highest in Genous (98.3%), followed by Combo (83.3%), and lowest in EES (52.7%) (p=0.025). Endothelial coverage between struts was nearly identical (Combo 93.3%, Genous 87.5%, EES 92.0%, p=0.714). By OCT, 28-day animals showed less area stenosis and less neointimal thickness in Combo and EES as compared to Genous. There were no significant differences between Combo and EES in terms of area stenosis, neointimal thickness, and uncovered struts. No stents showed thrombosis or restenosis at both 28-day and 45-day time points. The OCT analysis correlated significantly with histologic findings.
Conclusions: Compared to the EES stent, the Combo stent was found to have a similar reduction in neointimal proliferation, while exhibiting fewer uncovered struts and significantly greater endothelial coverage over struts.

TCT-820

First Approach to Stimulate Arteriogenesis using Monoclonal Antibodies: Blocking the Interferon-alpha/beta Receptor Subunit 1 Stimulates Restoration of Perfusion in a Murine Hindlimb-ischemia Model Without Affecting Atherosclerosis

Paul F. Teunissen[1], Marieke C. Boshuizen[2], Maurits Hollander[1], Nina W van der Hoeven[3], Marion Gijbels[2], Menno P de Winther[2], Anton J. Horrevoets[1], Niels van Royen[1]
[1]VU University Medical Center, Amsterdam, Netherlands, [2]Academic Medical Center, Amsterdam, Netherlands, [3]VU University Medical Center, Amsterdam, Noord-Holland

Background: Increased expression of interferon (IFN)-beta was shown in patients with insufficient coronary collaterals. Furthermore, mice treated with IFN-beta demonstrate inhibition of collateral artery growth (arteriogenesis). Interestingly, type I interferons (IFN-alpha and IFN-beta) have been identified as proatherosclerotic cytokines and in mouse models of atherosclerosis, IFN-beta treatment accelerated lesion formation and increased accumulation of macrophages in plaques. We hypothesized that arteriogenesis can be stimulated using monoclonal antibodies inhibiting IFN-beta signaling without accelerating atherosclerosis.
Methods: In an atherosclerotic murine hindlimb-ischemia model, LDLR-/- mice were treated during a 4-week period with monoclonal antibodies specific for mouse Interferon-alpha/beta Receptor subunit 1 (IFNAR-1) or murine IgG isotype as control. Hindlimb perfusion was measured using laser Doppler perfusion imaging (LDPI) directly after femoral artery ligation as well as at 2, 7, 14 and 28 days following ligation. We used a disease model to investigate effects of anti-IFNAR-1 on atherosclerosis, which was evaluated with histology to determine plaque area and composition.
Results: Hindlimb perfusion restoration after femoral artery ligation was improved in mice treated with anti-IFNAR-1 compared to controls as assessed by LDPI after 7, 14 and 28 days (treatment vs. control; 7 days: 35.6 ± 16.5% vs. 23.6 ± 8.7%, p=0.027; 14 days: 51.4 ± 17.2% vs. 35.0 ± 12.3%, p 0.010; 28 days 71.5 ± 13.8% vs. 54.0 ± 16.3%, p=0.005). Total plaque area (treatment vs. control: 118.8 ± 46.1x10^3 µm^2 vs. 139.3 ± 46.5 x10^3 µm^2, p=0.275) as well as composition were unaffected.
Conclusions: Blocking IFNAR-1 using monoclonal antibodies stimulates collateral artery growth in mice and has a neutral effect on atherosclerosis.

TCT-821

Stem Cell Mobilization by Granulocyte-Colony Stimulating Factor in Patients With Acute Myocardial Infarction: Five-year results of the REVIVAL-2 trial

Ilka Ott[1], Stefanie Schulz[2], Salvatore Cassese[2], Robert Byrne[3], Adnan Kastrati[3]
[1]Deutsches Herzzentrum, München, Germany, [2]Deutsches Herzzentrum, Munich, BAVARIA, [3]Deutsches Herzzentrum Munich, Munich, Germany

Background: The REVIVAL-2 study showed that stem cell mobilization by G-CSF does not influence infarct size, left ventricular function and coronary restenosis in patients with AMI that underwent successful percutaneous coronary intervention (PCI). The objective of the present analysis was to assess the impact of G-CSF treatment on 5-year clinical outcomes from the REVIVAL-2 trial.
Methods: In the randomized, double-blind, placebo-controlled REVIVAL-2 study, 114 patients with the diagnosis of acute myocardial infarction were enrolled 5 days after successful reperfusion by percutaneous coronary intervention. Patients were assigned to receive 10 µg/kg G-CSF (56 patients) or placebo (58 patients) for 5 days. The primary outcome for this analysis was the composite of death, myocardial infarction or stroke 5 years after randomization.
Results: The endpoint occurred in 7.1% of patients in the G-CSF group versus 15.5% assigned to placebo (relative risk [RR], 0.5; 95% confidence interval [CI], 0.1-1.4; p=0.17). The combined incidence of death or myocardial infarction occurred in 5.4% of the patients assigned to G-CSF and 13.8% of the patients assigned to placebo (RR, 0.4; 95% CI, 0.1-1.4; p=0.14). The major driver was mortality which was reduced from 10.3% in the placebo group to 3.6% in the G-CSF group (p=0.16).
Conclusions: These long term follow-up data show that G-CSF may reduce adverse events especially mortality in patients with acute myocardial infarction. ClinicalTrials.gov Identifier: NCT00126100

TCT-822

Effective Antegrade Cardiac Gene Therapy with VEGF-B167 for Pacing-induced Dilated Cardiomyopathy in a Pre-clinical Large Animal Model of Heart Failure

Felix Woitek[1], MaryKathryn Hurst[2], Nadja Ring[3], Anna M. Kulczycki[2], Amy Lam[2], Jeffrey C. Powers[2], Abdelkarim Sabri[1], Mauro Giacca[3], Fabio A. Recchia[2]
[1]Temple University - School of Medicine, Philadelphia, PA, [2]Temple University - School of Medicine, Philadelphia, PA, [3]International Centre for Genetic Engineering and Biotechnology, Trieste, Italy

Background: The selective VEGFR-1 activator VEGF-B has been shown to be antiapoptotic and cytoprotective in absence of angiogenic side effects. Thus