Background: The beta chemokines MCP-1 and RANTES activate and attract monocytes/macrophages and T-lymphocytes and thus, they can both stimulate antigen-independent cellular immune response. Autoantibodies to vascular endothelial damage-related externalized phosphatidylserine (aPS) or to its preferential cover annexin V (aANX-V), both indicate stimulation of humoral immune response. Aim of this study was to delineate if any type of immune response can be stimulated after acute coronary endothelial damage (CED)-related stent-percutaneous transluminal coronary angioplasty (stent-PTCA). Methods: 40 patients (pts) with coronary artery disease (CAD) underwent a primary successful, single- vessel, stent-PTCA. 20 CAD pts who underwent only coronary angiography (CA) and 20 healthy subjects (HS) served as controls. Peripheral blood was sampled at baseline before and 24 hours after PTCA or CA as well as 3 and 6 months after PTCA and was evaluated for plasma levels of MCP-1, RANTES, aPS and aANX-V.

Results: At baseline, PTCA pts presented plasma levels of MCP-1 (440 ± 62 pg/mL) and RANTES (25.5 ± 2.5 pg/mL) both similar to the respective levels of CA pts (MCP-1: 449 ± 87 pg/mL and RANTES: 24.2 ± 3.1 pg/mL) but higher than the respective levels of HS (MCP-1: 97 ± 12 pg/mL, p < 0.002 and RANTES: 10.1 ± 2.6 pg/mL, p = 0.001). After PTCA, only MCP-1 levels attained a gradual increase at all the interval times assessed (24 h after: 618 ± 76 pg/mL, 3 m after: 676 ± 79 pg/mL, 6 m after: 714 ± 64 pg/mL, p < 0.05 in all cases compared with the corresponding value of the previous interval assessing time). No other changes in MCP-1 and RANTES levels were noticed after PTCA or CA at all the interval times assessed, in comparison to the corresponding levels before the respective procedure. Both aPS and aANX-V were undetectable in plasma of all PTCA pts, CA pts and HS, at any time assessed. Conclusions: In CED-related CAD, MCP-1 and RANTES can both stimulate antigen-independent cellular immune response. However, in acute CED-related stent-PTCA, only MCP-1 can stimulate such a response. There is not enough evidence that CAD or stent-PTCA are associated in an important way to stimulation of any CED-related humoral immune response.

Alpha-Melanocyte Stimulation Hormone Inhibits Porcine Vascular Smooth Muscle and Endothelial Cell Responses to Tumor Necrosis Factor-Alpha

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Background: The long-term success of percutaneous coronary interventions (PCI) is limited by restenosis due to neointima formation. Early inflammation, apoptosis and proliferation at the site of injury play a role in neointima formation. Alpha-melanocyte-stimulating hormone (alpha-MSH) can inhibit inflammation by blocking intracellular pathways triggered by several inflammatory cytokines in cells expressing MSH receptors (MC-1). Alpha-MSH has previously been demonstrated to inhibit NF-kB transcription factor activation by TNF-alpha. However, the in vivo and in vivo effects of alpha-MSH on vascular smooth muscle cells (VSMC) and endothelial cells are not known. Methods: Immuno-labelling of cultured porcine VSMC and endothelial cells has identified positive MC-1 receptor surface expression. Stimulation with human or porcine TNF-alpha induced NF-kB activation both in VSMC and endothelial cells. NF-kB activation was determined by digital immunofluorescent nuclear tracking. Results: Alpha-MSH (10-9M) significantly inhibited TNF-alpha stimulated activation of NF-kB by 50% (± 9%) in VSM cells and 48% (±10%) in endothelial cells. Preliminary in vivo data obtained from oversize angioplasty injury to porcine coronary artery following local or systemic alpha-MSH delivery revealed a reduction in inflammation at the injury site one hour post-angioplasty. Conclusions: Our data suggests that alpha-MSH has potential for preventing local inflammation following angioplasty by inhibiting the NF-kBp65 pro-inflammatory signalling pathway. Alpha-MSH inhibition of stenosis following PCI in pig aortas is presently being investigated.

Stent Placement: A Cost Analysis From AVID

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Background: AVID (Angiography Vs. Intravascular ultrasound [IVUS]-Directed stent placement) is a multicenter randomized trial to determine the effect of IVUS-directed stent placement on clinical outcome. Results include a 12-month target lesion revascularization (TLR) rate of 4.9% in the IVUS group and 10.8% in the angiography group when protocol violations are excluded (p=0.02).

Methods: To determine the cost of IVUS- and angiography-directed stent placement, resource utilization was assessed for both groups within 12 months. Acute procedural resource utilization included the cost of IVUS catheters, PTCA balloons, stents and procedure time related to IVUS-directed additional therapy. Post-procedure costs included in-hospital complications, as well as readmission for MI, repeat coronary angiography, and repeat PTCA or CABG for TLR within 12 months. Medicare hospital reimbursements for MI, unstable angina, coronary angiography, PTCA, and CABG were obtained for 10 clinical sites and adjusted using institution-specific cost-to-charge ratios. Medicare schedules were used for physician fee reimbursement rates. Costs were compared using a two-sample t-test.

Results: At 24 centers 800 patients were randomized—394 to IVUS and 406 to angiography. The mean number of 15mm stents used was 1.5±0.9 in the IVUS group and 1.4±0.7 in the angiography group (p=0.02). In the IVUS group, 42% required additional therapy to fulfill criteria; 29% for an underdilated stent. The mean acute procedural cost per patient in the angiography group (p=0.27). The 12-month cumulative cost was $487±3240 in the IVUS group and $4274±3516 in the angiography group (p=0.05).

Conclusions: IVUS-directed stent placement results in significantly lower 12-month TLR costs compared to angiography-directed stent placement.