Results: Forty percent of veins harvested for aorto-coronary bypass had no functional viability (n = 39). HSPB1 expression and phosphorylation were inversely associated with relaxation in response to sodium nitroprusside (figure 1). Inhibiting HSPB1 phosphorylation by pretreatment with SB203580, a p38 MAPK inhibitor or a cell permeant peptide inhibitor of MK2, MK2i, enhanced relaxation ($p < 0.05$ figure 2). Rat aortic smooth muscle contains low levels of HSPB1; when treated with recombinant HSPB1 with a protein transduction domain allowing cell entry (rPTDHSPB1) led to increased HSPB1 impairing relaxation (figure 3).

Conclusions: Taken together, these studies support a role for HSPB1 in impaired relaxation of smooth muscle.

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PS234.

A Mouse Model of Vascular Grafting

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Objectives: Grafting of surgically transplanted arteries and veins to the arterial circulation is common in cardiovascular practice. Venous grafts degenerate rapidly following implantation with intimal hyperplasia playing an important role. In contrast, arterial grafts have excellent patency rates in the long-term and might be superior to vein grafts. Here we describe arterial and venous grafting to the mouse aorta.

Methods: A model for implantation of vascular grafts was established by transfer of the vena cava from donor animals to the abdominal aorta in recipients. Arterial grafting was performed by transfer of the abdominal aorta from donor mouse to the same site in recipients. Histology, scanning electron microscopy and confocal microscopy were used to study development of intimal hyperplasia and structural changes following transfer. Intravital microscopy was used to study interactions between leukocytes and graft endothelium.

Results: At different time points postop, scanning electron microscopy revealed that venous graft endothelium suffers structural injury whereas arterial grafts show no changes in endothelial integrity. By cross transfer of grafts from Tie2GFP mice that carry fluorescent endothelial cells into WT mice and subsequent confocal microscopy we determined that degenerated endothelium in venous grafts are of a mixed origin with most cells coming from the grafts but with contribution from arterial endothelium and/or circulating endothelial progenitor cells. Intimal hyperplasia was well developed at 28 days. Intravital microscopy showed rolling and recruitment of leukocytes in vein grafts at 28 days and no such interactions were observed in arterial grafts.

Conclusions: We've developed a stable and reproducible mouse model of vascular grafting. We show endothelial injury, intimal hyperplasia and inflammatory recruitment of leukocytes in vein grafts but not in arterial grafts. This animal model will be used in future experiments studying the roles of inflammation in the formation of intimal hyperplasia.

Author Disclosures: E. Eriksson: Nothing to disclose; **U. Hedin**: Nothing to disclose; **C. Tseng**: Nothing to disclose.

PS236.

Hydrophilic Surface Treatment of Thin Film Nickel Titanium Reduces Bacterial Biofilm Production Compared to Commercially Available Endograft Materials

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Objectives: Infections of indwelling medical devices remain a source of morbidity and mortality. We have been investigating the use of thin film nickel titanium (TFN) as a novel material to cover stents for a wide array of vascular applications, and have demonstrated that a super hydrophilic surface treatment prevents platelet adhesion and decreases bacterial adhesion. The current study aimed to show that biofilm producing bacteria will be unlikely to form biofilm on super hydrophilic TFN (S-TFN) and that any bacterial adhesion can be more effectively treated with therapeutic doses of antibiotics compared to commercially available endograft materials.

Methods: TFN was created using a sputter deposition technique to a uniform thickness of 5 microns. TFN then underwent surface treatment to create a hydrophilic layer. Bacterial studies were conducted using Staphylococcus Epidermidis strain 35984, a well characterized biofilm producing species. 1cm2 samples of Dacron, ePTFE, Untreated TFN and S-TFN were placed in 10ml tryptic soy broth, inoculated with 107 bacteria, and incubated at 37oC for 24 hours. Samples were then treated with therapeutic doses of rifampin/vancomycin for 24 hours. SEM images were taken both before and after treatment.

Results: SEM imaging studies demonstrated consistently decreased bacterial adhesion on S-TFN compared to all samples with significantly less biofilm deposition. Treatment with antibiotics for 24 hours demonstrated near clearance of bacteria on S-TFN with all other samples having evidence of persistent biofilm.

Conclusions: We demonstrate that the surface properties of S-TFN, namely its negatively charged, super hydrophilic, and ultra smooth surface reduce the likelihood of bacterial adhesion and significantly reduce biofilm deposi-

tion. This inability to form an adequate biofilm layer allows the S-TFN to be treated more effectively with antibiotics compared to commercially available endograft materials.

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PS238.

Regulation of Endothelin-1 and Endothelin Receptors by Shear Stress in Vascular Smooth Muscle Cells

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Objectives: Vascular interventional procedures often lead to endothelial denudation exposing vascular smooth muscle cells (SMCs) to fluid shear stress (FSS) exerted by the flowing blood. Intimal hyperplasia has been previously found to be influenced by Endothelin-1 (Et-1) through its receptors A and B (Et (A)/Et (B)). This study aimed to investigate the regulation of Et-1 and Et (A)/Et (B) by FSS in SMCs.

Methods: Rat aortic SMCs were exposed to FSS (14 dynes/cm2, 24 h) and endothelin-associated gene expression studied using microarrays. Cells were also were subjected to low shear (5 dynes/cm2) or high shear (14 dynes/cm2) and the expression of Et-1 and its receptors studied with RT-PCR. Following balloon injury to the rat carotid artery, RNA was isolated at 0-20 h after injury and expression of endothelin-associated genes studied with microarray technology. 10 days after injury, carotid arteries were studied by immunohistochemistry (IHC) using an Et (B) receptor antibody.

Results: Array analysis showed a decrease of Et-1 mRNA with a signal log ratio (SLR) of -5 ($p < 0.0025$) in FSS exposed SMCs in vitro. RT-PCR revealed an mRNA quantity of 29.9% ($p < 0.001$) and 13.3% ($p < 0.001$) for the low and high FSS group, respectively. Et (B) receptor mRNA was upregulated by FSS in SMCs (SLR 4.4, $p < 0.025$). RT-PCR showed a consistent upregulation ($p < 0.001$) in the low- and high FSS groups, but no significant dose-response effect (945.9% and 733.4% for the low- and high FSS groups vs control, respectively). Et (A) receptor expression was increased in the low FSS group (381.7%, $p < 0.001$) compared to control, but no increase was seen in the high FSS group. Following rat carotid injury, Et (B) receptor mRNA was upregulated at 5, 10 and 20 h by 388.3%, 495.4% and 141.9%, respectively ($p < 0.05$). IHC showed a prominent Et (B) receptor expression in adluminal SMCs exposed to FSS.

Conclusions: This data suggests that Et-1 and its receptors are regulated by FSS in SMCs. Further studies of the endothelin system in this context are warranted.

Author Disclosures: J. Ekstrand: Nothing to disclose; **U. Hedin**: Nothing to disclose; **A. Razuvaev**: Nothing to disclose; **J. Roy**: Nothing to disclose.

PS240.

Edaravone Suppresses Reperfusion Injury After Leg Ischemia in Rat Models

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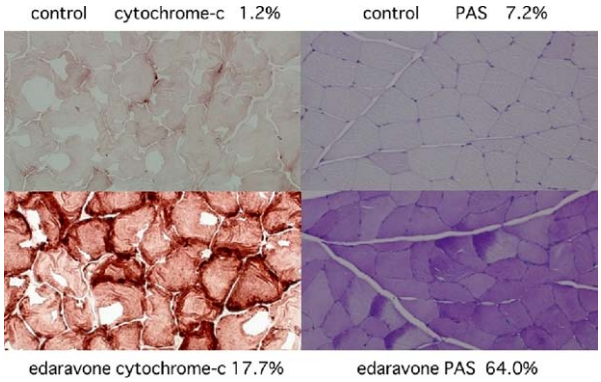
Objectives: Edaravone (Radicut®, Mitsubishi Tanabe Pharma Co., JAPAN), the first free-radical scavenger is presently used for acute cerebral infarction patients. We aimed to evaluate whether edaravone suppresses reperfusion injury focusing on mitochondrial activity and glycogen storage in the lower extremity muscles.

Methods: Male Lewis rats (508 ± 35 gm) were administrated a preoperative intraperitoneal injection of edaravone (3.0 mg/kg, edaravone group, n = 8) or the same dose of saline (control group, n = 8). Both common femoral arteries were clamped for 5 hours, and then declamped. The muscles of the bilateral lower extremities were harvested after more 5 hours from the start of reperfusion. They were stained with cytochrome-c oxidant as mitochondrial activity, and Periodic Acid Schiff (PAS) as glycogen storage. The percentages of cytochrome-c oxidant+ area and PAS+ area were measured and compared.

Results: The mean percentage of cytochrome-c oxidant+ area in the edaravone group was significantly higher than that in controls (13.3 ± 1.2 % vs 0.8 ± 0.1%, $p < 0.01$). The mean percentage of PAS+ area in the edaravone group was also significantly higher than that in controls (51.7 ± 6.8 % vs 7.3 ± 2.1%, $p < 0.001$, Fig. attached).

Conclusions: Our results suggested that edaravone might suppress reperfusion injury after leg ischemia by keeping a high level of mitochondrial activity, resulted in also a high level of glycogen storage in muscles.



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