

Connective tissue changes in experimental vein grafts – The influence of paclitaxel treatment on thrombosis, neointimal thickness, and apoptosis.

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Introduction: The extracellular matrix plays an important physiological role in the architecture of the vascular wall, e.g. by restraining smooth muscle cells. In arterialised vein grafts severe early changes, such as thrombosis and neointimal hyperplasia occur. Paclitaxel is in clinical use as antiproliferative coating of coronary stents. We aimed to investigate the early connective tissue changes in arterialized vein grafts and the influence of perivascular paclitaxel treatment.

Methods: C57 black mice underwent interposition of the vena cava into the carotid artery. Neointimal hyperplasia, thrombosis, acid mucopolysaccharides (Alcian), collagen fibers (trichrome Masson), elastic fibers, and apoptosis rate (TUNEL) were quantified in paclitaxel treated veins and controls.

Results: In both, controls and paclitaxel treated vein grafts acid mucopolysaccharides and elastic fibers were found predominantly in the neointima, whereas collagen fibers were found mainly in the media and adventitia. At 4 weeks postoperatively the neointimal thickness in controls was 52 (13-130) μm , whereas in paclitaxel (0.6 mg/ml) treated veins it was 103 (43-318) μm ($p=0.094$). At 8 weeks postoperatively paclitaxel treated veins showed a significantly increased neointimal thickness of 136 (87-199) μm compared with 79 (62-146) μm in controls ($p=0.032$). With higher concentrations of paclitaxel (6 and 1.5 mg/ml) high thrombosis rates (67% and 56% respectively) and severe vasculitis was present in the vein grafts. There was no difference in apoptosis rate between the two groups.

Conclusion: Early vein graft disease is characterised by an accumulation of acid mucopolysaccharides and elastic fibers in the thickened neointima. Paclitaxel treatment increases the neointimal hyperplasia in mouse vein grafts.