

AVASTIN INHIBITS CELLULAR REPLICATION AND INTIMAL HYPERPLASIA IN EXPERIMENTAL VEIN GRAFTS

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Objective: Studies on the role of vascular endothelial growth factor (VEGF) in the development of intimal hyperplasia (IH) have yielded conflicting results in both human and experimental vein grafts (EVGs). The VEGF gene is upregulated within 24 hours of implantation in EVGs. However its expression is variable in human arterialized and stenotic vein graft specimens suggesting that VEGF inhibition also plays a role. In this study we determined the effects of VEGF inhibition with Avastin on cellular replication, infiltration and IH in EVGs.

Methods: Epigastric vein to femoral artery interposition grafts were performed in 36 (8 month-old) male Lewis rats. The animals were divided into two groups. Each animal received either diluent (control group, n= 18) or avastin, (treatment group, n= 18), 15mg/kg intraperitoneally (IP) on days 1, 3, and 5 following graft implantation. The grafts were harvested at 7, 13, 21 and 53 days. They were examined histologically with H&E, von Giesson's elastic stain and by immunohistochemistry (IHC) with antibodies to myeloperoxidase, SMC α actin, VEGF and PCNA. The inhibitory effects of Avastin on VEGF was determined by Western immunoblotting.

Results: Avastin IP suppressed VEGF expression in EVGs for up to 21 days by western blot analysis. Vein grafts explanted within the first month showed a significant reduction in intimal/medial thickness and decreased cellular replication rate in the treatment group compared to controls ($P < 0.05$)

Conclusions: Avastin IP in the early period of graft implantation suppresses VEGF expression for up to 21 days in aged rats. The inhibition of VEGF blocks the inflammatory response and prevents SMC replication and infiltration and as a consequence reduces intimal hyperplasia in EVGs. The duration of Avastin induced VEGF inhibition and its long term effects on cellular proliferation and IH in both experimental and human vein grafts remain to be determined.