

**[F-FC157] Adventitial Proliferation Precedes Endothelial Proliferation in Arteriovenous Fistula Stenosis.**

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**Introduction:** Arteriovenous fistula (AVF) failure as a result of venous stenosis (due to a combination of intima-media thickening and lack of venous dilatation) is an important cause of hemodialysis vascular access dysfunction. Recent studies have documented the importance of the adventitia as an early site of cellular activation following vascular injury. However, it is unclear as to whether this paradigm (which could influence the development of local therapies for AVF stenosis) also applies to AVF failure. The AIM of this study was to describe the pattern of cellular proliferation within different layers of the vessel wall in a pig model of AVF stenosis.

**Methods:** 17 AVF were created between the femoral artery and vein of 10 Yorkshire cross pigs. Animals were sacrificed at 2d (2 pigs), 7d (2 pigs), 28d (2 pigs) and 42d (4 pigs). Bromodeoxyuridine (BrDU) was injected IP, 16 hrs prior to sacrifice. Formalin fixed, paraffin embedded sections from the venous segment were assessed for the degree of cellular proliferation using a standard immunohistochemical technique for BrDU. The degree of proliferation within different layers of the vessel wall (adventitia, intima-media and endothelium) was quantified using a semiquantitative scoring scale from 0-4+. **Results:** Maximal adventitial and intima-media proliferation (scores ranging from 1.57+/-0.48 to 1.89+/-0.26) occurred at the 2d and 7d timepoints, with lower levels of proliferation at both these sites at the 28d and 42d timepoints (scores ranging from 0.71+/-0.11 to 1.33+/-0.28). In contrast, cellular proliferation within the endothelium was lowest at the 2d time point (1.38+/-0.49) with maximal endothelial proliferation occurring at the 28d time point (2.13+/-0.35). **Conclusion:** Our data demonstrate that following creation of an AVF, there is early cellular activation within the adventitia and media of the venous segment. From a therapeutic standpoint, these results support the development of local perivascular therapies that are applied directly to the venous segment at the time of surgery.

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