Pathogenetic Role for Early Focal Macrophage Infiltration in a Pig Model of Arteriovenous Fistula (AVF) Stenosis

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Arteriovenous fistula (AVF) maturation failure as a result of a peri-anastomotic stenosis is currently a huge clinical problem. Despite the magnitude of the clinical problem, however, there is minimal information about the pathogenesis of this condition. The aim of this study was to describe the cellular (macrophage) infiltrate at different time points following AVF creation in a pig model of AVF stenosis.

Bilateral AVFs were placed in 8 pigs. Animals were sacrificed at 2d, 7d, 28d and 42d. Multiple formalin fixed paraffin embedded blocks were sequentially cut at 4 mm intervals for the first 2.5 cms of the venous segment beyond the anastomosis. Sections were stained for pig macrophages using a streptavidin biotin immunohistochemical technique and scored using a semi-quantitative scoring scale (Range 0-4+ with 0 = 0-10% macrophages; 1+ = 11-25%, 2+ = 26-50%, 3+ = 51-75%, 4+ = 76-100%). The adventitia (A), intima-media (IM) and endothelium (E) were separately scored at each of the time points and data from different blocks for a single AVF was averaged.

Maximal macrophage infiltration occurred at 2d (mean for all 3 layers combined = 1.14+/-.02). The individual scores for macrophage infiltration within the different vessel wall layers at 2 days were similar (A = 1.29+/-.0.04; IM = 1+/-.0; E = 1.2+/-.0.5). In marked contrast there was minimal infiltration at 7d (0.06+/-.03; p < 0.001 for a comparison of 2d versus 7d), with a complete absence of macrophages at 28d and 42d. Interestingly, many regions of the venous segment at 2d had a very marked macrophage infiltration (>75%) on one side of the vein only, with minimal infiltration of the opposite wall.

The early and transient infiltration of macrophages into the vessel wall (at 2d only) together with a selective infiltration to one side of the venous segment (perhaps due to differences in hemodynamic stress) suggest future novel therapeutic targets for AVF stenosis.

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Location: Exhibit Halls A/B/C

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