Regional heterogeneity and time-course of immunohistochemical changes in the venous wall of a porcine arteriovenous shunt model

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Objective: The majority of synthetic grafts become occluded within 18 months after placement, because of intimal hyperplasia at the venous anastomosis. This study examined the time-course and regional heterogeneity in the expression of cell migration [α-actin smooth muscle cells (α-SMA)] and proliferation markers (ki-67) in the venous wall of a porcine arteriovenous shunt (AVS) model.
Methods: AVS was created in 24 healthy male Landrace pigs between the common carotid artery and ipsilateral internal jugular vein using an ePTFE graft. The animals were randomized into three groups that were euthanized 2, 4, and 12 weeks post-surgery. The shunted and contralateral veins were resected and separated into three parts, in relation to region (proximal, central, and distal). The expression of α-SMA and ki-67 was detected immunohistochemically and analyzed.
Results: At 12 weeks, α-SMA expression centrally increased in tunica intima and adventitia of shunted than control veins (40.0±1.0% vs. 0.0±0.0%, 22.3±1.5% vs. 0.0±0.0%, $p<0.05$), but decreased in tunica media (16.5±0.8% vs. 33.8±2.0%, $p<0.05$). An increase in ki-67 expression was noticed in all tunicas of shunted veins (intima: 34.0±1.2% vs. 0.0±0.0%, media: 5.0±0.2% vs. 0.0±0.0%, adventitia: 17.6±1.1% vs. 7.4±0.4%, $p<0.05$). Differences among shunted and control vessels were less marked in the remaining regions (central>proximal>distal) and time intervals (12>4>2 weeks).
Conclusions: Creation of AVS with ePTFE graft induced extensive cell migration and proliferation leading to development of intimal hyperplasia, especially in the central region, with unfavorable consequences for graft patency and functionality. The present information on regional and temporal variations may further our appreciation of pathophysiological mechanisms entailed in graft access complications.

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