ABSTRACTS - Angiography & Interventional Cardiology

1031-176 Estrogen is Vasoprotective in Osteopontin Deficient Mice

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Background: Estrogen is vasoprotective in animal models of vascular injury, yet the mechanisms involved are incompletely understood. Many lines of evidence indicate that osteopontin (OPN) plays a role in neointima formation following arterial injury and that estrogen receptor (ER) modulates OPN expression. This study tested the hypothesis that estrogen reduces neointima formation following vascular injury via a mechanism that is dependent on modulation of OPN expression.

Methods: Male and female wild type (OPN+/+) mice and mice with homozygous deletion of the osteopontin gene (OPN-/-) were studied intact (INT) or following ovariectomy (OVX) and implantation of either estrogen (E2) or vehicle (V) pellets. Mice were randomized to 6 groups: INT females had a 72% reduction in neointima formation compared to OPN+/- males (1.21±0.20 x 10^4 mm^2 vs. 4.14±0.42 x 10^4 mm^2; p<0.05), and OPN+/- females had a 72% reduction in neointima formation compared to OPN+/- males (0.94±0.09 x 10^4 mm^2 vs. 3.61±0.51 x 10^4 mm^2; p<0.05). The sex-specific response was attenuated by OVX and restored by E2 replacement in both the OPN+/- and OPN-/- mice. Female OPN+/-+OVX+E2 mice had an 82% reduction in neointima formation compared to female OPN+/-+OVX-V mice (0.14±0.05 x 10^4 mm^2 vs. 2.63±0.37 x 10^4 mm^2; p<0.05), and female OPN+/-+OVX+E2 mice had a 59% reduction in neointima formation compared to female OPN-/-+OVX-E2 mice (0.55±0.09 x 10^4 mm^2 vs. 1.22±0.22 x 10^4 mm^2; p<0.05).

Conclusions: These results demonstrate that estrogen protects against neointima formation, and that the role of estrogen is dependent on modulation of OPN expression.