The Role of Hepcidin in Aortic Aneurysm Formation

Erik Scott, MD MS, Jolian J Dahl, MD; Gorav Ailawadi, MD MBA; Morgan Salmon, PhD
University of Virginia

Objectives: Hepcidin is a peptide hormone whose primary site of production is within the liver as the main iron regulatory hormone. Hepcidin decreases iron absorption by enterocytes and increases iron storage by macrophages and hepatocytes thus reducing serum iron levels. Excess iron causes tissue damage by oxidative stress. Iron deposits have been shown previously in abdominal aortic aneurysms (AAAs); however, the role of Hepcidin in AAA formation remains unknown. Our goal is to investigate the role of Hepcidin in aortic aneurysm formation.

Methods and Results: C57/BL6 male and female mice (WT/WT) underwent infrarenal peri-adventitial application of porcine pancreatic elastase (control; n=19) followed by harvest 14 days following AAA formation. Hepcidin heterozygous Knock-out male and female mice (WT/KO) underwent infrarenal peri-adventitial application of porcine pancreatic elastase (n=13) for 14 days. At day 14 the aortas were measured and harvested using video micrometry. Mann-Whitney tests were performed to statistically compare percent aortic dilation of WT/WT mice to the WT/KO Hepcidin mice. We found that female Hepcidin WT/KO mice had significantly larger aneurysms compared with WT/WT control mice at day 14 (WT/WT vs. WT/KO; WT/WT mean 135.4, Standard Deviation 36.06; WT/KO mean 100.1, Standard Deviation 19; p=.0079). In contrast, male Hepcidin WT/KO male mice had significantly smaller aneurysms compared with their WT/WT controls (WT/WT vs. WT/KO; WT/WT mean 56.79 Standard Deviation 5.22; WT/KO mean 120.5, Standard Deviation 37.63); p =.0128).

Conclusions: In conclusion, Hepcidin heterozygous elimination appears to have gender-dependent effects and suggests that hepcidin elimination using drug-based therapies could have gender-specific results.

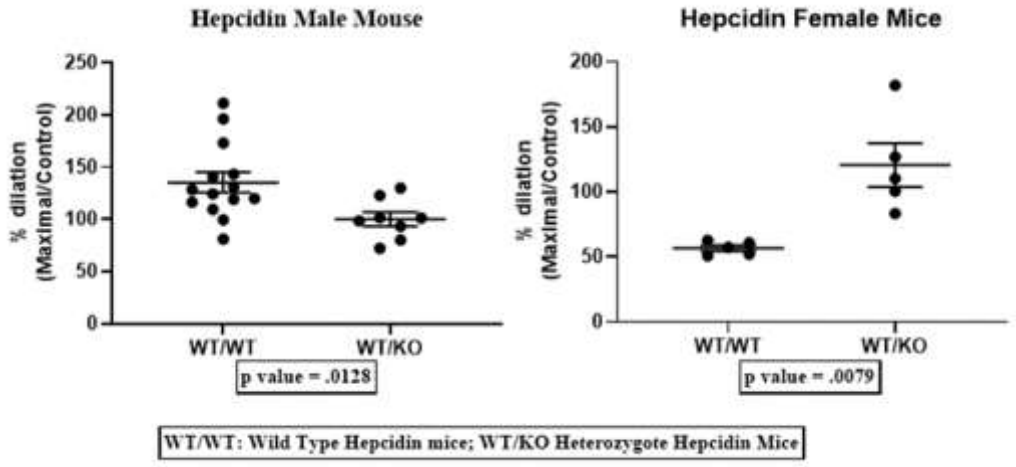

Figure 1. Aortic Dilation of Hepcidin Heterozygous Knock-out Mice versus Controls