



EFFECTS OF INHIBITING ADVANCED GLYCATION END PRODUCT RECEPTORS (RAGE) ON ARTERIOVENOUS FISTULA (AVF) MATURATION

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Chronic kidney disease (CKD) is the 9th leading cause of death in the United States affecting approximately 14% of the population [1,2]. Surgical creation of an arteriovenous fistulas (AVF) is the preferred method of vascular access for dialysis [3]. Advanced glycation end (AGE) products are high oxidant compounds that accumulate in vascular tissue due to high levels of oxidative stress in patients with CKD and end-stage kidney disease (ESKD) [4]. Interactions between AGEs and their receptors, including receptor for advanced glycation end product-specific receptor (RAGE), trigger various intracellular events, such as oxidative stress and inflammation, leading to cardiovascular and vascular access complications during dialysis treatment [4]. Carotid-jugular AVFs were created in two strains of mice: (a) C57/BL6 mice as the wild-type (WT) control. (b) RAGE KO mice on C57/BL6 background (RAGE KO or RAGE^{-/-}). CKD was not induced in these mice. Animals were sacrificed at 1 week after AVF creation. N=3 per condition type. AVFs were harvested for histology (embedding, sectioning, staining) and morphometry. The staining was the Verhoeff-Van Gieson (VVG) stain, which renders elastin fibers black (internal elastic lamina or IEL), collagen pink, and other tissues yellow. Images of VVG-stained slides were used for morphometric analysis to quantify the area within IEL, the area of open lumen, and the area of neointimal lesion (NL). Overall, the RAGE KO mice had smaller IEL areas ($p=0.1868$), NL areas ($p=0.2832$), open lumen areas ($p=0.1625$), and % open lumen areas ($p=0.0190$) than those in the WT mice. This observation suggests that RAGE inhibition (via genetic knockout) does not improve AVF remodeling. However, the sample size is small (only $n=3$ per condition) and the RAGE KO mice and WT control mice were not age-matched. In the future, similar research will need to be conducted on CKD mice that are age-matched to confirm results from this study.

References:

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