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Sex Differences in Limb Ischemia Recovery Following Conditional Endothelial Overexpression of Cept1

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Objectives: Choline ethanolamine phosphotransferase 1 (CEPT1) is essential for endothelial de novo lipogenesis (DNL) and is elevated in diseased peripheral arterial segments. Women are more sensitive to diet-induced DNL, and those with diabetes have higher incidence of severe peripheral arterial disease. We therefore hypothesized that women may have higher CEPT1 content in diseased peripheral arteries and that murine conditional endothelial overexpression of CEPT1 may lead to sex-specific differences in ischemic recovery.

Methods: CEPT1 expression was evaluated in diseased peripheral plaque of seven women and nine men. A murine endothelial CEPT1 overexpression model was engineered with Cre-induced expression of a CEPT1 transgene inserted in a C57BL/6J background. Endothelial CEPT1 overexpression was evaluated using reverse transcriptase polymerase chain reaction. Male (n = 5) and female (n = 5) received streptozotocin and unilateral femoral artery ligation. Limb perfusion, appearance, and use were then evaluated. Gastrocnemius was stained with hematoxylin and eosin, and endothelial isletin. Muscle fiber size and microvascular density were analyzed using the Student t test.

Results: Compared with males, female patients have higher CEPT1 in peripheral segments (n = 7, P < .005). Figure A. Murine endothelial CEPT1 overexpression had a seven-fold increase in expression compared with control (Figure B). Compared with female mice, males demonstrated improved perfusion (P < .05). Figure C, D, limb function (P < .05), Figure E, limb appearance (P < .05), Figure F, muscle fiber size (P < .05). Figure G, H, but both has adequate muscle microvascular density. Figure H, I. Conclusions: This study reveals a gender difference in peripheral arterial CEPT1 expression and ischemic recovery following overexpression. Differences do not seem to be directly associated with angiogenesis and may be due to underlying DNL metabolic consequences. These findings may have important implications for the prevalence of severe peripheral arterial disease in diabetic women.


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Sex Hormones Mediate Sex Differences in Hemodynamics and Inflammation during Arteriovenous Fistula Maturation

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Background: Arteriovenous fistulae (AVF) fail to mature, that is dilate and thicken, in women more than in men, leading to inferior outcomes and decreased utilization in women. As our mouse AVF model...