Sex-related differences in the intratubular renin-angiotensin system (RAS) in 2-kidney 1-clip hypertensive rats

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Objectives: The intratubular renin-angiotensin system (RAS) is thought to play an essential role in hypertensive renal disease, but information regarding sex-related differences in this system is limited. This study investigated the sexual differences in the intratubular RAS in 2-kidney 1-clip (2K1C) rats.

Methods: A 2.5-mm clip was placed on the left renal artery of Sprague Dawley rats, and the rats were euthanized 3 or 5 weeks following the operation.

Results: Systolic blood pressure (SBP) increased in 2K1C rats of both sexes but was significantly higher in males than in females, and an antihypertensive effect was not observed in 2K1C ovariectomized (OVX) female rats. Intratubular angiotensin-converting enzyme (ACE) and Ang II were repressed, and intratubular ACE2, Ang 1-7, and MasR were increased in both kidneys of 2K1C female rats at five weeks after surgery compared with those of male 2K1C rats. Intratubular mRNA levels of ACE and AT1R were augmented in OVX female rats regardless of clipping surgery at three weeks after operation in comparison with those in male and female rats. The AT1R was upregulated in female rats with or without OVX; thus, the AT1R/AT2 ratio was higher in female rats than in male rats.

Conclusions: Female rats were protected from hypertensive renal and cardiac injury after renal artery clipping. An increase in intratubular nonclassic RAS (ACE2/angiotensin 1-7/MasR) and a decrease in the AT1R/AT2 ratio could limit the adverse effects of classic RAS during renovascular hypertension in female rats, and estrogen is suggested to have a primary role in regulating intratubular RAS components.