Sexual Difference of Tubular Renin Angiotensin System (RAS) in 2kiney-1clip (2K1C) rats

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INTRODUCTION

Premenopausal female manifests lower blood pressure compared with age-matched male. Intrarenal RAS is thought to be an important role in hypertension and hypertensive renal disease, while there is rare information about sexual difference in intrarenal RAS. This study was performed to evaluate sexual difference of tubular RAS in 2 kidney 1 clip (2K1C) rat model.

METHODS

A 2.5-mm clip was inserted into the left renal artery of male and female Spargue-Dawley rats and they were euthanized at 5 week following the operation. Systolic blood pressure (SBP) was measured via the tail-cuff method at 10 day interval. Mainly medulla was analyzed for tubular RAS expression by immunohistochemistry and western blot.

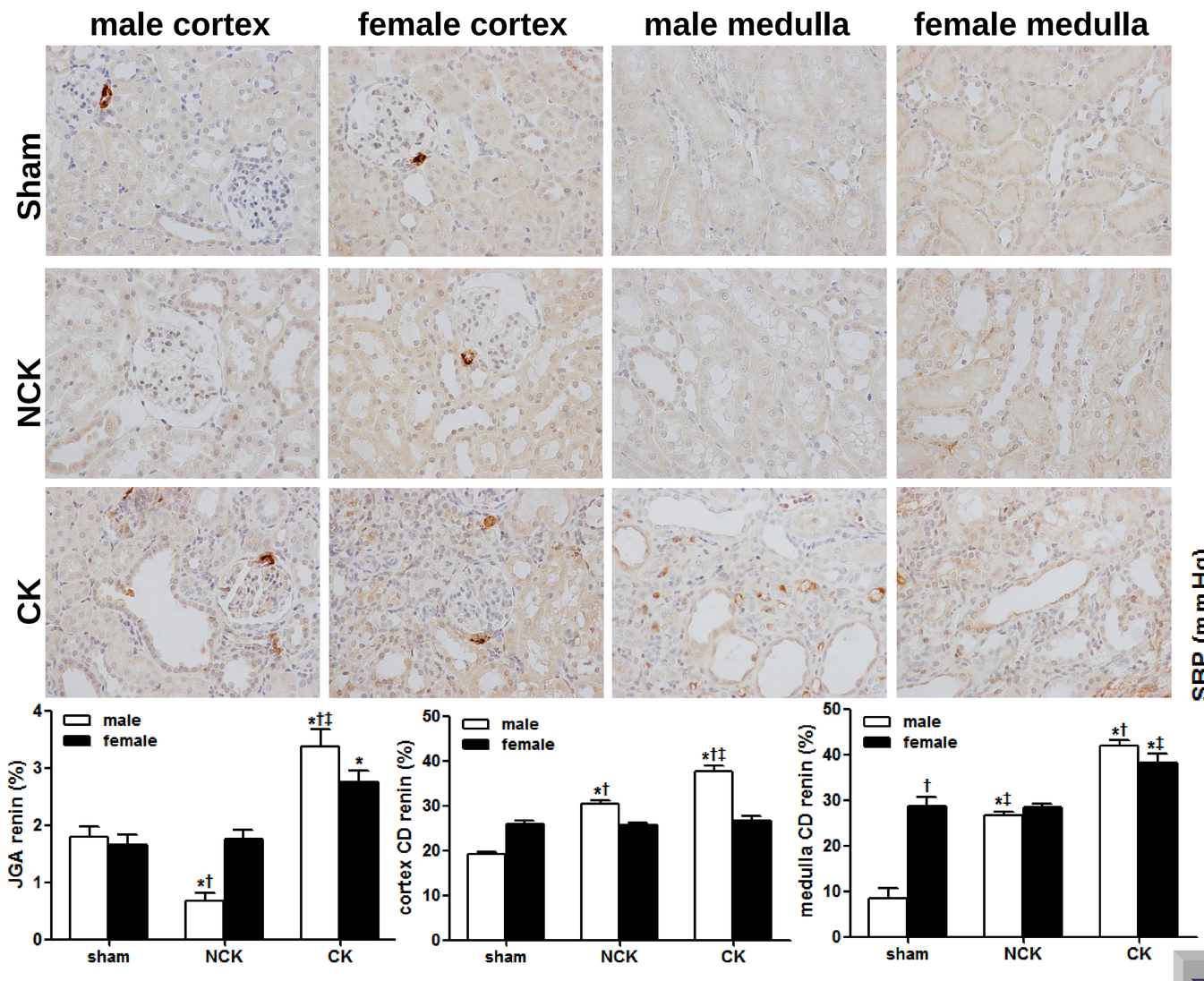

Figure1. Immunohistochemistry of intrarenal renin

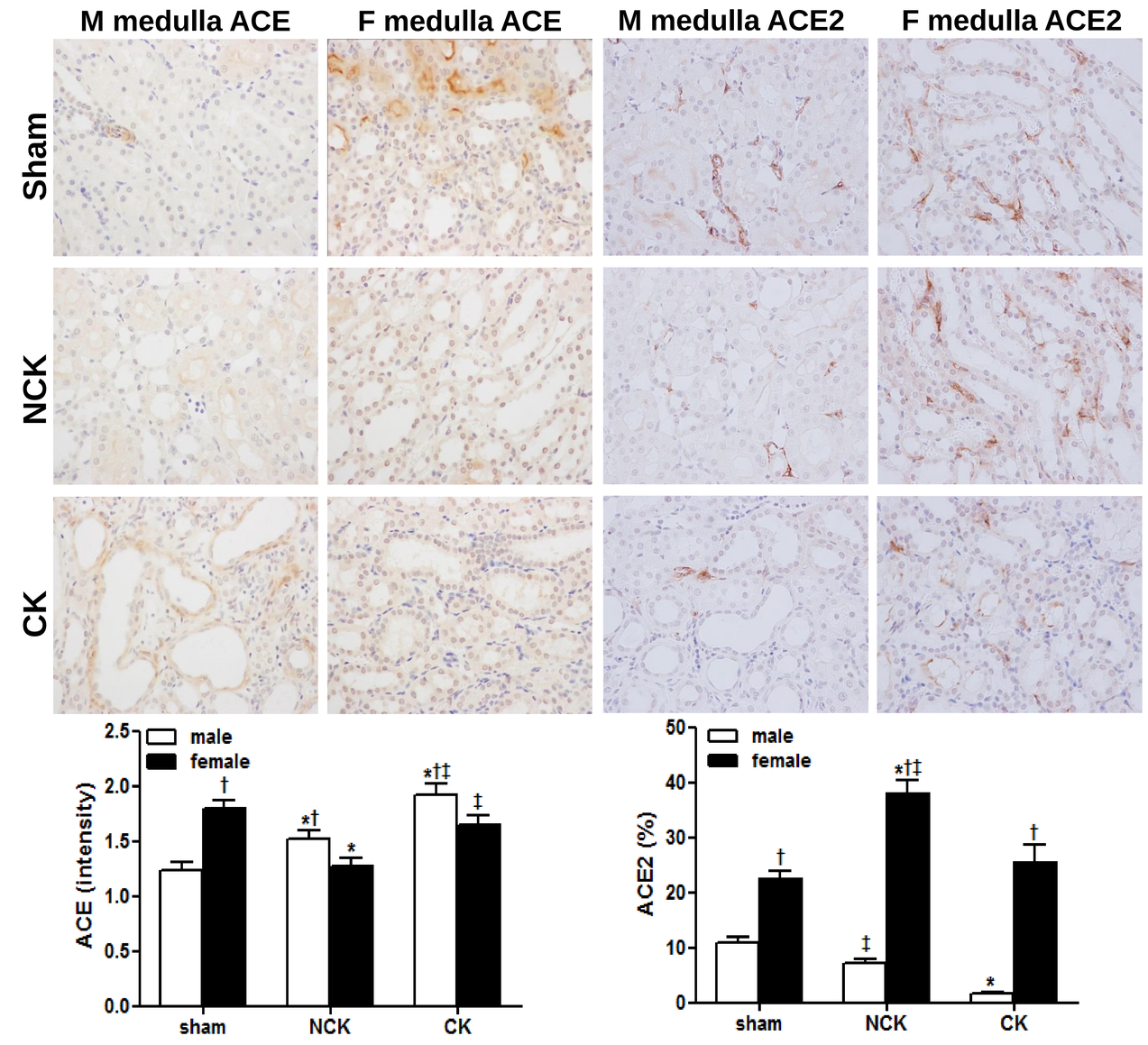

Figure3. Immunohistochemistry of medullary ACE and ACE2

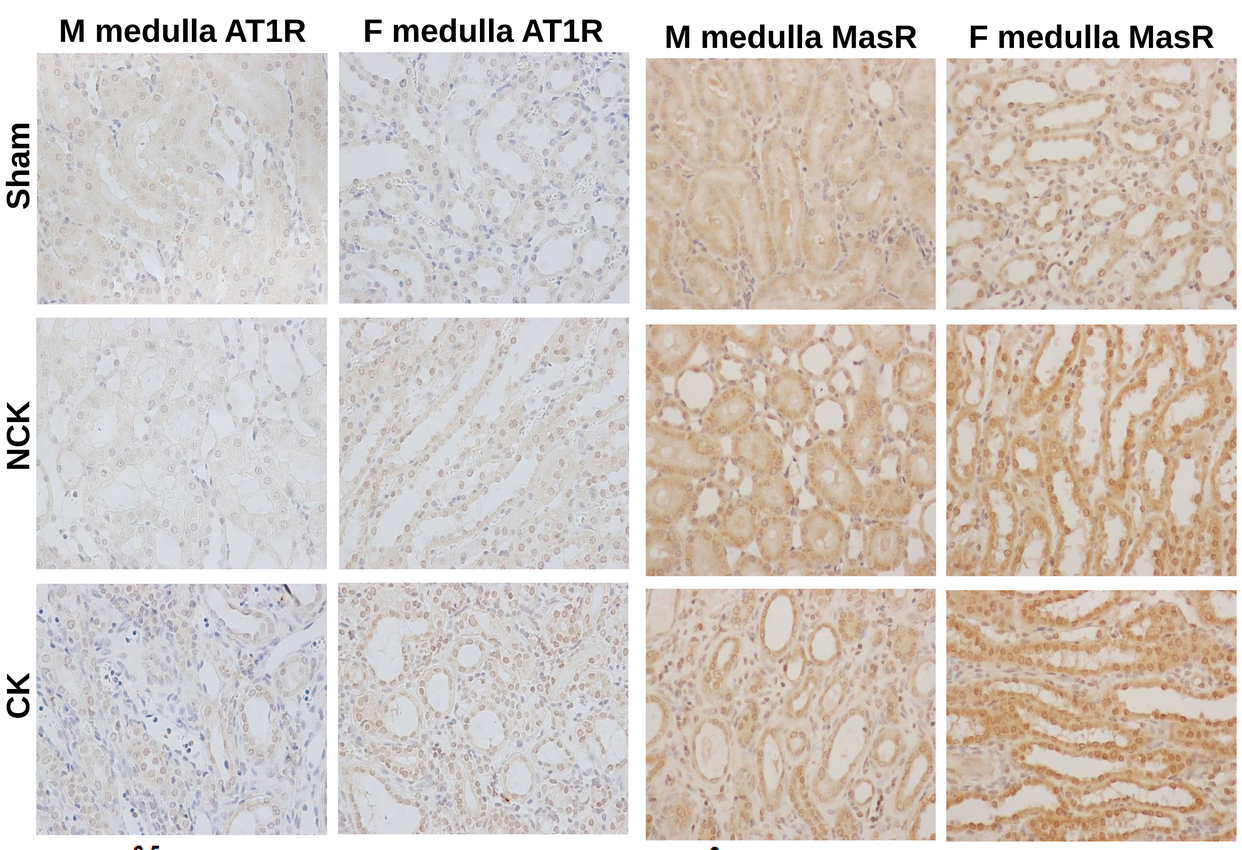

Figure3. Immunohistochemistry of medullary AT1R and MasR

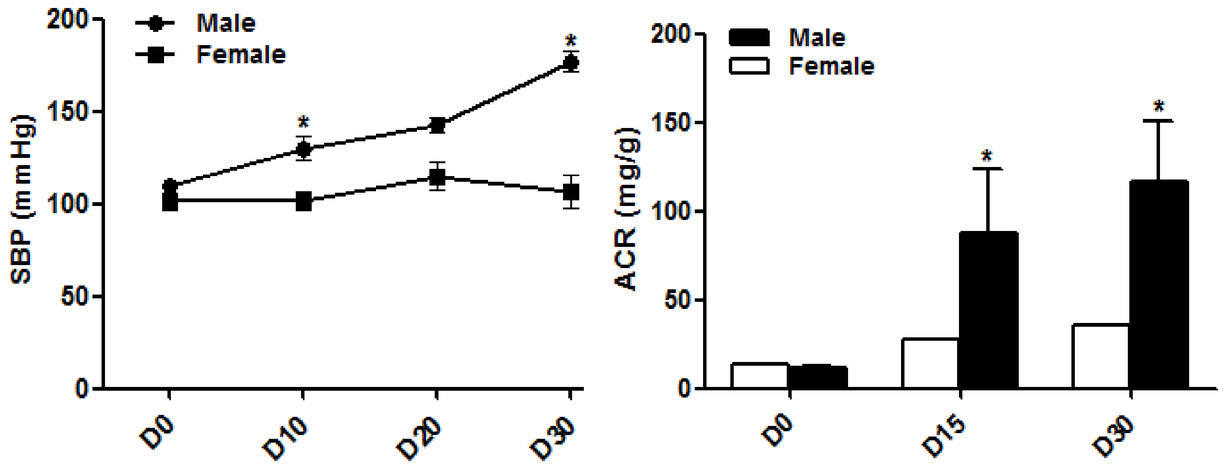

Figure14. Clinical characteristics

RESULTS

Clinical manifestation of hypertension, albuminuria and left ventricular hypertrophy was observed only in male rats. The clipped kidney (CK) of male rat presented worse glomerulosclerosis and more macrophage infiltration in comparison with CK of 2K1C female rat. In 2K1C male, Juxtaglomerular (JG) renin was increased in CK and reciprocally suppressed in non-clipped kidney (NCK), while collecting duct (CD) renin was enhanced in both kidneys. In 2K1C female, JG renin augmented in CK but the change of CD renin is subtle in both kidneys. ACE is up-regulated, while ACE2 was down-regulated in medulla of both kidneys in 2K1C male. In contrast, female identified reverse pattern of ACE and ACE2. Angiotensin type 1 receptor and Mas receptor was mildly elevated in both kidneys of 2K1C female. Female CK showed relatively lower level of angiotensin II, but rather higher level of angiotensin1-7 compared with them of male CK.

CONCLUSIONS

Same insult of renal artery stenosis aroused different clinical outcome in 2K1C male and female. Differently activated tubular RAS might influence difference in clinical manifestation. Superiority of nonclassic RAS in 2K1C female rat could limit the negative effect of classic RAS under renovascular hypertension.

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