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The role of ST2 as a biomarker and a treatment target in Hypertensive Kidney Injury

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Objectives: Increased sST2 serum levels are known to be associated with alterations of left ventricular geometry and increased systolic blood pressure. However, the role of ST2 in hypertensive injury of kidney is not discovered.

Methods: We enrolled 12 IgA nephropathy patients who had hypertension (hypertension group, n=6) or not (control group, n=6). We measured and compared ST2 levels in kidney tissue of the patients by immunohistochemical stain. For validation, we measured ST2 in hypertensive rat which induced by 5/6 nephrectomy. And ST2 blocking Ab was treated on primary cultured endothelial cell with hypertensive injury through rotational force-driven pressure.

Results: Hypertension and control groups were have similar ages ($p=1.000$) and they have no significant differences in eGFR (75.6 ± 35.4 vs. 68.4 ± 31.3 , $p=0.522$) and proteinuria (0.7 ± 0.7 vs. 1.9 ± 1.4 , $p=0.148$). Hypertensive group has significantly higher systolic blood pressure (119.0 ± 5.4 vs. 139.8 ± 9.9 , $p=0.006$) and diastolic pressure (73.5 ± 10.8 vs. 87.8 ± 10.0 , $p=0.030$). In immunohistochemical stain for ST2, hypertensive group showed significantly higher positive area compared to control group ($p=0.043$). In animal study, blood pressure was significantly higher in 5/6 nephrectomy rats compared to sham-operated rats (196.3 ± 25.8 vs. 125.9 ± 7.0 , $p=0.001$). ST2 positive areas were significantly larger in 5/6 nephrectomy rat kidney tissues compared to kidney from sham-operated rat ($p=0.024$). And both soluble and membranous ST2 mRNA levels were significantly elevated after 5/6 nephrectomy. For in vitro analysis, we induced hypertensive injury on primary glomerular endothelial cell through previously verified method by rotational force driven device. Then, we treated blocking antibody of ST2 on injured human glomerular endothelial cell. After 4 mmHg of rotational force induced, apoptotic cell proportions were significantly increased, and the apoptotic cells were alleviated after dose-dependent blockade of ST2. In addition, fibronectin expression was also reduced by ST2 in a similar manner after hypertensive injury.

Conclusions: ST2 has significant role on hypertensive injury of kidney.