論文の内容の要旨

論文題目
The role of renal sympathetic nerve in cardio-renal association
（心腎連関における腎交感神経の役割）

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Background:

Chronic kidney disease (CKD) is an indepent risk factor for cardiovascular disease (CVD) from its early stage. Clinically, CKD and heart failure (HF) often worsen each organ concurrently, reffered to as the cardiorenal syndrome (CRS). However, the mechanisms and mediators underlying this interaction are poorly understood. In this study, I tested my hypothesis that renal denervation has direct cardioprotective effect on cardiac function in CRS.

Methods:

Three-week-old male Sprague-Dawley rats were subjected to right uninephrectomy with or without left-side renal denervation, and fed normal-salt diet (0.3% NaCl) or high-salt diet (8% NaCl) for 6 weeks. LV diastolic function measured as time constant at the isovolumic relaxation phase (Tau) were investigated by cardiac catheterization. Protein level of sarcoplasmic

reticulum (SR) Ca^{2+}-ATPase type 2a (SERCA2a) and phospholamban (PLB) were determined by immunohistochemistry, and related gene expression was quantified by real time PCR.

Results:

High-salt loading induced a significant elevation of blood pressure (BP) and impaired left ventricular relaxation, accompanied by reduced SERCA2a protein and gene expression in the cardiac tissue. Renal denervation improved left ventricular relaxation accompanied by restoring SERCA2a protein and gene expression despite neither BP nor urinary protein levels were not altered. BP reduction by hydralazine at the early phase had the tendency to restore left ventricular relaxation, while SERCA2a gene and protein expression remained reduced. PLB-phosphorylation was not altered by renal denervation.

Conclusion:

In this CKD animal model, renal denervation has the cardioprotective effect on cardiac diastolic dysfunction independent from BP reduction as well as renal function recovery possibly through specific restoration of SERCA2a gene and protein expression, providing new insight into the mechanism of CRS.