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The Novel Therapeutic Strategy for Salt-Sensitive Hypertension Via Inhibition of Renal Sympathetic Nerve Activation

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Summary

Objectives: The mechanism of high-salt sensitive hypertension and it's induced cardiovascular injury are still unknown. However, renal sympathetic nerve activation was reported to be closely involved in various cardiovascular injuries. Hence, the present study was undertaken to examine whether long-term renal denervation (RDN) is involved in salt-sensitive hypertension and salt-induced cardiovascular injury (chronic kidney disease: CKD and cardiac diastolic heart failure: DHF).

Methods: (Experiment I) High-salt (HS) diet DS rats were divided into RDN group and a sham operation group to examine the effect of long-term RDN on cardiovascular injury. (Experiment II) Angiotensin II (Ang-II) infused Wild type (WT) and eNOS-/- mice were compared on blood pressure rhythm and cardio-renal injuries. (Experiment III) We evaluated the changes of cardiac function by echocardiography, and noninvasively assesses peripheral endothelial function as the reactive hyperemia-peripheral arterial tonometry index (RHI) in treatment-resistant hypertensive patients clinically treated with RDN therapies.

Results: (Experiment I) HS-diet DS rats exhibited severe hypertension, left ventricular (LV) hypertrophy and endothelial dysfunction, and RDN treatments significantly ameliorated them compared to hydralazine group despite of same degree of hypotensive effects in HS-diet DS rats. Furthermore, these beneficial effects were associated with the attenuation of vascular reactive oxygen species by dihydroethidium staining and of LV interstitial and peri-coronary fibrosis by Sirius-Red staining.

(Experiment II) Blood pressure of eNOS-/- mice was significantly higher than that of WT, and eNOS-/- mice exhibited a nondipper-type hypertension. Moreover, cardiovascular injuries in Ang-II-infused WT mice treated with RDN were significantly improved compared to sham operated Ang-II-infused WT mice.

(Experiment III) RHIs in RDN responder group in treatment-resistant hypertensive patients were lower than that in RDN non-responder patients, and were improved by RDN treatment, indicating the feasibility of RHI measurements in selecting therapeutic responder for RDN. Furthermore, cardiac diastolic function estimated by E/e' in echocardiography was improved by RDN treatments.

Conclusions: These studies suggested that salt sensitive hypertension and salt-sensitive hypertensive cardiovascular injuries are closely associated with renal sympathetic nerve activation, and RDN could be new therapy for salt sensitive hypertension and it's induced cardiovascular injuries. Furthermore, clinical RDN therapy also improved endothelial dysfunction and diastolic dysfunction in treatment-resistant hypertensive patients.