Print this Page for Your Records Close Window

Control/Tracking Number: 2012-SS-A-12664-AHA
Activity: Abstract
Current Date/Time: 6/4/2012 8:13:30 PM

Mechanisms of Cardiac Diastolic Dysfunction in a Model of Cardiorenal Syndrome

Author Block: An-sheng Lee, Fang-Yu Chen, Shih-sheng Chang, Chia-Chi Pan, Hua-Chen Chan, Chi-Tzong Chang, China Medical Univ Hosp, Taichung, Taiwan; Ming-Jai Su, Natl Taiwan Univ, Taipei, Taiwan; Chu-Huang Chen, Texas Heart Inst, Houston, TX; Kuan-Cheng Chang, China Medical Univ Hosp, Taichung, Taiwan

Abstract:
Background: Advanced-stage chronic kidney disease (CKD) may contribute to left ventricular hypertrophy, fibrosis, and diastolic dysfunction, which increase risk of cardiovascular mortality. However, whether cardiac remodeling occurs in early stages of CKD is unclear. In rats subjected to single nephrectomy, we examined cardiac structural changes and their underlying mechanisms in early stages of CKD.
Methods and Results: Adult male Sprague-Dawley rats underwent single nephrectomy (SNx; n=8) or sham (n=8) operations. Eight weeks later, the SNx group had a higher serum blood urea nitrogen (18.58±0.67 vs 13.40±0.78 mg/dL; *P*<.02) level, creatinine (0.45±0.02 vs 0.36±0.02 mg/dL; *P*<.02) level, systemic pulse pressure (48±5 vs 33±1 mmHg; *P*<.02), and echocardiographic transmitral deceleration time (65.3±2.6 vs 51.2±2.8 ms; *P*<.02) than the sham group. Doppler imaging and pressure-volume relationship (PVR) analysis performed in both groups revealed impaired diastolic function in SNx rats, which was manifested by significant (*P*<.05) increases in end-diastolic (ED) pressure, EDPVR, and the isovolumic relaxation constant. Compared to sham rats, SNx rats also had higher intracellular Ca^{2+} transient (0.08±0.03 vs 0.04±0.01 AUC; *P*<.05) and decay tau (342±46 vs 227±13 ms; *P*<.02) without cell length shortening in isolated cardiomyocytes (CMs). These changes were accompanied by an outward K^{+} current reduction and action potential prolongation. In SNx but not sham rats, inducible nitric oxide synthase (iNOS) and lectin-like oxidized LDL receptor-1 (LOX-1) were overinduced, and sarcoplasmic reticulum Ca^{2+} ATPase (SERCA), the enzyme that regulates Ca^{2+} transfer during muscle relaxation, was nitrosylated by peroxynitrite (produced by iNOS). Plasma LDL of SNx but not sham rats induced apoptosis in CMs through LOX-1signaling. In SNx rats, mitochondria permeability transition pores of CMs were oversensitive to Ca^{2+}, which is indicative of mitochondrial dysfunction and ATP depletion.
Conclusions: Chronic SNx affects global and cellular diastolic cardiac function via enhanced atherogenic LDL production, which contributes to SERCA nitrosylation and mitochondrial dysfunction. Our findings suggest that cardiac remodeling occurs in early stages of CKD.
:

Author Disclosure Information: A. Lee: None. **F. Chen:** None. **S. Chang:** None. **C. Pan:** None. **H. Chan:** None. **C. Chang:** None. **M. Su:** None. **C. Chen:** None. **K. Chang:** None.
Category (Complete): 501. Cardiac Failure and Remodeling
Keyword (Complete): Kidney ; Electrophysiology ; Calcium ; Lipoproteins ; Pressure – volume relation
Presentation Preference (Complete): Oral or Poster
Additional Info (Complete):
*: E. Have Submitted in the Past
*: No
***Disclosure**: There are no unlabeled/unapproved uses of drugs or products.
*: Yes

Payment (Complete): Your credit card order has been processed on Sunday 3 June 2012 at 9:58 PM.
Status: Complete

American Heart Association
7272 Greenville Avenue
Dallas, Texas 75231
OASIS Helpdesk