

Novel biomarkers for diastolic heart failure

Samuel C Dudley Jr, Euy-Myoung Jeong, Vikram Brahmanandam, Mihai Raicu, Song Yi Lee, Jae Hoon Chung, Cody A Rutledge, Ge Gao and Harvey Lardin

University of Illinois at Chicago, USA

Diastolic heart failure (DHF) is increasing in prevalence and incidence, but there are no specific treatments or diagnostic biomarkers known. Recently, we reported that that impaired relaxation is associated with nitric oxide synthase (NOS) uncoupling that results in oxidative modification of cardiac myosin binding protein C (MyBP-C), induces slowed myofilament cross-bridge kinetics, and leads to diastolic dysfunction. NOS uncoupling is enhanced by asymmetric dimethylarginine (ADMA). Plasma ADMA, L-arginine, and symmetric dimethyl arginine (SDMA) levels were determined from human plasma samples from patients with DHF or systolic HF (SHF) and from a healthy control group. Plasma ADMA level were elevated in both DHF patients ($0.77 \pm 0.04 \mu\text{M}$, $P < 0.05$) and SHF patients ($0.68 \pm 0.03 \mu\text{M}$, $P < 0.05$) compared to control group ($0.57 \pm 0.02 \mu\text{M}$). The ratio of L-arginine/ADMA was significantly reduced in the DHF group (139.5 ± 9.5 , $P < 0.05$) but not in the SHF group. Acute and chronic patients with DHF showed elevated plasma ADMA levels ($0.71 \pm 0.03 \mu\text{M}$, $P < 0.05$, Acute; $0.74 \pm 0.03 \mu\text{M}$, $P < 0.05$, Chronic) compared to control, but there was no difference based on the acutely of the illness. Human plasma from DHF patients showed elevated MyBP-C and S-total glutathionylated MyBP-C fragments compared to healthy control group (4.2 ± 1.4 -fold, $N=12$, $P < 0.05$). Elevated plasma ADMA level, the ratio of L-arginine/ADMA, and cardiac-specific S-glutathionylation of MyBP-C may be a useful biomarkers of DHF.

Biography

Dudley completed his MD and Ph.D. at the age of 26 years from the Medical College of Virginia. Dudley is a Professor of Medicine and Physiology at the University of Illinois at Chicago. Currently, he is an Editorial Board Member for JACC and a member of the Association of University Cardiologists and the American Society for Clinical Investigation. His research program focuses on mechanisms and treatments of arrhythmia and diastolic heart failure. He has published more than 80 articles and chapters and has submitted more than 15 patent applications on new therapeutics in these areas.

scdudley@uic.edu