Oxalate Diet Induced Chronic Kidney Disease in Dahl-Salt-Sensitive Rats Induces Uremic Cardiomyopathy

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Background: Patients with chronic kidney disease (CKD) often develop "uremic" cardiomyopathy characterized by left ventricular hypertrophy and cardiac remodeling, causing high morbidity and mortality. Increased levels of dietary oxalate, a renally-eliminated terminal toxic metabolite, can lead to CKD. Dahl-salt-sensitive rats (SS) are mainstay models of hypertensive renal disease; however, characterization of other diet-induced CKD models with uremic cardiomyopathy would allow for comparative studies.

Objective/Hypothesis: Our objective was to characterize a clinically relevant diet-induced rodent model of uremic cardiomyopathy. We hypothesized that SS rats fed a high oxalate diet will develop cardiac dysfunction compared to SS rats fed a normal chow diet.

Methods/Results: Ten-week-old male SS rats were fed either 0.2% salt normal chow (SS-NC) or 0.2% salt and 0.67% sodium oxalate (SS-OX) for five weeks (n=6-8/group). SS-OX rats demonstrated increased 24-hour urinary protein excretion (97% vs SS-NC, $p<0.01$), plasma Cystatin C (135% vs SS-NC, $p<0.01$), and hypertension (23% increase in systolic blood pressure vs. SS-NC, $p<0.05$). Renin-angiotensin-aldosterone-system profile demonstrated significant ($p<0.05$) increases in circulating plasma angiotensin (128% vs SS-NC), angiotensin I (56% vs SS-NC), and suppression of aldosterone (-54% vs SS-NC). SS-OX also displayed increased cardiac tissue fibrosis (188% vs. SS-NC, $p<0.05$) and inflammation (75% vs. SS-NC, $p<0.0001$). Echocardiography of SS-OX rats showed increased posterior wall thickness (128% vs. SS-NC, $p<0.01$), increased septal wall thickness (113% vs. SS-NC, $p<0.05$), indicating left ventricular hypertrophy.

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Conclusion: Oxalate diet induces significant renin-angiotensin-aldosterone-system activation, hypertension, cardiac fibrosis, inflammation, left ventricular remodeling, introducing a novel diet-induced model to study the cardiovascular complications of CKD.

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