

Gender specific differences in left ventricular hypertrophy in DOCA-salt mice with hypertensive kidney disease

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In chronic renal failure, volume overload and hypertension due to aldosterone excess lead to combination of concentric and eccentric hypertrophy. Deoxycorticosterone acetate (DOCA) mimics aldosterone by stimulation of sodium reabsorption in the kidney collecting ducts. Consequently, mice develop renal disease and left ventricular hypertrophy within 3-6 weeks. Signaling by the calcium-dependent phosphatase calcineurin contributes to cardiac hypertrophy in response to pathologic stimuli. Whether or not activation of calcineurin-signaling displays gender-specific differences has not been investigated yet. We hypothesized that putative gender differences in the activation of calcineurin-signaling in DOCA-salt model are estrogen dependent and mediated through estrogen-receptors. In order to differentiate blood pressure dependent from independent effects, we will employ pharmacological intervention with hydralazine. DOCA pellets were implanted to uninephrectomized female and male C57BL/6J mice receiving a high salt diet. Blood pressure and urinary excretion were monitored weekly. At the endpoints, after 3 or 6 weeks the invasive blood pressure measurement was performed and hearts and kidneys were harvested. We studied structural and molecular markers of cardiac and renal hypertrophy and fibrosis. We preliminary show that DOCA-salt induces volume overload and hypertension in a gender independent manner. Yet, female mice display a trend of increased renal and decreased cardiac hypertrophy implicating better adaptation to injurious stimulus. Hearts and kidneys show signs of beginning fibrosis and glomerulosclerosis in a gender dependent manner. Further experiments are directed to investigate gender specificity in the calcineurin pathway and the role of estrogen receptors.