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Ovariectomy Induces Early Changes in Cardiac Fibrosis and Angiotensin II Gene Expression

Anisha Patel
University of Massachusetts Amherst, aspatel@kin.umass.edu

Espen E. Spangenburg
University of Maryland

Sarah Witkowski
University of Massachusetts Amherst, switkows@kin.umass.edu

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Ovariectomy induces early changes in cardiac fibrosis and angiotensin II gene expression
Anisha Patel‡, Espen E. Spangenburg†, Sarah Witkowski‡
‡University of Massachusetts, Amherst, MA
†University of Maryland, College Park, MD
Contact E-mail: aspatel@kin.umass.edu
Postmenopausal women have an increased risk for heart disease. Ovariectomized mouse models show changes in body weight, adipose tissue, and systemic inflammation within 8-12 weeks following ovariectomy. These pathological changes may contribute to cardiac dysfunction after menopause. However, early changes in cardiac markers that may lead to dysfunction and disease remain unclear. **Objective:** To evaluate differences in cardiac gene expression between 8-week post-ovariectomy and control mice. **Methods:** Myocardial RNA was isolated from ovariectomized (OVX, n=10) and sham surgery (SHAM, n=10) adult mice 8 weeks following surgery. Fetal gene program, fibrosis, and angiotensin II gene expression were determined via RT-PCR. Differences between groups were analyzed using two sample t-tests. **Results:** Compared to SHAM, OVX mice exhibited a fetal gene expression pattern similar to that observed in failing hearts including increased B-type natriuretic peptide (p=0.02), atrial natriuretic peptide (p=0.06) and alpha skeletal actin (p=0.01) and decreased alpha and beta myosin heavy chain isoform expression (p=0.05, p=0.02, respectively). Expression of fibrotic genes vimentin (p=0.01), fibronectin (p=0.02), collagen1 (p=0.04), and collagen3 (p=0.03) were greater in OVX compared with SHAM. Lastly, angiotensin II was also significantly greater in OVX (p=0.001). **Conclusion:** Ovariectomized mice begin to exhibit maladaptive gene expression within 8 weeks after surgery, indicating that ovarian hormone loss initiates a pathological response in the heart at early time points that may be related to angiotensin II-induced cardiac fibrosis.