

Ovariectomy induces early changes in cardiac fibrosis and angiotensin II gene expression

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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.