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

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Et al.

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.