Evaluating the Role of Female Sex Hormones on Left Ventricular Mechanics in Aortic-Banded Mini-Swine

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ABSTRACT

Heart failure with preserved ejection fraction (HFpEF) comprises approximately 50% of all human heart failure cases. HFpEF has twice the incidence in woman compared to men, despite previous studies suggesting estrogen may be protective against the development of heart failure. Recent studies have proposed increasing the clinical use of two-dimensional speckle-tracking echocardiography (2D-STE) given its practicality and reduced expense compared to Magnetic resonance imaging. For this study, 28 female Yucatan miniature swine were placed into four groups (N=7/group): intact control (CON), intact aortic-banded (AB), ovariectomized control (CON-OVX), and ovariectomized aortic-banded (AB-OVX). For 2D-STE six segments of the left ventricle (LV) and septum were generated from apical four-chamber and short-axis two-dimensional views (acquired at the mitral-valve and apex levels) and averaged to determine global strain, strain rate, and displacement in the longitudinal, transverse, radial, and circumferential dimensions over three cardiac cycles. Torsion was calculated as the difference between mitral and apical end systolic rotation (degrees) and normalized to both LV hypertrophy (wall thickness) and end diastolic chamber length.

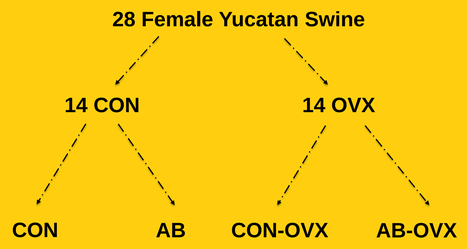
Objective

The objective of this study was to determine the role of female sex hormones on left ventricular mechanics of the hart following chronic pressure-overload using 2D-STE.

Hypothesis

Global LV strain will be decreased primarily in the longitudinal direction in the AB group. Longitudinal strain will be further impaired by the loss of female sex hormones.

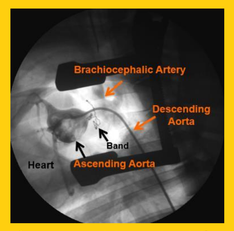
METHODS



- Yucatan mini-swine were delivered at 6 months of age
- Ovariectomy (OVX) was performed at 7 months of age
- Aortic-banding (AB) was performed at 8 months of age
- Aortic-banded animals were subject to pressure overload for a total of 6 months
- Terminal experiments were performed at 14 months of age

METHODS (cont.)

Aortic Band Placement:



A left second space intercostal Thoracotomy was performed. A sterile zip tie surrounded by Gore-Tex tubing was placed around the ascending aorta proximal to the brachiocephalic artery. An approximate 70 mm systolic transtenotic gradient (measured using a fluid-filled catheter – femoral artery insertion) was achieved while maintaining a peripheral vascular mean arterial pressure of approximately 90 mmHg under anesthesia using phenylephrine (I.V. 1-3 ug/kg/min) at a heart rate of 100 beats/min.

2-D Speckle Tracking Echocardiography

Transthoracic echocardiography was performed under sedation in lateral recumbence at 14 months of age. Using GE EchoPac software, kernels following the LV wall motion were tracked to assess LV wall mechanics over a total of three cardiac cycles. Strain is calculated using initial and final kernel positions as follows: $\frac{L_1 - L_0}{L_0}$

Strain rate represents how fast longitudinal, circumferential, and radial deformation occurs. Rotation rate indicates the speed of LV twisting at either the level of the apex or the base. Torsion is the net difference between apical and basal rotation.

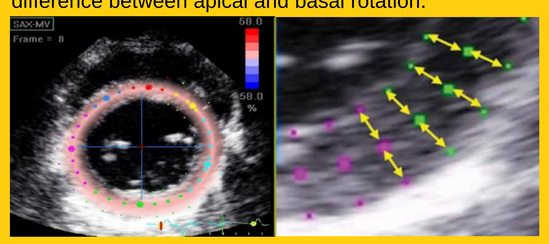


Figure 1. Radial strain measures myocardial deformation of the left ventricle toward the center of the cavity.

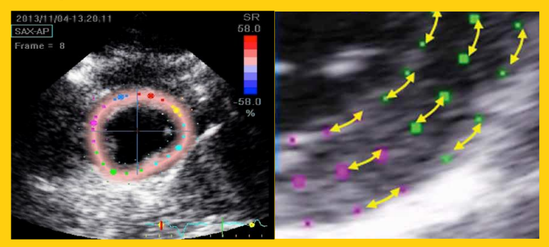


Figure 2. Circumferential strain measures myocardial fiber shortening along the circular perimeter of the left ventricle.

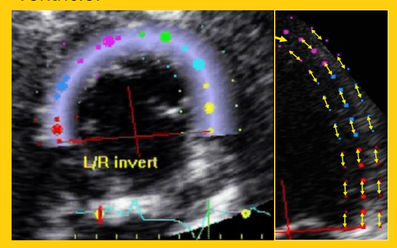


Figure 3. Longitudinal strain measures apex to base deformation of the left ventricle.

RESULTS

Systolic Function

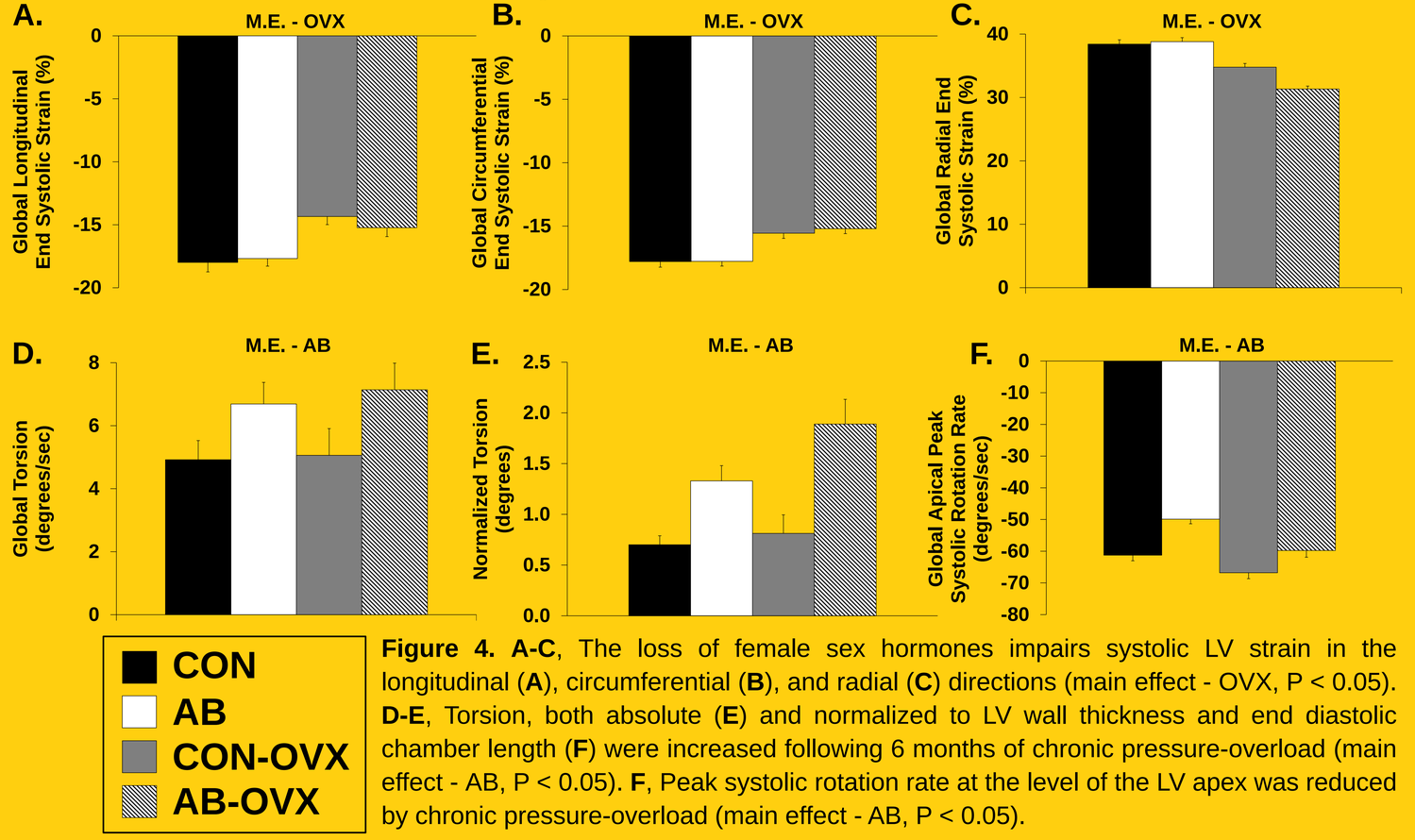


Figure 4. A-C, The loss of female sex hormones impairs systolic LV strain in the longitudinal (**A**), circumferential (**B**), and radial (**C**) directions (main effect - OVX, $P < 0.05$). **D-E**, Torsion, both absolute (**E**) and normalized to LV wall thickness and end diastolic chamber length (**F**) were increased following 6 months of chronic pressure-overload (main effect - AB, $P < 0.05$). **F**, Peak systolic rotation rate at the level of the LV apex was reduced by chronic pressure-overload (main effect - AB, $P < 0.05$).

Diastolic Function

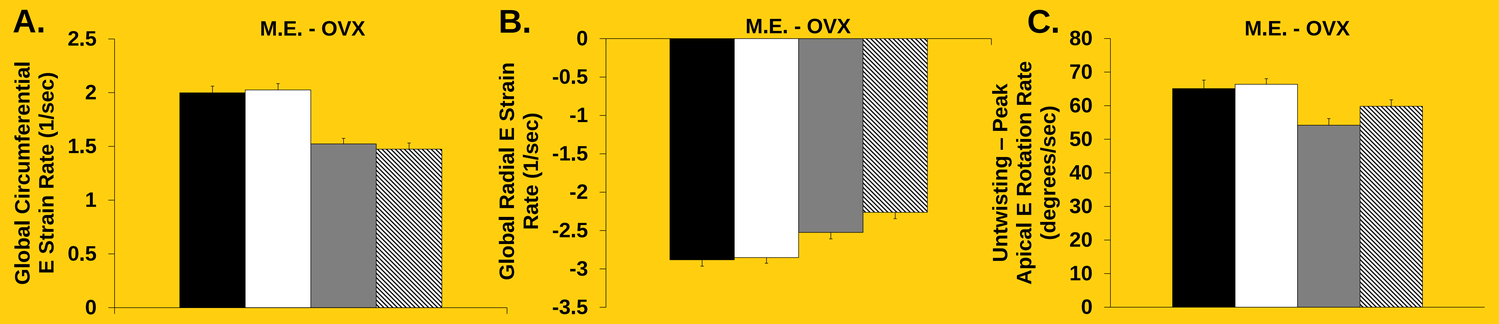


Figure 5. A-B, The loss of female sex hormones impairs early (E) diastolic LV strain rate in the circumferential (**A**) and radial (**B**) directions (main effect - OVX, $P < 0.05$). **C**, Early diastolic peak rotation rate at the level of the LV apex is also decreased 7 months post-ovariectomy (main effect - OVX, $P < 0.05$).

CONCLUSION

The loss of female sex hormones impairs both systolic and early diastolic LV mechanics. Pressure-overload induced specific changes to LV systolic twisting which are characterized by increased torsion and slower apical rotation. Our results suggest both menopause and hypertension can influence the development of heart failure through independent alterations to LV mechanics.

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