The Effect of Hormone Therapy on Vascular Function in a Male-to-Female Transgender Endurance Athlete

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Introduction

Biological sex is an independent predictor of cardiovascular outcomes. While there has been ample research conducted on the incidence of cardiovascular disease in biologically male and female individuals, there is much to understand regarding the specific cardiovascular risk in transgendered individuals[1]. At the time of this study in 2017, little was known about the cardiovascular consequences of female sex hormone exposure on human male physiology.

Research Question

Does gender affirming hormone therapy (GAHT) effect vascular function and subsequently change the risk of cardiovascular disease in a male-to-female transgendered endurance athlete?

Methods

The participant in this case study was a 27-year-old biologically male endurance athlete undergoing male-to-female gender transition.

- This study was reviewed and approved by the IRB at Arizona State University.
- Details of all procedures, data, and risks were discussed with the participant and written informed consent was completed before any testing was performed.
- A statement for permission to publish all collected data was included in the informed consent.
- There were no controls, and no other subjects were recruited in this study.

Testing occurred at 4–8-week intervals:

- Two baseline assessments.
- Six assessments on an estrogen-only treatment regimen (10 mg subcutaneous estradiol valerate every seven days).
- Three assessments after switching to oral estriol/estradiol (2 mg oral 80:20 estriol/estradiol per day) and the addition of a testosterone blockade (100 mg oral Spironolactone per day).

At each visit, testing included:

- Blood hormone levels
- Brachial blood pressure
- Body mass index (BMI)
- DEXA scan
- Ultrasound quantified brachial artery flow-mediated dilation (FMD)
- Non-invasive central aortic blood pressures and pulse wave velocity (PWV)

Results

Hormone Levels

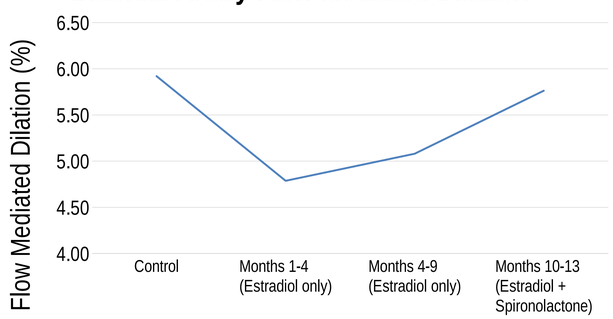
- Prior to initiating GAHT, the participant's testosterone level was within reference range for a male: total serum testosterone 323.00 ng/dL. Total serum testosterone levels were within range for a female, 30-100 ng/dL, by month 10 of the study, after the addition of the testosterone blocker Spironolactone.
- The participant's estradiol level was within reference range for a male, 9 pg/mL, prior to the study. Over nine months of estradiol only GAHT, the participant's estradiol was over 800 pg/mL. The target range for feminizing GAHT is estradiol less than 200 pg/mL. Over the course of 13 months of GAHT, the participant did not reach target estrogen levels.

Visceral Fat

- Throughout estradiol only treatment, the participant's visceral fat increased from 143 cm^2 to 190.5 cm^2.
- After treatment with spironolactone, the participant's visceral fat fell below the baseline control value of 133.25 cm^2.

Blood Pressure

- Over the course of GAHT, brachial blood pressure measurements increased slightly.
- A Spearman Correlation relative to time was assessed, and peripheral systolic blood pressure (SBP) and central systolic blood pressure (cSBP) were significantly positively correlated with time in this study (Pearson Correlation Coefficient r = 0.667, p = 0.049 and Pearson Correlation Coefficient r = 0.678, p = 0.045 respectively).



Figures 1: Flow mediated dilation (FMD) and time to peak FMD showed similar U-shaped trends, decreasing after the initiation of GAHT but then returning towards baseline. FMD was not correlated with other measures in this study. Time to peak was negatively associated with time, but the correlation was not statistically significant (Pearson Correlation Coefficient r = -0.617, p = 0.077).

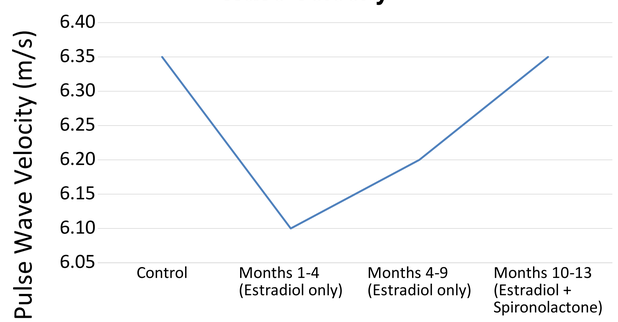


Figure 2: Pulse wave velocity (PWV), inversely related to vascular stiffness, decreased after the addition of estradiol therapy indicating increased vascular stiffness. However, the PWV returned to baseline within the timeframe of the study.

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Summary

High blood pressure is one of the most significant risk factors for vascular disease[2]:

- Systolic and diastolic brachial blood pressures increased throughout treatment with GAHT.
- Both peripheral and central systolic blood pressures were positively correlated with time in this case study.

Arterial stiffness is independent predictive factor for cardiovascular events[3]:

- Vascular stiffness increased and arterial reactivity decreased after the initiation of feminizing GAHT.

The distribution of visceral body fat is a significant and independent risk factor for cardiovascular disease and related mortality[4]:

- Visceral fat increased by 47.2 cm^2 after 9 months of estradiol only GAHT.

Conclusion

Our data suggests that feminizing GAHT may impact vascular function and these short-term changes may have the potential to subsequently increase the long-term risk of cardiovascular disease in this population.

Evidence published in 2019, from The Behavioral Risk Factor Surveillance System, suggested that transgendered men and women have a greater than 2-fold increase in the rates of myocardial infarction compared to their age-matched, cis-gendered peers, even after adjusting for cardiovascular risk factors[5]. This was the first large-scale analysis demonstrating an association between transgendered individuals and cardiovascular disease in a United States population.

Unfortunately, this case study was limited in its duration and sample size. More participants and a longer study time are needed to comprehensively assess the impact of GAHT on vascular physiology and cardiovascular risk in transgendered individuals.

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