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LETTERS

RESEARCH LETTER

Change in the QT Interval During Gender-Affirming Hormone Therapy

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The corrected QT interval (QTc) is longer in women than in men.[1] This difference starts in puberty and narrows with age, suggesting a role for sex steroids.[1] Study of QTc variation in states of sex steroid hypo- or hyperfunction (eg, hypogonadal men) have reinforced the role of sex steroids in QTc variation.[2] Gender-affirming hormone therapy for transgender and gender-diverse (TGD) patients provides a unique model to evaluate the impact of sex steroids independently from other sex-specific characteristics that may affect the electrocardiogram (ECG).

TGD individuals under 27 years of age who had received hormone therapy (including testosterone, estrogen, or gonadotropin-releasing hormone analogues [GnRHas]), had at least 1 ECG before hormone initiation, and at least 1 ECG after 40 days of hormone use were included. Patients with documented cardiac abnormalities, including arrhythmias such as long QT syndrome, were excluded.

Age, race, biological sex, cardiac medical history, medications, and ECG parameters were abstracted from the medical record. QTc was calculated according to Bazett's formula. Changes in QTc were analyzed for each treatment group with the use of generalized linear mixed models, adjusting for concomitant use of known QTc-prolonging medications. To account for multiple observations recorded for each subject, a random intercept for participant ID was included in the model. The study was conducted under the ethical oversight of the Lifespan Institutional Review Board.

A total of 11 records were excluded due to overdose-related ECGs, 1 record was excluded due to being the only individual designated male at birth (DMAB) in the GnRHa cohort, leaving 39 individuals for analysis. Of these, 23 were treated with testosterone (all designated female at birth [DFAB]; 22 via testosterone cypionate injection, 1 via topical gel), 10 with oral estrogen (all DMAB), and 6 with GnRHas (all DFAB; via leuprolide injection). Three individuals treated with testosterone had received previous GnRHa treatment.

Among patients receiving testosterone, the mean QTc decreased significantly from 422.1 ± 24.3 ms to 408.5 ± 23.5 ms (estimate: −14.0; 95% CI: −22.5 to −5.5; F ratio = 10.8; $P < 0.01$) (**Figure 1**). In the estrogen cohort, the QTc increased significantly from 417.0 ± 25.2 ms to 432.0 ± 13.4 ms (estimate: 16.1; 95% CI: 5.6 to 26.6; F ratio = 9.7; $P < 0.01$) (**Figure 1**).

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For the DFAB individuals who received GnRHa, the QTc increased significantly from 416.1 ± 19.8 ms to 430.0 ± 23.4 ms (estimate: 17.0; CI: 1.3-33.0; F ratio = 4.8; $P = 0.03$) (Figure 1).

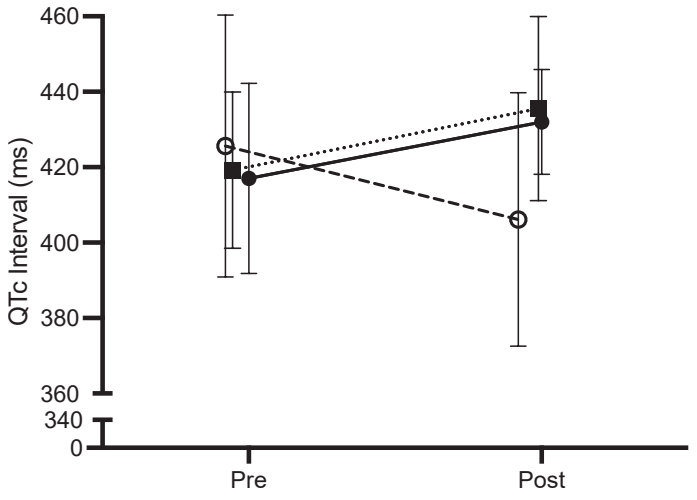
The QTc interval decreased during testosterone therapy in DFAB individuals and increased in DMAB individuals receiving estrogen, as consistent with the decrease in QTc during testosterone-driven puberty in males and QTc prolongation in hypogonadal males.[2] Our findings agree with previous reports of QTc alterations in transgender adults.[3]

GnRHa treatment was associated with a significant increase in QTc. Previous studies of the effect of GnRHa on QTc in TGD youth did not observe an effect; however, lack of stratification by designated sex may have obscured a designated sex-specific effect.[4] QTc prolongation is described in men receiving GnRHa for treatment of prostate cancer, likely secondary to a more significant androgen deprivation.[5] GnRHa-related suppression of testosterone may likewise contribute to the observed QTc prolongation in our cohort.

This study is limited by its retrospective nature and small sample size. Dose changes of QTc-prolonging concomitant medications were not considered in the analysis, though we would not expect such changes to uniformly influence our sample. Future work should prospectively evaluate ECG changes to better assess potentially confounding comorbidities and medications.

We report additional evidence that sex steroids affect cardiac repolarization leading to a decrease in the QTc with increasing testosterone exposure, and a novel finding of QTc lengthening in DFAB adolescents using GnRHa. Clinicians should consider sex steroid exposure when interpreting QTc, including in the evaluation for long QT syndrome.

FIGURE 1 Change in QTc Before and During Gender-Affirming Medical Treatment



Solid circles and solid line represent individuals designated male at birth treated with estrogen (n = 10). Solid squares and dotted line represent individuals designated female at birth (DFAB) treated with gonadotropin-releasing hormone analogues (n = 6). Open circles and dashed line represent DFAB participants treated with testosterone (n = 23). Vertical lines represent SD around the mean.

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REFERENCES

1. Rabkin SW, Cheng XBJ, Thompson DJ. Detailed analysis of the impact of age on the QT interval. *J Geriatr Cardiol*. 2016;13(9):740–748.

2. Charbit B, Christin-Maître S, Démolis JL, Soustre E, Young J, Funck-Brentano C. Effects of testosterone on ventricular repolarization in hypogonadic men. *Am J Cardiol*. 2009;103(6):887–890.

3. Saito N, Nagahara D, Ichihara K, Masumori N, Miura T, Takahashi S. Gender-affirming hormone treatment causes changes in gender phenotype in a 12-lead electrocardiogram. *Heart Rhythm*. 2021;18(7):1203–1209.

4. Waldner RC, Doulla M, Atallah J, Rathwell S, Grimbly C. Leuprolide acetate and QTc interval in gender-diverse youth. *Transgender Health*. 2023;8(1):84–88.

5. Gagliano-Jucá T, Travison TG, Kantoff PW, et al. Androgen deprivation therapy is associated with prolongation of QTc interval in men with prostate cancer. *J Endocr Soc*. 2018;2(5):485–496.

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