The Effect of Sex Steroids on Electrocardiogram Measurements in Transgender and Gender Diverse Youth

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Background

Cisgender women have a longer calculated QT interval than cisgender men. This difference starts at puberty, suggesting that sex steroids may play a role.[1] Transgender and gender diverse (TGD) individuals may be treated with sex steroids to align their physical appearance with their gender identity (i.e., testosterone treatment in transmasculine individuals or estrogen treatment in transfeminine individuals) or with GnRH analogs to halt the production of endogenous sex steroids. Previous reports in older cisgender men undergoing androgen deprivation therapy for prostate cancer treatment have shown that GnRH analog therapy may prolong QTc length; however, there have been no studies in TGD adolescents and young adults.[2] Furthermore, TGD individuals have a high burden of psychiatric co-morbidities and are frequently prescribed psychiatric medications that are known to prolong QTc. Therefore, understanding the relationship between patient characteristics and QTc length in patients undergoing gender affirming medical treatments is especially important. Elucidating this association will help to identify and appropriately triage patients with prolonged QTc who are at risk of subsequent arrythmias.

Objectives

In this retrospective study, we aim to characterize changes QTc length in TGD patients receiving testosterone, estrogen, and/or GnRH analog therapy. A better understanding of the changes in EKG parameters in TGD patients receiving gender affirming care will improve the care of our TGD patients by providing context to QTc lengths in patients undergoing hormone therapy. We hope that this study will provide pilot data for a prospective study which is currently underway.

Methods

We obtained the electronic health records of all patients who (1) presented to the Division of Adolescent Medicine at Hasbro and (2) have at least one electrocardiogram in their medical records. Records are being manually reviewed and relevant data is currently being collected and stored in a REDCap database. The following information is being gathered:

- **Demographic information**, including age, sex, race, gender identity,
- **Medical History**, including type of hormone therapy, age at hormone therapy start and all further measurements, comorbid medical conditions, and current medications,
- **Anthropometric data**, including height, weight, blood pressure, and Tanner stage,
- **Laboratory data**, including sex hormone levels, a basic metabolic panel, and magnesium if available
- **EKG data**, including RR, PR, and QR intervals.

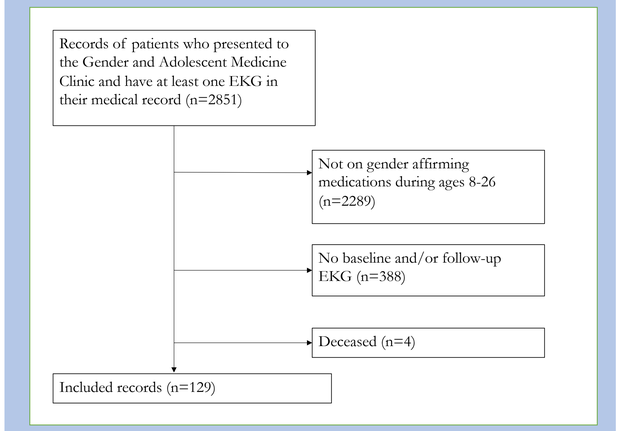

Figure 1. Schematic of record inclusion and exclusion screening

Data

A total of 2,851 charts were obtained based on the above criteria. Patient charts were further excluded if they have not been on gender affirming medications (i.e. GnRH analogs, testosterone, and/or estradiol) during ages 8-26, lack a baseline and/or follow-up EKG, have an unknown medication start date, or are deceased. A total of 129 records will be included in the final analysis (Fig. 1).

Results

As of now, results are pending. However, we anticipate that our results will adhere to the following categorization, adjusting for time before and since starting gender affirming medications, age, and Tanner stage:

Group	Testosterone group (n=?)	Estrogen group (n=?)	GnRH group (n=?)	Testosterone + GnRH group (n=?)	Estrogen + GnRH group (n=?)
Baseline QTc (ms)					
Follow-up QTc (ms)					
Change in QTc (ms)					
Testosterone level (ng/dL)					
Estradiol level (pg/mL)					
Sodium (mEq/L)					
Potassium (mEq/L)					
Magnesium (mEq/L)					

Conclusion

As of now, data collection is still pending. However, we hypothesize that transmasculine patients on testosterone will have a decreased QTc from baseline, transfeminine patients on estrogen will have an increased QTc from baseline, and patients on GnRH analogs alone will have minimal QTc change from baseline. We further hypothesize that patients on a combination of testosterone and a GnRH analog or a combination of estrogen and a GnRH analog will see a greater change in their QTc from baseline compared to the testosterone and estrogen groups alone. These changes, especially in the estrogen cohort, may have implications for these patients' medical management. TGD youth tend to have a high burden of psychiatric comorbidities which are treated with medications known to prolong QTc and predispose to arrhythmias. Furthermore, common comorbidities in the TGD populations such as eating disorders may result in electrolyte abnormalities known to alter QTc length. We hope that our study will elucidate any cardiac risk factors associated with gender care in real-world setting, and thereby improve care for TGD individuals.

References

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Acknowledgements

The authors would like to thank Deanna M. Salter, MS, PhD, at the data engineering team at Lifespan BERDI for their help with patient record abstraction, The Division of Gender and Adolescent Medicine at Hasbro Children's Hospital for guidance in the study design process, and the Warren Alpert Medical School for their support.

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