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Executive Overview

Transgender-Affirming Hormone Therapies, QT Prolongation, and Cardiac Repolarization • Baseline quantitative ECG parameters do not fully predict class 1 antiarrhythmic effect in Brugada patient: Drug-induced ECG changes in Brugada patients • Products News • AMPS People.

Editorial

We continue covering the AMPS tradition of research participation in this TAI issue, as we feature 2 new papers published this past quarter: *Transgender-Affirming Hormone Therapies, QT Prolongation, and Cardiac Repolarization*

IMPORTANCE Transgender women (assigned male at birth) usually take antiandrogens associated with estrogens (or are castrated) to induce feminization, whereas transgender men (assigned female at birth) take testosterone to induce masculinization. However, the cardiovascular outcomes of these gender-affirming hormone therapies (GAHTs) remain poorly studied.

OBJECTIVE To examine the association between GAHT intake and cardiac repolarization alterations on electrocardiography in transgender individuals.

DESIGN, SETTING, AND PARTICIPANTS In this cohort study, data from a prospective cohort of adult transgender individuals from a single center in France were collected from January 1, 2021, to January 1, 2023. GAHT consisted of injectable testosterone in transgender men and transdermal estradiol with mostly oral cyproterone acetate as antiandrogens in transgender women.

MAIN OUTCOMES AND MEASURES Electrocardiographic features, including QTc, T-wave maximal amplitude (TAmp), and QT peak (QTp; distance between Q onset and T peak), were studied. Circulating sex hormones, including total testosterone, estradiol, progesterone, and gonadotrophins, were assessed concomitantly to electrocardiographic intake.

RESULTS In the overall cohort of 120 transgender individuals (mean [SD] age, 29.7 [11.9] years; 64 transgender men and 56 transgender women), mean (SD) QTc was similar between 35 transgender women receiving GAHT (406 [20] milliseconds) and 23 transgender men before GAHT (400 [16] milliseconds) but prolonged versus 41 transgender men receiving GAHT (378 [19] milliseconds) ($P < .001$) or 21 transgender women before receiving GAHT (384 [21] milliseconds) ($P < .001$). The start of GAHT in 15 transgender women was associated with increased QTc (mean [SD], 20 [12] milliseconds versus before receiving GAHT; $P < .001$) and decreased QTc in 18 transgender men (mean [SD], −17 [16] milliseconds versus before receiving GAHT; $P < .001$). No participant had a QTc greater than 480 milliseconds or QTc change greater than 60 milliseconds after the start of GAHT in this study. Nonlinear mixed models (eg, integrating age, calcemia, relevant circulating hormones levels, and torsadogenic drug intake) showed that QTc was associated with total testosterone in transgender men (mean [SD] estimate, −1.6 [0.6] ms/ng/mL; $P = .007$) and prolactin (mean [SD], 0.4 [0.1] ms/ng/mL; $P < .001$). In transgender women, QTc was associated with total testosterone (mean [SD] estimate, −3.5 [0.8] ms/ng/mL; $P < .001$). Variation of QTp and TAmp observed after the start of GAHT and associated

hormonal alteration were globally associated with those observed with QTc, although in opposite directions for transgender women and transgender men.

CONCLUSIONS AND RELEVANCE In this cohort study, testosterone use in transgender men was associated with QTc and QTp shortening and increased TAmp. Androgen deprivation in transgender women was associated with opposite observations. The magnitude of QTc sexual dimorphism seen in cisgender adults was also observed in the transgender population. This work highlights that potential GAHT effects on cardiac repolarization warrant attention in the exponentially increasing transgender population, which is often exposed to coprescribed drugs prolonging QTc and at risk of TdP.

The full article, as well as other recent journal publications authored or co-authored by our staff can be found on the AMPS website

Baseline quantitative ECG parameters do not fully predict class 1 antiarrhythmic effect in Brugada patient: Drug-induced ECG changes in Brugada patients

Background: Drug challenge is useful to identify patients with Brugada syndrome (BS) without spontaneous ECG type 1 pattern. Effect of class I antiarrhythmic challenge is difficult to anticipate and potentially associated with complications.

Objective: Assess the response to class I antiarrhythmic challenge.

Methods: We included patients from the French multicenter MUTAVIT registry with a drug induced BS. Using digitized ECG, we automatically quantified 12-lead ECG parameters on lead V1-V3.

Results: Among 157 patients (72 % males, mean age 43 ± 13 years), baseline ECG did not show a type 2 or 3 BS pattern in 58 %. Drug infusion induced a QRS prolongation from 96 ± 20 to 117 ± 25 ms and an increase of ST amplitude from 107 ± 82 to 345 ± 231 µV (lead V2).

Amplitude of drug-challenge effect was associated with homogeneous response across groups (with and without baseline BS pattern). Baseline ST elevation correlated with a pronounced response to the induction

test (on V1: $r = 0.697$ (0.568; 0.792), $p < 0.001$, $R2 = 0.486$). Conversely, on-drug QRS duration was poorly correlated with baseline QRS duration (on V2: $r = 0.215$ (0.0527; 0.366), $p < 0.05$, $R2 = 0.046$). SCN5A variant carriers had longer QRS duration at baseline but not during drug challenge. Male patients had prolonged baseline QRS and baseline and post-induction ST amplitude.

Conclusion: Amplitude of sodium blockade effect on ST elevation was correlated with baseline ST amplitude but dugs effect on QRS duration was only slightly correlated with baseline QRS duration. Presence of (likely) pathogenic SCN5A variant was associated with different baseline ECG characteristics and response to sodium channel blockade.

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Products News

- Work continues on ACG v. 2.1.0 with the addition of MERGE and SPLIT for analysis, plus the ISHNE export
- CalECG 4.3.0 released. Changes: a BF, some changes to the API, command-line use, licensing, and plugin and library management methods.
- ECG Anonymization Service:
  AMPS has refined its processes to deliver an increasingly efficient ECG anonymization service. If you have ECGs containing sensitive data subject to privacy regulations, our team can ensure full anonymization. Simply contact us, and AMPS will quickly customize the solution to meet your specific formats and data requirements.

AMPS People

The AMPS team celebrating 25 years of innovation and teamwork with an unforgettable trip to the stunning Dolomites. Here's to the journey — past, present, and future!