Comments on "QT interval prolongation in Takotsubo syndrome: a frightening feature with no major prognostic impact"

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Dear Editor,

Pinho *et al*. reported on the acquired corrected QT (QTc)-interval prolongation in a retrospective analysis of 113 patients (aged 67.6±11.7, 94.7% female), of whom 43 (38%) had a prolonged QTc (QTc≥460 ms) and 70 (62%) had a normal QTc (460 ms) [1]. Notably, QTc categorization was based on any electrocardiogram (ECG) at admission or during hospitalization, with the highest QTc value. The authors did not find any differences between the two subgroups in reference to baseline characteristics [including relevant (*i.e*., which could have caused prolongation of the QTc) chronically administered medications], save for a history of atrial fibrillation and syncope, which were more frequent in the patients with prolonged QTc. In-hospital complications [including ventricular arrhythmias (VA) and complete atrioventricular block (CHB)] were not different between patients with prolonged and normal QTc. The only in-hospital mortality observed was in a patient with a prolonged QTc. Also, at a mean follow-up of 4.8±3.8 years, all-cause mortality and the composite endpoint of major adverse cardiac and cerebrovascular events (MACCE) were not different between the subgroups. The authors concluded that QTc prolongation has no major prognostic in-hospital and long-term implications in Takotsubo syndrome (TTS) patients.

QTc prolongation is feared in the setting of TTS; however, there has been controversy about whether QTc is associated with VA and other MACCE during hospitalization and at long-term follow-up. There is variation in the literature regarding the source of QTc measurements, with some authors employing the admission ECG, others using multiple ECGs with the ECG with the longest QTc taken as the study-relevant measurement, and others using the longest QTc measured during the first 48 or 72 hours after admission. Some have employed automated QTc measurements, while others have employed manual measurements, without or after magnification of the ECG tracings; there is great variation in ECG leads used, with some employing the ECG lead with the longest QTc, or the mean of all ECG leads employed, or specifically using single or multiple precordial ECG leads. Some have observed prolongation of the QTc late during the inpatient clinical course, and many have emphasized recording of many ECGs and ECG monitoring of the QTc throughout hospitalization for TTS patients. Finally, some have reported prolonged prolongation of the QTc beyond several months after the index TTS episode. QTc prolongation has been associated with regional myocardial edema detected by cardiac magnetic resonance imaging [2,3]. Some authors have made a distinction between TTS-related QTc prolongation and the need to evaluate whether some of the patients have chronic QTc prolongation before the inception of TTS due to drug-QTc-prolonging effects or due to congenital long QT syndromes. As of late, there is an interest in other repolarization metrics being explored in patients with TTS, with interest in the T-peak to T-end measurements, with some authors reporting that this metric outperforms the QTc as a predictor of VA and other in-hospital and follow-up MACCE.

I have some remarks and inquiries for the authors' consideration: i) whether prolonged QTc has an in-hospital and/or long-term MACCE prognostic role would be eventually decided upon by analyses from very large databases and/or TTS patient registries; ii) such controlled analyses should include QTc-prolonging drugs that the patients, who had been admitted with TTS, had been treated with prior to the inception of their illness; iii) it is conceivable that other variables, in conjunction with QTc prolongation may be responsible for the emergence of VA and CHB in patients with

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TTS; iv) it would be contributory if the authors supplied the information about the number of recorded ECGs in their patients, and the recording time from the hospital admission (in days) of the ECGs that they used for the study measurements; v) it would be of interest if the authors supplied the QTc measurements post-hospitalization and during follow-up, even from a few of their patients, to ascertain the long-term course of QTc following hospital discharge of their TTS patients.

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