CJC Pediatric and Congenital Heart Disease 3 (2024) 22–23

Editorial

Prolonged QTc in the Setting of Eating Disorders

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The QT interval is an electrocardiographic representation of ventricular depolarization and repolarization. A prolonged QT interval represents a prolonged action potential of ventricular myocytes and is mediated by an increase in inward current of sodium or calcium channels or a decrease in outward current through potassium channels. Initial assessments aim to differentiate congenital vs acquired long QT syndrome as subsequent investigation and management will differ based on the etiology of the QT prolongation. Acquired long QT syndrome is characterized by prolongation of the corrected QT interval (QTc), which is typically due to electrolyte imbalances, pharmaceutical influences, and certain medical conditions.[1] There may also be genetic predispositions that can influence the development of acquired long QT syndrome by providing a substrate for vulnerability.[1] Acquired long QT syndrome is associated with an established risk of syncope, sudden cardiac arrest, and sudden cardiac death due to a potentially lethal arrhythmia called torsades de pointes that can degenerate into ventricular fibrillation. The finding of a prolonged QTc interval in any clinical setting should trigger further evaluation and a search for underlying causes.

A prolonged QTc interval has been proposed as a risk for cardiovascular death in patients with an eating disorder including anorexia nervosa and bulimia nervosa. It is an important question whether patients with eating disorders are more prone to develop a prolonged QTc or whether their risk is comparable to the general population. Studies have shown conflicting evidence of rate of cardiac events and its relation to baseline QTc in patients with eating disorders.[2] A more recent and large population cohort study in 2020 by Krantz et al.[3] assessed QTc prolongation in 1026 adults with anorexia nervosa and bulimia nervosa. The incidence of prolonged QTc >450 ms was found in 12% of subjects, and only 1.2% had markedly prolonged QTc >500 ms.[3] They concluded that QTc prolongation was not intrinsic to eating disorders as marked prolongation occurred only in patients with extrinsic factors, particularly IKr-inhibiting drugs and electrolyte disturbances.[3] Studies have tried to elucidate the etiology of a prolonged QTc interval and QT dispersion in patients with eating disorders, but data have been inconsistent. Risk assessment for cardiac events in patients with eating disorders remains unclear because QT prolongation does not correlate with markers of disease severity such as body mass index, left ventricular mass, left ventricular mass index, or resting energy expenditure.[4] In the adult population, while long-term follow-up in patients with anorexia nervosa demonstrated a higher risk of cardiac events and all-cause mortality compared with healthy controls, it did not correlate with the baseline QTc interval.[2]

The Relationship of Eating Disorders in Children and QT Intervals

Benayon et al.[5] conducted a retrospective analysis of 264 patients aged 7-17 years who were diagnosed with an eating disorder. Relevant clinical and laboratory data and electrocardiograms (ECGs) from their initial visit were collected. A QT interval corrected for heart rate using the Bazett formula was calculated. They defined a QTc of >460 ms as prolonged, 440-460 ms as borderline prolonged, and <440 ms as normal. ECG parameters, electrolyte values, and use of QTc-prolonging antidepressants and/or antipsychotics were analysed to determine whether extrinsic factors influenced QTc interval prolongation rather than factors inherent to the patient's eating disorder. The electrolyte values were taken at the time closest to the performance of the ECG. Their cohort had a mean age of 14 ± 2 years and a mean heart rate of 66 ± 16 bpm, and 90.5% were female. The mean QTc was 411 ± 26 ms, with a range of 347-483 ms.[5]

The authors found that the prevalence of a QTc >440 ms in their study population of children with eating disorders without electrolyte abnormalities or psychotropic medication use (10.1%) was similar to that of a large adult cohort study (8.7%) with a sample size of 36,301.[6] There was no association between QTc prolongation and electrolyte abnormalities in the paediatric cohort reported by Benayon et al.[5] Importantly, the use of psychotropic medications (9% of the cohort) had an association with a longer QTc interval, with 34.8 vs 12% and 21.7 vs 2.5% having a QTc >440 and >460 ms, respectively. Logistic regression modelling demonstrated that the use of psychotropic medications was associated with borderline prolonged and prolonged QTc intervals in the

Received for publication November 19, 2023. Accepted November 24, 2023.

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https://doi.org/10.1016/j.cjcpc.2023.11.003

cohort. These results suggest that eating disorders in children alone may not lead to QTc interval prolongation; however, the concurrent use of QTc-prolonging medications may be an important factor in the finding of prolonged QTc intervals in children with eating disorders.

Strengths and Limitations of the Current Study

The study by Benayon et al.[5] is the largest known retrospective analyses of QTc interval prolongation in children with eating disorders. The study attempted to isolate the influence of an eating disorder from the extrinsic factors that are commonly known to prolong QTc intervals to determine the relative influence of each on QTc prolongation in children with eating disorders.

This study has limitations that are worth further discussion, which relate primarily to the retrospective design and the presumably small sample sizes if the authors were to attempt to compare additional subgroups. The population was generalized as having eating disorders instead of separately analysing disease processes (anorexia nervosa and bulimia nervosa) that may influence QTc intervals differently.[3] The effect of puberty was not taken into account, but it is known that sex hormones act as modulators of ventricular repolarization through regulation of ionic currents. Testosterone has a QTc shortening effect with the QTc interval in males shortening during puberty while remaining unchanged in females during puberty.[7,8] The correct timing of QT interval measurement is crucial in assessing the influence with different factors such as electrolyte imbalances, acute/chronic intake of psychotropic drugs, or significant clinical changes in eating disorder severity. Of note, there were missing data regarding electrolytes in 12.5% of the cohort with varied intervals between electrolyte measurement and ECG correlation. Data regarding psychotropic drug intake, dosage, or documentation of QT interval changes before and after initiation of psychotropic drugs were unavailable. It is common to have sinus bradycardia in patients with eating disorders. The Bazett formula, while considered by many as the standard, leads to overcorrection of QT intervals in bradycardia. Other formulae such as Hodges and Fridericia's formula can be used and may be more accurate in this setting.[9,10] Lastly, the presence of cardiovascular events was not documented or associated with prolonged QTc in this population, an area that can be explored in future studies.

Overall, the study by Benayon et al.[5] supports the theory that external factors, particularly the use of QT-prolonging psychotropic medications, are the primary cause of prolonged QTc in the paediatric eating disorder population. This study emphasizes the need for QTc monitoring of patients taking psychotropic drugs in the setting of eating disorders. Whether patients with eating disorders are more susceptible to QT-prolonging effects of medications is an area that requires further study.

Conclusions

Mortality associated with eating disorders is largely cardiovascular in origin, and prolonged QTc has been one of the significant cardiac findings.[11] The retrospective analysis by Benayon et al.[5] emphasizes that a prolonged QTc interval is most likely related to acquired causes and is not an inherent feature of eating disorders. In patients with eating disorders, attention should be given to reversible factors including electrolyte abnormalities and use of QT prolonging medications. The results of the study by Benayon et al.[5] highlight the importance of QTc surveillance and appropriate management of potential causes of acquired QTc in children with eating disorders. Lastly, it is important to consider that bradycardia, a common finding in eating disorders, can confound the QTc calculation when using the Bazett formula, and alternative formulae may be considered in this setting to avoid overcorrection of the QTc.

Ethics Statement

The information reported in this paper adhered to relevant ethics guidelines.

Funding Sources

No funding was received for this study.

Disclosures

The author has no conflicts of interest to disclose.

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