Göteborg, 2023

Repolarization studies in the long QT syndrome

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Hjärtats Aula, Sahlgrenska Universitetssjukhuset, Vita Stråket 12, Göteborg den 17 november 2023, klockan 9.00

av Pia Dahlberg

Fakultetsopponent:
Professor Jacob Tfelt-Hansen
Copenhagen University Hospital, Copenhagen, Denmark

Avhandlingen baseras på följande delarbeten

I. Dahlberg P, Diamant U-B, Gilljam T, Rydberg A, Bergfeldt L. QT correction using Bazett´s formula remains preferable in long QT syndrome type 1 and 2. *Ann Noninvasive Electrocardiol. 2021 Jan;26(1):e12804*.

II. Dahlberg P*, Axelsson KJ*, Jensen SM, Lundahl G, Vahedi F, Gransberg L, Bergfeldt L. Accelerated QT adaptation following atropine-induced heart rate increase in LQT1 patients versus healthy controls: A sign of disturbed hysteresis. *Physiol Rep. 2022 Nov;10(21):e15487.*

III. Dahlberg P, Axelsson KJ, Rydberg A, Lundahl G, Gransberg L, Bergfeldt L. Spatio-temporal repolarization dispersion before and after exercise in patients with long QT syndrome type 1 vs controls. *Accepted. AJP - Heart and Circulatory Physiology. 2023*

IV. Dahlberg P, Axelsson KJ, Jensen SM, Lundahl G, Gransberg L, Bergfeldt L. Greater overshoot in the adaptation of repolarization dispersion following atropine-induced heart rate increase in LQT1 patients and healthy controls**.** *In manuscript*

**Both authors contributed equally*

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR MEDICIN

GÖTEBORGS UNIVERSITET

Göteborg, 2023

Repolarization studies in the long QT syndrome

Pia Dahlberg

Department of Molecular and Clinical Medicine, Institute of Medicine
Sahlgrenska Academy, University of Gothenburg, Sweden

Abstract

Background: Sudden cardiac death in the young is predominantly caused by inherited cardiac conditions. Long QT syndrome (LQTS) is one of the most common of these disorders. Since risk stratification relies largely upon the heart rate (HR) corrected QT interval (QTc), it is crucial to identify an appropriate method for QT correction. Furthermore, cardiac events in LQTS type 1 (LQT1) occur commonly at HR increase. Repolarization duration and dispersion was therefore studied at HR increase.

Aims: The objectives were to describe the electrocardiographic and vectorcardiographic phenotype in LQTS patients and to compare repolarization response including dispersion to HR increase between LQT1 and healthy controls.

Methods: Paper I compared four different methods for HR correction of the QT interval in a group of LQTS patients using linear regression. In a subgroup, comparisons were made before and after the initiation of betablockers. In paper II and IV we used an intravenous bolus injection of atropine to increase HR in LQT1 patients and healthy controls. Vectorcardiography (VCG) was continuously recorded and VCG parameters were compared. Paper III compared the VCG reaction to increased HR induced by an exercise stress test in LQT1 patients and healthy controls.

Results: Bazett´s method yielded the only correction resulting in a QTc without relation to HR, irrespective of initiation of betablockers. Although a similar HR response to atropine, the QT adaptation was faster in LQT1 than in healthy controls. As a response to exercise, the QTcB and its components, the HR corrected QTpeak and Tpeak-end intervals, but not global dispersion parameters, separated LQT1 patients from controls.

Following a rapid HR increase induced by atropine, the majority in both groups showed a biphasic response for global measures of VR dispersion, including an overshoot; in LQT1 the overshoot was more pronounced.

Conclusions: Although questioned**,** Bazett´s method remains preferable for QT correction in LQT1 and 2. Faster QT adaptation following a rapid HR increase in LQT1 patients indicates a disturbed QT hysteresis. Timing of repolarization duration but not global dispersion parameters distinguished LQT1 patients from controls after exercise. The biphasic response in VR dispersion was exaggerated in LQT1 patients which could play a role in arrhythmogenesis, but further studies are warranted.

Keywords: long QT syndrome, vectorcardiography, repolarization, hysteresis, QT adaptation, ventricular repolarization

ISBN: 978-91-8069-449-0 (PRINT) http://hdl.handle.net/2077/77763
ISBN: 978-91-8069-450-6 (PDF)