

Adaptation of ventricular repolarization to heart rate change in humans

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i hörsal Arvid Carlsson, Academicum, Medicinaregatan 3, Göteborg den 29 oktober 2021, klockan 9.00 av

Karl-Jonas Axelsson

Fakultetsopponent:

Professor Henrik Engblom

Karolinska Institutet, Stockholm

Avhandlingen baseras på följande delarbeten

- I. Axelsson KJ, Brännlund A, Gransberg L, Lundahl G, Vahedi F, Bergfeldt L. Adaptation of ventricular repolarization duration and dispersion during changes in heart rate induced by atrial stimulation. *Ann Noninvasive Electrocardiol.* 2020;25(3):e12713.
- II. Axelsson KJ, Gransberg L, Lundahl G, Vahedi F, Bergfeldt L. Adaptation of ventricular repolarization time following abrupt changes in heart rate: comparisons and reproducibility of repeated atrial and ventricular pacing. *Am J Physiol Heart Circ Physiol.* 2021;320(1):H381-H392.
- III. Axelsson KJ, Gransberg L, Lundahl G, Bergfeldt L. Adaptation of ventricular repolarization dispersion during heart rate increase in humans: A roller coaster process. *J Electrocardiol.* 2021;68:90-100.
- IV. Dahlberg P*, Axelsson KJ*, Jensen SM, Lundahl G, Vahedi F, Gransberg L, Bergfeldt L. QT adaptation hysteresis during atropine induced heart rate increase: comparison between patients with long QT syndrome type 1 and healthy subjects. In manuscript.
*Both authors contributed equally.

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Karl-Jonas Axelsson

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

Abstract

Background: Life-threatening cardiac rhythm disturbances and sudden death are common manifestations of heart disease. Disturbances in electrical recovery (ventricular repolarization; VR) are important mechanisms behind ventricular arrhythmias, which often occur in relation to changes in heart rate (HR). It is therefore of both theoretical and clinical interest to study the adaptation of VR to changes in HR.

Aims: To investigate the adaptation of VR duration (QT and QT_{peak}) and VR heterogeneity (aka dispersion; T area, T amplitude and ventricular gradient) in response to changes in HR in subjects without structural heart disease and in patients with long QT syndrome type 1 (LQT1).

Methods: VR adaptation to HR changes was investigated in three clinical studies (four papers). In Paper I, patients scheduled for ablation of supraventricular tachycardia were incrementally paced in the atrium to an HR of 120–140 bpm, and the pacing was halted after 5 min. In Papers II and III, the HR increase was induced by sudden atrial or ventricular pacing, repeated at intervals comprising at least one month and was performed with the use of permanent pacemakers in patients with sick sinus disease. In Paper IV, an intravenous bolus of atropine was used to increase HR in patients with LQT1 and in healthy subjects. In all studies, vectorcardiography was used to record the electrical activity of the heart.

Results: Papers I and II: The adaptation of VR duration to a sustained HR change was mono-exponential, took 1.5–2.5 min and was longer following decreasing vs increasing HR. The intra-individual coefficient of variation for QT adaptation to increasing HR was ≤10%. Paper III: There were significant differences in the adaptation of global measures of electrical heterogeneity (dispersion) between HR increase induced by atrial vs ventricular pacing. For both pacing modes, the adaptation occurred in 2–3 rapidly changing phases. QT adaptation was faster in LQT1 patients vs healthy controls.

Conclusions: The adaptation of VR duration is gradual, takes longer in response to decreasing vs increasing HR and is intra-individually a stable process over time. The bi- or tri-phasic VR dispersion response possibly identifies a time period of electrical vulnerability. The atropine ‘stress test’ for VR adaptation is safe and feasible in LQT1 and could potentially be used as a future tool for risk assessment and prognosis.

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