

ANALYSIS OF QT DYNAMICITY BEHAVIOUR IN RELATIONSHIP TO THE RISK OF SUDDEN CARDIAC DEATH. A PILOT STUDY

ŠIŠÁKOVÁ M.¹, TOMAN O.¹, FLORIÁNOVÁ A.¹, VÍT P.², GAILLYOVÁ R.³, KADLECOVÁ J.³,
CHROUST K.⁴, PAPOUŠEK I.⁴, ŠPINAR J.¹

¹Department of Internal Cardiology Medicine, Faculty Hospital in Brno, Faculty of Medicine,
Masaryk University, Brno

²Secondnd Department of Pediatrics, Faculty Hospital in Brno, Faculty of Medicine,
Masaryk University, Brno

³Department of Medical Genetics, Faculty Hospital in Brno, Faculty of Medicine, Masaryk
University, Brno

⁴Department of Genetics and Molecular Biology, Faculty of Science, Masaryk University in Brno

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Abstract

Processes of myocardial repolarisation are reflected in the QT interval of surface ECG and are influenced by heart rate, autonomous nervous system, metabolic situation and pharmacotherapy. Its prolongation is a marker of an increased risk of malignant ventricular arrhythmias and sudden cardiac death. A new method for QT interval behaviour assessment is the QT dynamicity expressed by the linear regression curve of the QT interval and RR interval relationship. The aim of this pilot study is to compare QT dynamicity in patients with ischemic heart disease and in the Long QT Syndrome (LQTS) patients, where abnormal myocardial repolarisation is strictly defined.

In this pilot study 29 individuals were investigated. In 7 of them (3 males, 4 females) a KCNQ1 gene mutation was found; 9 patients (8 males, 1 female) had a diagnosis of myocardial infarction (MI) with the left ventricle ejection fraction lower than $\leq 35\%$. The control group consisted of 13 healthy individuals (7 males, 6 females). The QT dynamicity was automatically analysed from 24-hour ECG recordings using "QT Guard" software. The differences of slopes of QT/RR curves were statistically compared in the 3 groups.

The slopes of QT/RR curves were significantly different in the LQTS group compared to the healthy individuals ($p < 0.001$). No statistical difference was found between the MI group and healthy individuals.

The QT dynamicity reliably reveals individuals with severe impairment of myocardial repolarisation - patients with Long QT Syndrome. The contribution of this method for sudden cardiac death risk stratification remains to be established in a larger group of patients with coronary artery disease and congestive heart failure.

Key words

Long QT syndrome, QT/RR slope, Repolarisation

INTRODUCTION

Recently, intensive research has focused on the repolarisation phase of the electrocardiogram. The pathophysiology of repolarisation processes is based on multiple changes of the cardiac ion channel function. This could lead to a prolongation of action potential (AP) duration or differences in AP duration in different layers of myocardium. The repolarisation phase is influenced by heart rate, autonomous nervous system, metabolic situation and pharmacotherapy. Its prolongation is a marker of an increased risk of malignant ventricular arrhythmias and sudden cardiac death (SCD). In surface ECG the QT interval is a reflection of repolarisation.

Myocardial repolarisation is assessed as the leading symptom of the congenital long QT syndrome (LQTS), which is a clearly defined monogenic disorder of repolarisation (1). The assessment of repolarisation also becomes a part of SCD risk stratification in patients with populationally important cardiovascular diseases. QT interval changes are also a marker of proarrhythmia risk related to treatment with many, not only cardiovascular, drugs.

Most often the so-called static correction models are used for QT interval correction (according to Bazett, Fridericia, Framingham study, etc.) (2). However, their important limitations have been repeatedly discussed (3). These discussions have been an inspiration for seeking new methods for a more precise assessment of the repolarisation phase using the so-called dynamic parameters reflecting immediate changes of the QT interval in relation to the heart rate. In this study we use the QT dynamicity which is expressed by a linear regression line of the QT interval and the RR interval relationship, so-called "QT/RR slope" (4, 5).

MATERIALS AND METHODS

In this pilot study 29 individuals were investigated. In 7 of them (3 males, 4 females) a KCNQ1 gene mutation was found; 9 patients (8 males, 1 female) had a diagnosis of myocardial infarction (MI) with the left ventricle ejection fraction lower than $\leq 35\%$. The control group consisted of 13 healthy individuals (7 males, 6 females). The average age of LQTS patients was 24.6 ± 18.6 years, of healthy individuals 29.5 ± 7.1 years, and in the MI group 63.3 ± 11.0 years. All the MI patients and 5 of 7 patients in the LQTS group were treated with a beta-blocker; healthy individuals received no pharmacotherapy. None of the investigated individuals was treated with drugs with a known influence on myocardial repolarisation. The QT dynamicity was automatically analysed from 24-hour ECG recordings using QT Guard software of MARS Unity Workstation, GE Medical Information Technologies (6). The linear regression slope QT/RR is mathematically defined as $QT = a \cdot RR + b$, where "a" expresses the slope of the curve, "RR" is the distance between 2 R waves on ECG, and "b" expresses position of the curve in relationship to the "y" axis (Fig. 1). The data were statistically analysed using Student t-test; the parameter compared was "a".

RESULTS

The average values of the parameter "a" expressing the slope of QT/RR regression curves in the investigated groups were the following: 0.316 ± 0.074 in LQTS patients, 0.202 ± 0.060 in MI group, and 0.191 ± 0.030 in healthy individuals. These

values were significantly different in the LQTS group compared to healthy individuals ($p < 0.001$); this means that the QT/RR slopes were steeper in the LQTS group. No statistical difference was found between the MI group and healthy individuals.

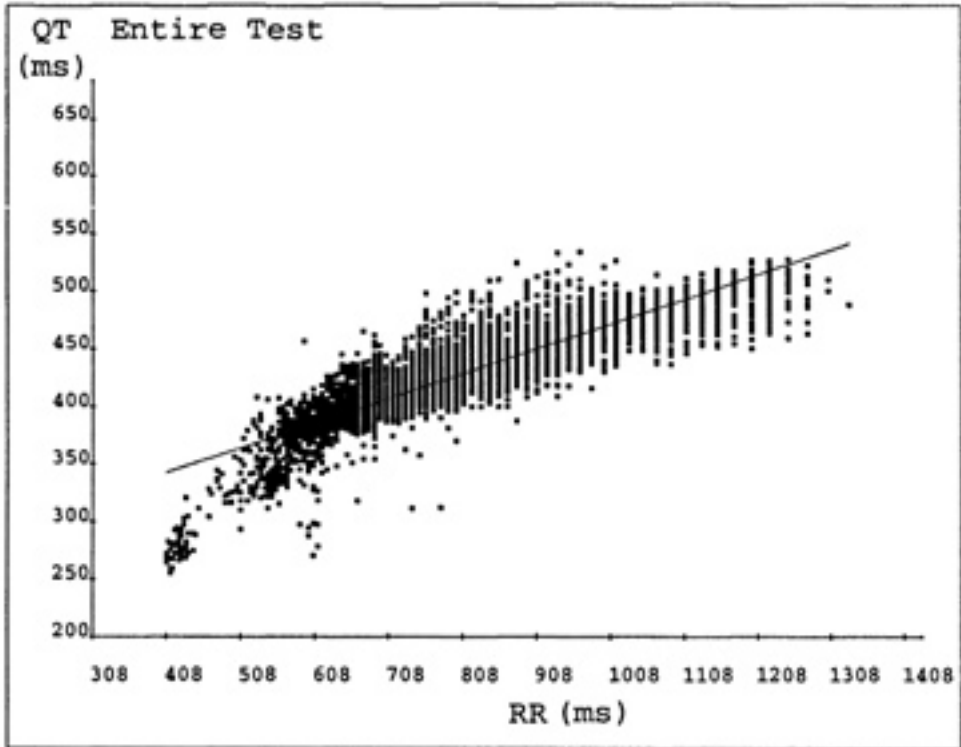


Fig. 1

An example of linear regression curve. Heart rate expressed by R-R intervals in milliseconds is shown on the horizontal axis and QT interval duration in milliseconds on the vertical axis. The group of points represent QT intervals plotted against RR intervals. Through them the linear regression line is drawn.

DISCUSSION

In our pilot study the QT dynamicity analysis was able to differentiate individuals with severe impairment of myocardial repolarisation (i. e. LQTS individuals). In this small group no statistically significant difference was found between the high risk coronary artery disease patients (post-MI with severe left ventricle dysfunction and $EF \leq 35\%$) compared with healthy individuals. Nevertheless, in the MI group the QT/RR slope was markedly different in one patient in whom malignant

ventricular arrhythmias were recorded. Thus, the QT dynamicity evaluation could be contributive in risk stratification of post-MI patients. The hypothesis will be evaluated in a larger group of individuals.

The importance of the evaluation of QT dynamicity is in the possibility of detecting some differences of the QT/RR slopes in the individuals whose correlated QT intervals are identical (the QT/RR slopes at this point can cross themselves). Recently published population based studies showed a familial cumulation of SCD even in normal wide population. Being aware of external risk factors shared in a particular family it is obvious that there must exist genetically determined variations of physiological processes that increase the risk of SCD. Hypothetically, in these families a different QT/RR behaviour can be detectable which could be used for risk stratification (7). The behaviour of QT dynamicity has until now been analysed only in smaller groups of patients. The physiological diurnal differences were discovered: the QT/RR slope is steeper during the day (QT dynamicity is larger). The QT/RR slopes are different in men than in women; in women the slopes are steeper (8, 9, 10). This difference starts to be significant just after the adolescence; it is in agreement with the experimentally proved direct influence of the sex hormones on the expression of the potassium repolarisation currents (11). In patients with coronary artery disease it is suspected that those at the highest risk after myocardial infarction have steeper QT/RR slopes, mainly during the day, the steepest just after the awakenings (12). The physiological day/night difference can be smaller; this is probably true in patients with chronic heart failure as well (13). In patients with LQTS the QT dynamicity is larger, but these patients exhibit a slower adaptation after a sudden change of the heart rate (14). The QT/RR slope during the day can in these patients be less steep than the slope during the night. According to the evaluation of QT dynamicity we can clinically differentiate subtypes of LQTS. The influence of drugs on QT dynamicity has to date been analysed mainly in the antiarrhythmic agents; so, e.g., dofetilide (class III antiarrhythmic agent) enhances QT dynamicity, the QT/RR slope during the therapy being steeper (15). More detailed data are missing.

The QT dynamicity expressed by the linear regression curve of the QT/RR relationship is a modern way of description of myocardial repolarisation. It reliably reveals individuals with severe impairment of myocardial repolarisation with a high risk of malignant ventricular arrhythmias and SCD - patients with LQTS. The contribution of this method for SCD risk stratification will be evaluated in a larger group of patients with coronary artery disease and congestive heart failure.

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ANALÝZA CHOVÁNÍ QT DYNAMICITY VE VZTAHU K RIZIKU NÁHLÉ SRDEČNÍ SMRTI - VÝSLEDKY PILOTNÍ STUDIE

Souhrn

Repolarizační fáze EKG křivky je v poslední době intenzivně zkoumána. Proces repolarizace myokardu, kterému v povrchovém EKG odpovídá interval QT, je ovlivňován srdeční frekvencí, aktuálním stavem autonomního nervového systému, metabolickou situací i farmakoterapií. Prodloužení repolarizace je markerem zvýšeného rizika náhlé srdeční smrti. Nekončící diskuse o limitacích dosud používaných korekčních matematických modelů (nejčastěji podle Bazetta, Fridericii či Framinghamské studie) inspirovaly k hledání nových metodik pro přesnější posuzování repolarizační fáze myokardu, především dynamických parametrů odrážejících okamžitě změny QT intervalu ve vztahu k aktuální srdeční frekvenci.

Cílem naší pilotní studie bylo posouzení přínosu hodnocení dynamicity QT intervalu u jedinců s organickým onemocněním srdce ve srovnání s pacienty s Long QT syndromem – s jasně definovanou poruchou repolarizace.

Vyšetřili jsme 29 pacientů, z toho 7 s geneticky prokázaným Long QT syndromem, 9 pacientů s ICHS po myokardiálním infarktu a s dysfunkcí levé srdeční komory (EF LK \leq 35 %) a 13 zdravých jedinců. Repolarizaci myokardu jsme hodnotili z 24hodinového Holterovského záznamu s pomocí lineární regresní křivky QT/RR, tzv. QT/RR slope.

Regresní křivky QT/RR se u pacientů s Long QT syndromem výrazně odlišovaly od zdravých jedinců ($p < 0,001$). Rozdíl mezi ischemiky a zdravými jedinci nedosáhl v této pilotní studii významného rozdílu.

Prokázali jsme, že regresní křivka QT/RR jednoznačně odlišuje jedince s hrubou poruchou repolarizace. Přínos této metody pro stratifikaci rizika náhlé srdeční smrti bude dále posuzován na větším souboru nemocných s ischemickou chorobou srdeční a u pacientů se srdečním selháním.

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