THE COMPONENT OF PATHOGENESIS OF SUDDEN NOCTURNAL DEATH IN PATIENTS WITH HEART FAILURE

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Patients with chronic heart failure (CHF) constitute the bulk of the group at the highest risk of sudden death (SD). The majority of SDs occur at night. However, CHF grade and ejection fraction do not always determine the risk of SD in the outcome of the disease. The following view has been expressed based on the research on the topic and the described mechanisms underlying SD: impaired QT interval adaptation ("hyperadaptation": QT/RR slope > 0.24) to HR in patients with CHF who show maximum QT interval prolongation during the night, capable of triggering life-threatening ventricular tachyarrhythmias that trigger the mechanism of SD associated with CHF, can play some role. It is possible that identification of QT interval hyperadaptation in patients with CHF makes it possible to form the group at high risk of SD associated with HF and can become an additional indication for implantation of cardioverter-defibrillator.

Keywords: sudden death, heart failure, night, QT dynamics, Holter monitoring

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ЗВЕНО ПАТОГЕНЕЗА НОЧНОЙ ВНЕЗАПНОЙ СМЕРТИ ПРИ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТИ

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Основную часть группы с наибольшим риском внезапной смерти (ВС) составляют больные с хронической сердечной недостаточностью (ХСН). В большинстве случаев ВС происходит в ночное время. При этом степень ХСН и фракция выброса не всегда определяет риск именно ВС в исходе заболевания. Основываясь на анализе исследований по теме и описанных механизмов ВС, высказано мнение о возможной роли нарушенной адаптации («гиперадаптации»: QT/RR slope > 0,24) интервала QT к ЧСС у больных с ХСН, с максимальным удлинением интервала QT именно в ночное время, что может приводить к запуску жизнеугрожающих желудочковых тахиаритмий, запускающих механизм ВС при ХСН. Возможно, что выявление «гиперадаптации» QT у больных с ХСН может формировать группу повышенного риска по ВС при СН и быть дополнительным показанием в имплантации кардиовертера дефибриллятора.

Ключевые слова: внезапная смерть, сердечная недостаточность, ночь, QT-динамика, холтеровское мониторирование

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Sudden death (SD) is one of the main challenges for modern cardiology. People with chronic heart failure (CHF) associated with coronary artery disease (CAD) are at the highest risk of SD. Up to 20% of patients in this group die suddenly [1]. Analysis of the PRAISE (Prospective Randomized Amlodipine Survival Trial) study results has shown that patients with ischemic heart failure significantly more often (44%) died during sleep between 4 and 8 hr am compared to other four-hour blocks of the day [2].

QT interval prolongation is a well-known independent risk factor of SD. Studying the circadian variation in QT dispersion showed that patients with CHF had a more prolonged QT interval compared to both healthy people and patients with CAD and no CHF [3]. However, the study revealed no significant differences in the values of QT dispersion between nighttime and daytime. The method for assessment of the QT interval/heart rate (or QT interval/RR interval) relationship based on the Holter monitoring data known as QT dynamics has been relatively recently widely implemented in clinical practice [4]. When using the method, it is assumed that the main indicator of QT dynamics, the linear regression coefficient (slope) between QT and RR intervals, defines the degree of QT variability related to changes in heart rate (Fig. 1). In the adopted interpretation of QT dynamics, the steep and flat QT/RR slopes are distinguished with the low or high values of the linear regression slope [4].

The criteria for physiologically normal QT dynamics (QT/RR slope = 0.13–0.24) were previously identified, the approach to clinical interpretation of QT dynamics was proposed that defined the concepts of the QT interval "hyperadaptation" and "hypoadaptation" [5–7]. QT interval hyperadaptation is determined when QT/RR slope > 0.24 and is characterized by excessive QT prolongation associated with bradycardia and QT shortening associated with tachycardia. QT interval hypoadaptation (QT/RR slope < 0.13) is characterized by insufficient QT interval adjustment to heart rate with any heart rate changes. These criteria for QT dynamics interpretation were included in the National Russian Guidelines on Application of the Methods of Holter Monitoring in Clinical Practice [8]. This approach was pioneered in healthy neonates with age-related sinus tachycardia [5]. However, when assessing the proposed interpretation of QT dynamics, M. Malik, one of the world's leading experts on electrocardiology, noted its prospects: "Their concept or hypo- and hyperadaptation of QT interval to heart rate might be worthy of further studies in different populations…." [9]. We also found in promising to use this approach in assessing possible mechanisms underlying SD in patients with CHF. We did not assess groups of patients with CHF, although a few isolated cases of nocturnal SD in patients with CHF were available (Fig. 2 and 3). We have found no Russian reports of using the QT dynamics method in

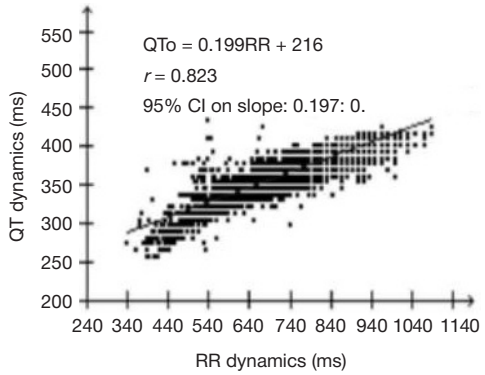

Fig. 1. Assessment of the 24-hr QT dynamics in healthy male aged 22 using the modern Holter monitoring system. QT/RR slope (QTo) = 0.199

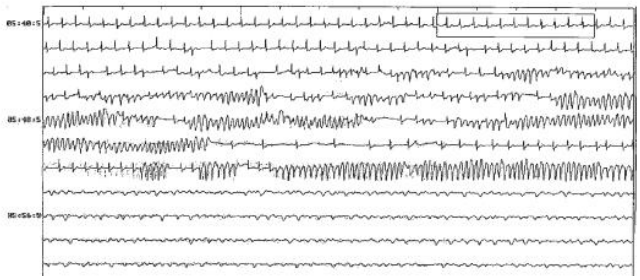

Fig. 2. Ventricular tachyarrhythmia that occurs at 05:44 am, ventricular fibrillation and sudden death that occur at 05:56 am in female patient aged 77 with ischemic cardiomyopathy and ejection fraction of 38%. No option for assessment of QT dynamics was installed in the system

patients with CHF, but, in our opinion, some global studies have provided interesting results. Thus, when predicting the risk of SD in patients with ischemic cardiomyopathy during the European Myocardial Infarct Amiodarone Trial (EMIAT), it was shown that patients with CHF, who died suddenly, had the significantly higher QT/RR slope values compared to those who survived (0.26 vs. 0.16, respectively) [10]. According to other researchers, QT/RR slope exceeding 0.28 was a strong independent predictor of SD in patients with CHF (relative risk 3.47; 95% confidence interval 1.43–8.40; $p = 0.006$) [11]. Both studies showed that QT hyperadaptation to heart rate with disproportionate QT prolongation associated with bradycardia during night-time was typical for patients with CHF who died suddenly.

The records of implantable cardioverter-defibrillators obtained from patients with CHF showed that the decrease in ejection fraction below 30% resulted in the higher incidence of ventricular tachycardia during the second half of the night compared to the first half [12]. This period of sleep is characterized by the daily minimum heart rate [13] and therefore by maximum QT interval prolongation in case of QT hyperadaptation. Higher abundance of REM sleep is typical for the second half of the night [13]. Ventricular extrasystoles are more often registered in patients with CHF during the REM sleep phase (163.0 vs. 118.4) [14], despite the fact that this phase accounts for only 20% of total sleep. It could be this combination of factors (prolonged QT interval and increased arrhythmogenic electrical instability of myocardium) that makes this period the most vulnerable to fatal arrhythmias in patients with CHF.

As explained in the opening lecture of the ISHNE Sudden Cardiac Death World Wide Internet Symposium, "… despite the fact that congenital long-QT syndrome is rather rare compared to other cardiovascular disorders, we could understand the whole problem of sudden cardiac death by studying the underlying mechanisms of arrhythmias". In support of this thesis, it can be noted that QT interval hyperadaptation is typical for patients with the molecular genetic type 3 long-QT syndrome (Fig. 4), who most often die during sleep [15]. This may indicate the common mechanisms underlying pathogenesis of SD in patients with the same main cause of the disease.

CONCLUSION

Based on the above, we have formulated the following hypothesis:

– QT interval hyperadaptation in patients with CHF associated with disproportionate prolongation of the QT interval and higher incidence of ventricular tachyarrhythmias in the night-time makes this group more susceptible to life-threatening nocturnal arrhythmias and SD.

– Identification of QT interval hyperadaptation in patients with CHF makes it possible to form the group at high risk of SD associated with HF and become an additional indication for implantation of cardioverter-defibrillator.

Confirmation or refutation of this hypothesis requires targeted research, which obviously pose no practical differences, since there is sufficient number of Holter recordings obtained from patients with CHF in numerous studies.

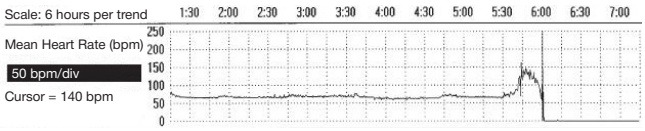

Fig. 3. Nocturnal heart rate trend with sudden death occurring at 05:56 am (see Fig. 1) during the period of the increased heart rate variability that corresponds to REM sleep phase according to conventional somnography [8, 13] in the 77-year-old female patient with ischemic cardiomyopathy

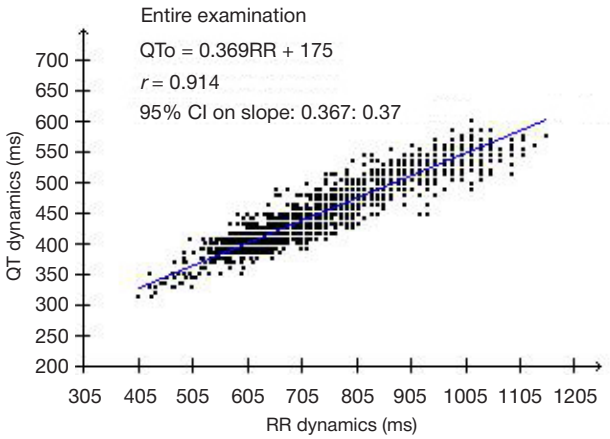

Fig. 4. QT hyperadaptation in male patient with type 3 long QT syndrome. QT/RR slope (QTo) = 0.369 (normal range: 0.13–0.24)

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