

# Electrophysiological predictors of sudden cardiac death on physical exercise test in young athletes

L A Balykova<sup>1</sup>, A A Kotlyarov<sup>2</sup>, S A Ivyanskiy<sup>1</sup>, A A Shirokova<sup>1</sup>, K A Miheeva<sup>1</sup>,  
L M Makarov<sup>3</sup>

<sup>1</sup> N.P.Ogarev Mordovia State University, Saransk, Russia

<sup>2</sup> Obninsk Institute for Nuclear Power Engineering Moscow, Russia

<sup>3</sup> Center for Syncope and Cardiac Arrhythmia in Children and Adolescents of Federal Medico-biological Agency Clinical Hospital Moscow, Russia.

E-mail: [larisabakykova@yandex.ru](mailto:larisabakykova@yandex.ru)

**Abstract.** The problem of sudden death of young athletes continues to be actual. Among its reasons, primary electric myocardium diseases along with organic heart troubles (cardiomyopathies, cordites, anomalies of coronary arteries) take an important place. The most frequent variant of channelopathies long QT syndrome (LQTS). Both inherited and acquired LQTS may be the reason of sudden cardiac death during physical activity and have to be revealed prior to sports admission. LQTS diagnostics in young athletes become problematic due to secondary exercise-related QT prolongation. Physical load test may reveal myocardium electric instability and enhance LQTS diagnostics accuracy without genetic testing. The aim was to study electrophysiological parameters of myocardium repolarization and reveal the signs of electrical instability as predictors of the life-threatening arrhythmias in young athletes during physical exercise test. In conclusion, electrophysiological myocardium parameters during physical exercise test noted to be markers of electrical myocardial instability and in combination with the other Schwartz criteria, was evidenced the inherited or acquired LQTS. QTc prolongation in athletes at the peak of exercise as well as in early recovery period were noted to be additional predictor life-threatening arrhythmias and sudden cardiac death in young athletes

## 1. Introduction

Professional athletes are a special risk group for sudden cardiac death SCD [1]. Undiagnosed myocardium diseases (myocarditis, cardiomyopathies), coronary artery anomalies, channelopathies, heart defects and other considered cardiac reasons can be the causes of fatal events in sport activities [2,3]. Nevertheless quite often the cause of athletes' death remains unresolved. Therefore, thorough medical examination of children to reveal cardiovascular diseases prior to sport admission is so important. However, the volume of this examination so far is under discussion [4-5]. American preparticipation screening protocol means careful evaluation of anamnesis, family history and carrying out a physical examination of athletes, whereas European ones, which proved their efficiency for SCD prevention, recommends in addition carrying out standard 12-leads ECG [6,7].

According to the order of the Ministry of Health №314H from 01.03.2016 Russian preparticipation screening includes not only physical examination and resting ECS, but an obligatory echocardiography and exercise test [8]. However up till now accurate aims of exercise testing in young



athletes have not yet been established. Traditionally in sports medicine an exercise test was used to assess physical working capacity and to reveal latent coronary failure [9,10]. But now, there are a lot of evidences concerning stress test importance for diagnostics of inherited arrhythmias, especially long QT syndrome [11, 12]. Different variants of LQTS respond differently to stress. In some cases this helps to make an accurate diagnosis without genetic testing [12, 13].

Different variants of LQTS respond differently to stress. In some cases this helps to make an accurate diagnosis without genetic testing [12, 13].

On the other hand, some of young athletes have secondary QT prolongation (associated with athletic training and other problems), which requires in-depth examination to rule out the primary LQTS [14].

The aim of our study was to establish the norm values of electrophysiological parameters (characterized myocardium repolarization) on exercise stress and to develop simple efficient technology of noninvasive long QT diagnostics and SCD prevention in athletes.

## 2. Methods

100 young athletes 11-16 yrs old (including 56 boys) - sport school attendants and 100 untrained healthy children of a similar age and gender were enrolled in our study. All the children underwent complex examination, including exercise bicycle test by Bruise protocol with synchronic ECG recording. Intervals RR and QT were measured manually. Corrected QT interval was calculate by Bazett and Fridericia formulas [15, 16]. Dispersions of absolute and corrected QT interval as well as QT delta (variability) during test were calculated.

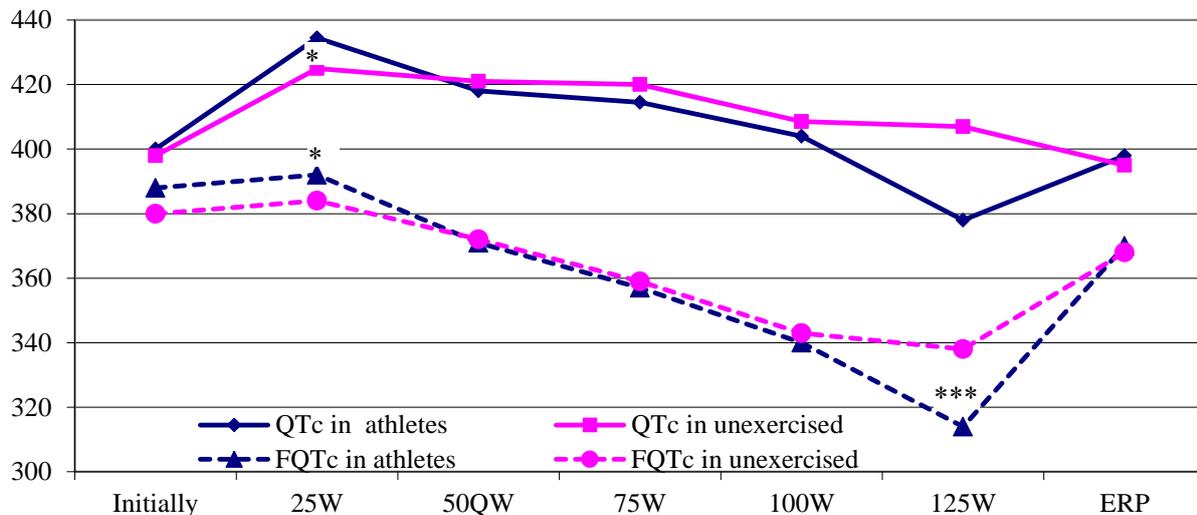
## 3. Results

Potentially dangerous changes - inverted T-waves, long QTc (exceeding 460-470 ms) and short QTc (less than 320ms) were not revealed at resting ECG in any of the athletes. Nonsignificant QTc prolongation (440-460 ms) and shortening were recorded in 2 athletes. Our data corresponds to Basavarajiah S. findings that QTc prolongation at rest occurs only in 0.4% of adult athletes and requires careful monitoring, temporary deconditioning and additional examination (including exercise test) to rule out primary LQTS, particularly if QTc exceeds 500 ms [17].

In our study mean QTc in the athletes at rest was compared to that in untrained, but absolute QT at rest and at the 1-st stage of exercise was higher in the athletes, due to bradycardia and myocardial hypertrophy.

Dynamics of myocardium repolarization in the young athletes during exercise-test was similar to that in healthy untrained adolescents (18). Gradual, smooth QT interval shortening in both groups were recorded, which correlated with gradual intensification of exercise. But at peak load QT in the athletes was considerably lower than in untrained due to hyperadaptation of repolarization processes to the heart rate grows (19). During recovery period QT duration in athletes returned to the original values more promptly than in untrained.

QTc interval in both groups increased ad maximum during low-intensity load despite the heart rate growth, but did not exceed 450-460 ms for boys and girls respectively(Figure 1). Minimal QTc values in both groups were recorded at peak load. But the athletes showed a more marked QTc shortening (less than 390 ms) compared to untrained- so-called "QTc hyperadaptation". During recovery period QTc returned to the original level in most of the athletes similar to the control group.



**Figure 1.** Dynamics of the QTc interval during exercise load test. ERP – early recovery period, \* - athletes vs untrained  $p < 0,05$ ; \*\*\* - athletes vs untrained  $p < 0,005$

As established by Doctor I.A. Gorbunova, QTc prolongation in athletes exceeding 450 ms in early recovery period suggests myocardium pathology and requires additional examination to rule out primary and secondary LQT. According to Peter J. Schwarts latest recommendations QTc duration over 480 ms during early recovery in adults is an additional diagnostic criteria of LQT syndrome (20). But Sy R.W. and coauthors (whose findings underlie this thesis) stated that LQTS can be diagnosed with high probability if QTc already exceeds 450 ms (21).

As Dong-Cheng showed QT adaptation to RR in early recovery period is impaired both in primary and secondary QT prolongation [22]. 17 children in our group had no adequate QTc short ending at peak load or early recovery period, in 3 out of them rhythm disturbances during test were recorded. Thorough medical examination showed myocarditis in 1 athlete, congenital and acquired LQTS in 2 athletes, signs of myocardial athletic remodeling, medication-induced damage or/and overtraining - in 14.

As an example, we can present a case history and exercise-test protocol of a 15-year old girl who has been in gymnastics for 9 years. Her training regime has been 8-9 hours per week. Her family history is negative, but she had one presyncope not connected with exercise. 12-lead ECG showed bradycardia, normal QTc. EcoCG indices also were normal for athletes. Graded exercise test resulted in significant QTc prolongation (up to 500 ms per 75 Wt), which persisted up to 8 minutes of recovery. Measurement data were similar in automatic and manual estimation. 24 hours monitoring revealed bradycardia, T-wave alteration, QTc prolongation over 460 ms for more than 80% of the assessment time. Potential LQTS was diagnosed by the sum of 3.5 scores by Swartz's criteria.

Dynamics of the QTc interval, estimated by different formulas was similar in both groups, but Bazett QTc values were higher than the Fridericia ones. We have determined the norm values of an absolute and corrected (by Bazett and Fridericia formulas) QT interval in young athletes during exercise test.

Dispersions of absolute and corrected QT interval during moderate exercise (50-100W) in athletes exceeded the corresponding indices in untrained children, while at peak load they were considerably lower. Like in a control group QT dispersion in athletes increased significantly during early recovery, up to the highest value in the test (did not exceed 35-40ms). Although QT dispersion alone cannot be a strong predictor of SCD, its prognostic significance is considerably growing in the presence of structural myocardial pathology.

**Table 1.** Dynamics of the QTc interval, estimated by different formulas.

	QT, ms	QTcBazett, ms	QTcFridericia, ms
Rest	373 (334-401)	400 (375-448)	390 (357-402)
1 st. (25W)	340 (310-366)	423 (400-460)	390 (369-410)
2 st. (50 W)	295 (270-308)	418 (396-449)	373 (344-395)
3 st. (75 W)	265 (247-289)	413 (394-445)	356 (330-380)
4 st. (100W)	240 (228-254)	404 (389-419)	335 (325-355)
5 st. (125 W)	228 (220-235)	392 (374-405)	325 (312-337)
6st. (150W)	220 (212-228)	380 (360-390)	315 (305-328)
Recovery	320 (300-340)	390 (361-450)	378 (330-400)

**Table 2.** Dynamics of myocardium repolarization dispersion (50, 5 and 95 %) in young athletes during loading test.

	<i>QTd</i> , ms		<i>dQTc</i> , ms		<i>FdQTc</i> , ms	
	Untrained	Athletes	Untrained	Athletes	Untrained	Athletes
Initially	22 (20-30)	28 (20-30)	(18-30)	(20-37)	(17-31)	(18-29)
25 W	18 (10-30)	22 (14-30)	18 (14-32)	(15-31)	(19,5-26)	(14-26)
50 W	14 (10-20)	15 (10-21)	(15-31)	(13-38)	(16-26)	(14-28)
75 W	12 (10-18)	13 (10-20)	23 (12-26)	19 (16-31)	(11-21)	(12-27)
100 W	8 (5-10)	7 (5-10)	15 (8-17)	12,5 (14-17)	(7-14)	(7-14,5)
125 W	7 (5-10)	6 (5-7,5)	(8-16)	(7-14)	(7-13)	(7-14)
Early recovery period	26 (19-35)	20 (15-30)	(16-40)	(13-37)	(18-35)	(16-36)

Another significant sign of electrical instability of the myocardium is QT variability that is the difference between maximal and minimal QTc during the exercise test. As Wong showed in healthy untrained children this index was less than 40 ms, while in patients with LQTS it exceeds 60-70 ms [23]. In our study permissible QT variability in athletes was 50-60ms. More significant QT variability was noted in 21% of athletes, 17 of whom had cardiac remodeling and overtraining syndrome, 3 - structural cardiovascular diseases and 1 - probably LQTS.

#### 4. Conclusions

In young athletes, as well as in the untrained maximal QTc (by Bazett) have been recorded at the initial stages (not exceeding 460 ms) and minimal - at the peak of exercise.

QTc prolongation over 390 ms at peak load and over 450 ms at min 4 of recovery, as well as QTc variability more than 50 ms during exercise test in young athletes can be considered as a signs of cardiac pathology. They require an extensive medical examination to rule out primary and secondary LQT.

Maximal QT and QTc interval dispersions have recorded at the initial stage of exercise and during recovery, they did not exceed 35 and 40 ms, respectively.

Assessment of myocardial repolarization dynamics during exercise in young athletes can be a significant diagnostic method for revealing some conditions associated with SCD.

#### References

- [1] Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, Elliott PM, Fitzsimons D, Hatala R, Hindricks G, Kirchhof P, Kjeldsen K, Kuck KH, Hernandez-Madrid A, Nikolaou N, Norekvål TM, Spaulding C, Van Veldhuisen DJ. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). *Eur Heart J*. 2015 Nov 1;36(41):2793-867.
- [2] Harmon KG, Drezner JA, Wilson MG, Sharma S. Incidence of sudden cardiac death in athletes: a state-of-the-art review. *Heart* 2014;100:1227–1234.
- [3] Schmied C, Borjesson M. Sudden cardiac death in athletes. *J Intern Med* 2014;275:93–103.
- [4] Assanelli D1, Levaggi R, Carré F, Sharma S, Deligiannis A, Mellwig KP, Tahmi M, Vinetti G, Aliverti P Cost-effectiveness of pre-participation screening of athletes with ECG in Europe and Algeria. *Intern Emerg Med*. 2015 Mar;10(2):143-50.
- [5] Menafoglio A, Di Valentino M, Porretta AP, Foglia P, Segatto JM, Siragusa P, Pezzoli R, Maggi M, Romano GA, Moschovitis G, Gallino A. Cardiovascular evaluation of middle-aged individuals engaged in high-intensity sport activities: implications for workload, yield and economic costs. *Br J Sports Med* 2015 Jun;49(11):757-61.
- [6] Maron B.J., Thompson P.D., Ackerman M.J., Balady G., Berger S., Cohen D., Dimeff R., Douglas P.S., Glover D.W., Hutter A.M. J.R, Krauss M.D., Maron M.S., Mitten M.J., Roberts W.O., Puffer J.C. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: A scientific statement from the American heart association council on nutrition, physical activity, and metabolism: endorsed by the American College of Cardiology Foundation // *Circulation*. – 2007.-№115.- P.1643-1655.
- [7] Corrado D., Pelliccia A., Bjørnstad H., Vanhees L., Biffi A., Borjesson M., Panhuyzen-Goedkoop N., Deligiannis A., Solberg E., Dugmore D., Mellwig K.P., Assanelli D., Delise P., van-Buuren F., Anastasakis A., Heidbuchel H., Hoffmann E., Fagard R., Priori S.G., Basso C., Arbustini E., Blomstrom-Lundqvist C., McKenna W.J., Thiene G.. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol Consensus Statement of the Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology // *Eur. Heart*. – 2005.-№26.-P.516–524.
- [8] The order of the Russian Ministry of Health from 01.03.2016 N 134N "About the Order of the organization of delivery of health care to the persons playing physical culture and sport ..." The Official Internet portal of legal information <http://www.pravo.gov.ru>
- [9] Chou R, Arora B, Dana T, Fu R, Walker M, Humphrey L Screening asymptomatic adults with

- resting or exercise electrocardiography: a review of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2011 Sep 20;155(6):375-85
- [10] Sarma S, Levine BD. Beyond the Bruce Protocol: Advanced Exercise Testing for the Sports Cardiologist. *CardiolClin.* 2016 Nov;34(4):603-608.
- [11] Dillenburg R.F. and Hamilton R.M. Is Exercise Testing Useful in Identifying Congenital Long QT Syndrom? *Am Heart J.* 2002 Oct. 140(4): 678-83.
- [12] Takenaka K, Ai T, Shimizu W, et al. Exercise stress test amplifies genotype-phenotype correlation in the LQT1 and LQT2 forms of the long-QT syndrome. *Circulation.* 2003;107:838–844.
- [13] Wong J.A., Gula L.J., Klein G.J., Yee R., Skanes A.C., Krahn A.D. Utility of Treadmill Testing in Identification and Genotype Prediction in Long-QT Syndrome *CircArrhythmElectrophysiol* 2010;3;120-125;
- [14] Corrado D, Pelliccia A, Heidbuchel H, et al. Recommendations for interpretation of 12-lead electrocardiogram in the athlete. *Eur Heart J* 2010; 31(2): 243-59.
- [15] Bazett H. Analysis of the time relations of electrocardiograms. *Heart* 1920;7:353-70.
- [16] Fridericia L. Die systolendauer im Elektrokardiogramm bei normalen Menschen und bei Herzkranken. *Act Med. Scand.* 1920;53: 469-472
- [17] Basavarajaiah S, Wilson M, Whyte G, Shah A, Behr E, Sharma S  
Prevalence and significance of an isolated long QT interval in elite athletes. *EurHeart J.* 2007 Dec;28(23):2944-9.
- [18] Makarov L.M., Balykova L.A., Komolyatova V.N., Gorbunova I.A., Changes of an interval of QT in the course of assay with the dosed exercise stress at healthy teenagers of 11-15 years//the *Cardiology* - 2012 No. 9 of Page 15-21.
- [19] Balykova L.A., Makarov L.M., Gorbunova I.A., Markelova I.A. QT Interval Adaptation in Young Athletes During Physical Load Test Abstract Congress ISHNE Moscow 2010.
- [20] Schwartz P.J., Crotti L. QTc Behavior During Exercise and Genetic Testing for the Long-QT Syndrome // *Circulation* -2011-№124- P.2181-2184.
- [21] Sy R.W., van der Werf C., Chatta I.S., Chockalingam P., Adler A., Healey J.S., Perrin M., Gollob M.H., Skanes A.C., Yee R., Gula L.J., Leong-Sit P., Viskin S., Klein G.J., Wilde A.A., Krahn A.D. Derivation and validation of a simple exercise-based algorithm for prediction of genetic testing in relatives of LQTS probands // *Circulation* -2011-№124- P.2187-2194.
- [22] Dong-sheng Gao, Wei-yi Fang, Christine Chiu-Man, Joel Kirsh, Gil Gross, Robert M Hamilton QT hysteresis in long-QT syndrome children with exercise testing. *Chin. Med. J.* 2007; Feb;120(3):179-82.
- [23] Wong JA, Gula LJ, Klein GJ, Yee R, Skanes AC, Krahn AD. Utility of Treadmill Testing in Identification and Genotype Prediction in Long-QT Syndrome. *CircArrhythmElectrophysiol.* 2010;3:120-125.