Behavior of Repolarization Variables during Exercise Test in the Athlete's Heart

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Background: T peak–T end, QT peak/QT ratio and T peak–T end/QT ratio are markers able to test myocardial repolarization homogeneity, their increase has been related to a higher risk of ventricular tachyarrhythmias. These parameters have not yet been studied in left ventricular hypertrophy due to training. Aim of the research was to test the behavior of these variables in the athlete's heart during exercise.

Methods: We examined 70 athletes, all males, divided into two groups according to the absence or the presence of a left ventricular mass index over $49 \text{ g/m}^{2.7}$ and a control group composed of 35 healthy, untrained males. All study participants underwent electrocardiogram at rest, transthoracic echocardiogram, and ergometric test. Repolarization markers (QT, corrected QT, QT dispersion, T peak–T end, QT peak/QT, T peak–T end/QT) were calculated at rest, at peak exercise and during recovery.

Results: There was no statistically significant difference among the groups regarding all the parameters studied, except for corrected QT at rest between athletes with left ventricular hypertrophy and control group. The behavior of repolarization markers during exercise was not dissimilar in the three groups.

Conclusions: Athlete's heart is not associated to any alteration in ventricular repolarization homogeneity, neither at rest nor during physical activity nor during recovery. Training-induced left ventricular hypertrophy does not affect relationship QT parameters/RR interval.

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athlete's heart; exercise; repolarization; T-peak–T-end; T-peak–T-end/QT ratio

INTRODUCTION

The athlete's heart is characterized by a thickening of the walls, an enlargement of the chambers and an increase in left ventricular mass (LVM), as a result of training.¹ Not all agree on the physiological nature of such adaptations nor, consequently, on the absence of possible negative consequences.²

A pathological hypertrophy is associated to alterations of the electrophysiological properties of

cardiomyocytes, closely related to a higher susceptibility towards malignant tachyarrhythmias. In the hypertrophic human heart, in presence of interstitial fibrosis, the ventricular repolarization is abnormal³ and a correlation between left ventricular hypertrophy (LVH) and sudden death (SD) has been yet demonstrated.⁴

Previous studies have found a relationship between pathological LVH and an increase in some electrocardiographic markers, able to test ventricular repolarization homogeneity.^{5,6}

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The only parameter studied till now in athletes is the QT dispersion (QTd), given by the difference between the maximum and the minimum QT interval in the 12-lead electrocardiogram (ECG).⁷ These researches have reached contrasting results.^{8,9}

Novel electrocardiographic variables such as T peak-T end (Tpe), Tpe/QT ratio,¹⁰⁻¹² and QT peak/QT end (QTp/QT)¹³ were investigated in some clinical conditions, resulting suitable to study ventricular repolarization¹³ and to reveal a high-arrhythmic risk.^{11,12}

Tpe interval was associated to an increased incidence of life-threatening ventricular arrhythmias in Brugada syndrome, with most of the recurrences in patients with an average value of Tpe > 100 ms.¹¹ Tpe/QT ratio was used as marker of arrhythmogenesis in hypertrophic cardiomyopathy (HCM)⁵ and in long QT syndrome (LQTS), with a value greater than 0.28 in V₅ that was able to predict the risk of ventricular arrhythmias in LQTS.¹²

These parameters have not yet been investigated within the sport population; we don't know if they increase in athletes who develop, in consequence of training, a left ventricular hypertrophy and their behavior during physical activity is unknown.

This study tested, in the physiological remodeling due to training, the possible presence of electrophysiological alterations at rest, during exercise, and recovery, by means of various electrocardiographic parameters which indirectly assess ventricular repolarization homogeneity.

METHODS

The study participants were 70 trained athletes, involved in agonistic sports. In order to receive a specific sport eligibility they underwent the Italian preparticipation examination program including family history, physical examination, urine examination, spirometry test, 12-lead ECG at rest, and exercise test.

On the basis of the results of an echocardiographic study they were divided into two different groups: without (first group) and with (second group) evidence of LVH. Both groups were composed of 35 athletes and compared with a third control group of 35 healthy untrained subjects.

The ECG was recorded with a standard digital recorder at a paper speed of 25 mm/s. The QT interval was measured in lead D II from the QRS

onset to the T-wave end, defined as the intersection between the tangent to the downslope of the T wave and the isoelectric line,¹⁴ when U waves were present the QT interval was measured to the nadir of the curve between T and U waves. Heart rate(HR)-corrected QT interval (QTc) was obtained using Bazett's formula ($QTc = QT/\sqrt{RR}$).¹⁵ QTd was determined as the difference between the maximum and minimum QT intervals,¹⁶ without using any formula to correct QTd for HR.¹⁷

Tpe interval was measured in precordial leads from the peak to the end of the T wave; in the case of negative T waves QT peak was measured to the nadir of the T wave. The Tpe value reported is the maximum (max) obtained. Tpe/QT ratio was calculated dividing the Tpe interval by the QT interval.¹² QTp/QT ratio was calculated dividing the QT peak by the QT interval.¹³

Heart dimension was evaluated by a transthoracic echocardiographic study. LVM was calculated by Devereux formula considering the diastolic measurements of left ventricular internal diameter (LVID), interventricular septal thickness (IVST) and posterior wall thickness (PWT): $LVM \text{ (in grams)} = 1.04 [(LVID + IVST + PWT)^3 - LVID^3] \times 0.8 + 0.6$.¹⁸ LVMI was calculated dividing LV mass (in grams) by height (in meters)^{2,7} as described by de Simone.¹⁹ LVH has been defined as $LVMI \geq 49 \text{ g/m}^{2,7,20}$

An exercise test was performed on a bicycle ergometer until volitional exhaustion. Athletes were specifically assessed for the development of ischemic changes, abnormal or flat blood pressure (BP) response and tachyarrhythmias.

QT, QTc, QTp, QTd, Tpe, QTp/QT ratio, and Tpe/QT ratio were manually measured at rest, at exercise peak, and during recovery by one observer who had no knowledge of the clinical data.

Statistical analysis was accomplished with the aid of R' software.²¹ The three groups were compared using a one-way analysis of variance (ANOVA). The comparison between the data at rest and during ergometric test inside the same group, was performed using the Student's *t*-test for paired data. To better understand the relationship between repolarization parameters and RR interval, simple linear regression models have been used, separately, for each group.

The predetermined α level was 0.05. Data are presented as mean $\pm$ SD.

Table 1. Baseline and Clinical Characteristics of Study Participants

	Group 1	Group 2	Group 3
Total number athletes	35	35	35
Age (years)*	21.4 ± 13.1	24.1 ± 7.7	20.3 ± 10.6
SBP (mmHg)*	110.4 ± 10.0	113.7 ± 10.1	111.7 ± 12.2
DBP (mmHg)*	71.7 ± 7.5	73.4 ± 7.5	72.4 ± 8.2
BMI*	21.6 ± 1.8	22.5 ± 2.1	21.8 ± 2.0
Height (cm)*	171.9 ± 10.3	175.6 ± 5.0	171.4 ± 12.6
LVMl (g/m ^{2.7})**	33.0 ± 5.7	56.9 ± 4.0	28.9 ± 7.9
HR**	64.8 ± 4.9	62.9 ± 6.2	73.2 ± 11.9
HPP(mmHgxbats/minx10 ⁻³)**	30.0 ± 3.4	33.1 ± 2.6	26.6 ± 3.1

Group 1 = athletes without left ventricular hypertrophy; Group 2 = athletes with left ventricular hypertrophy; Group 3 = control group; SBP = systolic blood pressure; DBP = diastolic blood pressure; BMI = body mass index; LVMl = left ventricular mass index; HR = heart rate; HPP = heart rate-systolic blood pressure product at peak exercise;* (P > 0.05); ** (P < 0.05). P values are from ANOVA tests.

RESULTS

A total of 105 male subjects, subdivided in three groups, were evaluated. Baseline and clinical characteristics of study participants are shown in Table 1.

The groups were homogeneous for age, height, body mass index (BMI), BP; a statistically significant difference, as a result of training, was present for HR, HR-systolic BP product at peak exercise, and left ventricular mass index (LVMl).

None took any drug including oral supplements of electrolytes or had cardiac or systemic diseases, electrolyte disorders, electrocardiographic abnormalities included evidence of bundle-branch blocks; all were in sinus rhythm.

No statistically meaningful difference was highlighted among the three study groups in terms of QT, QTp, Tpe max, QTd, QTp/QT, and Tpe/QT neither at rest nor at peak exercise nor at recovery with a P > 0.05 for all the parameters (means and standard deviations are shown in Table 2).

Only a meaningful difference regarding QTc at rest was found between athletes with LVH and untrained subjects (P = 0.04). All parameters, including QTc, were normal in all study participants. Athletes, in particular with LVH, showed longer QT and QTc intervals than untrained subjects, but these differences reach the statistical significance only for QT corrected for HR, according to Bazett's formula; however no athlete had QTc higher than 440 msec.

QTd, Tpe max, Tpe/QT, and QTp/QT took values very close in the three groups.

Repolarization markers response to exercise was fully superimposable in the three groups. When RR intervals decreased during exercise a QT, QTp, and Tpe shortening occurred (P < 0.05). QTd showed no statistically significant difference (P > 0.05). QTp/QT ratio (P > 0.05) and Tpe/QT ratio (P < 0.05) showed a trend to increase, statistically significant only for the second parameter. Changes in Tpe, Tpe/QT, and QTp/QT occurring during exercise in athletes without and with LVH are shown in Figure 1.

Regarding QT parameters/RR relationship the same features were found in the three groups. Linear regression method has not been applied to QTc because this parameter is jet relativized to RR interval. It was highlighted the presence of high values of linear correlation between RR and QT (0.93 in the first group, 0.94 in the second and in the third group), between RR and QTp (0.92 in the first group, 0.94 in the second group, 0.92 in the third group), and between RR and Tpe (0.81 in the first group, 0.78 in the second group, 0.82 in the third group). If RR intervals increased or decreased there was a consensual response of the aforementioned parameters.

As regards QT interval, the regression line assessed for the first group was $QT = 186.83 + 0.20 RR$, for the second group $QT = 191.92 + 0.20 RR$, for the third group $QT = 193.95 + 0.19 RR$. Both the intercept and the slope parameter were statistically significant (P < 0.05) in every model; the overall adaptation of the models was satisfactory with a R² respectively equal to 0.87, 0.89, and 0.88. For an unit increase in the RR, on average, there was a QT interval increase of 0.20 in the first and second groups and 0.19 in the third one.

The linear regression function of QT peak was $QTp = 135.83 + 0.16 RR$ for the first group, $QTp = 136.52 + 0.16 RR$ for the second group, $QTp = 144.19 + 0.14 RR$ for the third group. Either the intercept or the slope parameter were statistically significant (P < 0.05); the overall adaptation of the models was satisfactory with a R² respectively equal to 0.84, 0.88, and 0.84. For an unit increase in the RR, on average, there was a QTp increase of 0.16 for the first and second groups, of 0.14 for the third one.

The regression line of Tpe was $Tpe = 44.34 + 0.05 RR$ in the first group, $Tpe = 48.67 + 0.05 RR$ in the second group, $Tpe = 48.06 + 0.05 RR$ in the third one.

Table 2. Repolarization Markers in the Three Groups at Rest, at Peak Exercise, during Recovery

	QT	QTc	QTd	QTp/QT	Tpe max	Tpe/QT
REST						
Group 1	360.0 ± 28.1*	394.5 ± 24.4*	29.4 ± 13.7*	0.75 ± 0.03*	89.1 ± 11.7*	0.22 ± 0.03*
Group 2	366.3 ± 19.7*	405.5 ± 25.8**	28.6 ± 8.8*	0.75 ± 0.02*	91.7 ± 10.7*	0.23 ± 0.03*
Group 3	356.3 ± 28.7*	390.8 ± 25.5**	27.7 ± 9.7*	0.75 ± 0.03*	90.3 ± 9.8*	0.22 ± 0.02*
EXERCISE						
Group 1	262.8 ± 14.5*	419.6 ± 23.3*	23.7 ± 10.9*	0.76 ± 0.02*	64.3 ± 8.1*	0.25 ± 0.02*
Group 2	265.4 ± 11.7*	422.8 ± 15.4*	25.1 ± 8.9*	0.75 ± 0.03*	66.3 ± 7.7*	0.24 ± 0.03*
Group 3	262.0 ± 12.5*	420.9 ± 18.0*	24.6 ± 12.4*	0.76 ± 0.03*	64.8 ± 7.0*	0.24 ± 0.02*
RECOVERY						
Group 1	330.6 ± 18.0*	400.0 ± 23.8*	23.7 ± 9.4*	0.74 ± 0.02*	85.4 ± 8.2*	0.26 ± 0.09*
Group 2	332.0 ± 21.2*	409.9 ± 32.4*	26.8 ± 10.8*	0.74 ± 0.02*	85.1 ± 7.8*	0.26 ± 0.09*
Group 3	329.7 ± 22.0*	399.1 ± 23.7*	24.3 ± 9.2*	0.75 ± 0.03*	83.4 ± 8.4*	0.25 ± 0.02*

Group 1 = athletes without left ventricular hypertrophy; Group 2 = athletes with left ventricular hypertrophy; Group 3 = control group. QTc = corrected QT; QTd = QT dispersion; QTp = QT peak (QTp); Tpe = T-peak-T-end. *(P > 0.05); ***(P < 0.05). P values are from ANOVA tests.

ATHLETES WITHOUT LVH

ATHLETES WITH LVH

Figure 1. Frequency distribution of Tpe max, Tpe/QT, QTp/QT in athletes without and with LVH at rest (R) and at peak exercise (E).

the third group. Both the intercept and the slope parameter were statistically significant ($P < 0.05$) with a R^2 respectively equal to 0.66, 0.61, and 0.67. For an unit increase in the RR, on average, a Tpe increase, much less than the two previous parameters, was observed; it was exactly of 0.05 for all groups.

QTd, Tpe/QT ratio, and QTp/QT showed a low linear correlation with RR. Considering the ab-

sence of a linear trend when varying RR interval no linear regression model was calculated for these variables.

DISCUSSION

The heart adapts to training through some morphologic changes which include an increase in LVM.¹ Not all the authors agree to consider the

athlete's heart as a benign condition without adverse cardiovascular consequences.²

In pathological hypertrophy the electrophysiological abnormalities can be related to a myocardial architecture deformity. One of the anatomopathological hallmarks of hypertensive cardiomyopathy, besides to myocyte hypertrophy, is the increase in interstitial collagen matrix,²² able to provoke a distortion of the tissue architecture which is responsible for regional differences in the recovery of excitability, demonstrated by an increase in QTd.²³

In the same way, in HCM myocyte disarray and fibrosis lead to ventricular repolarization abnormalities proven by an increase of QT, QTd, and Tpe/QT ratio.⁵⁻²⁴

In our study, on the contrary, there is no evidence of negative consequences on electrophysiological properties of athlete's heart, as demonstrated by the absence of abnormal values of all electrocardiographic markers suited to assess ventricular repolarization.

QT, QTd, Tpe max, QTp/QT, and Tpe/QT are normal in athletes, who develop a training-induced LVH and their behavior during exercise and recovery does not show any alteration.

It can be explained by the histological characteristics of the athlete's heart, as assessed by ultrasonic myocardial reflectivity.²⁵ Both abnormal deposition of fibrous tissue and abnormal myocardial fiber architecture can increase the reflectivity.²⁶ Physiological hypertrophy, which is characterized by myocyte hypertrophy without or with minimum increase in the interstitial collagen, shows a normal reflectivity.²⁵ Myocyte hypertrophy together with the absence of fibrous tissue allows athlete's heart to increase its own functionality keeping a homogeneous repolarization, as demonstrated by the present study.

Considering the normal electrophysiological characteristics of the left ventricle, training induced LVH cannot be the cause of SD. The study gives an additional proof that the athlete's heart is an innocent consequence of training, that doesn't lead to any change in the ventricular repolarization homogeneity. Moreover these electrocardiographic parameters may be used as a screening strategy useful when there is a diagnostic doubt between physiological and pathological hypertrophy. The distinction between HCM and athlete's heart²⁷ is a common problem for sports doctors. During anamnesis athletes often hidden alarm symptoms which may trigger disqualification from competi-

tive sports. A simple 12-lead ECG is able to direct to the right diagnosis because it often results abnormal in patients with HCM. Sometimes also athletes can show electrocardiographic abnormalities, but unlike what happens in HCM, they never have altered repolarization markers. A prolongation of these parameters in athletes requires additional investigations and cannot be explained by the presence of a physiological remodeling.

CONCLUSIONS

In the athlete's heart the ventricular repolarization, assessed by the several electrocardiographic markers studied, does not show any alteration neither at rest nor during exercise nor during recovery. The behavior of QT, QTd, Tpe, Tpe/QT, and QTpeak/QT during exercise is not dissimilar in athletes with and without LVH and untrained subjects; QT parameters/RR relationship is superimposable. QT, QTp, and Tpe decrease, Tpe/QT increases, QTd and QTp/QT do not show statistically significant changes.

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