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Original Research Article

Evaluation of QT interval and QT dynamics in healthy male adults following isotonic and isometric exercise

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Abstract

Introduction: Electrocardiogram can be used an objective tool to assess cardiovascular response to physical exercise. The QT interval in ECG denoting ventricular depolarization and repolarization is particularly important in this regard as any change in its duration is known to be associated with arrhythmia. Studies reporting a change in QT duration in the post exercise period have variable results. Cardiac repolarization normally adapts to heart rate; therefore, various rate correction formulas have been used to calculate the corrected QT interval or QTc. Of these Bazzet's formula and Fridericia formula are commonly used. These correction formulas are best suited for steady state conditions only. Hence, QT dynamics may be a better measure of QT dependence on heart rate in the post exercise period.
Objectives: The aim of the study was to assess changes in QT interval and QT dynamics in healthy male adults following isotonic and isometric exercise.
Materials and Methods: The study was conducted in 30 healthy male subjects. Temporal sequence of QT interval and QT dynamics before and after both isotonic and isometric exercise were measured. QT dynamics was assessed by linear regression analysis method.
Results: The QTc calculated with standard rate correction formulae showed inconsistent values in the post exercise period. The slope of QT-RR relationship increased especially following isotonic exercise.
Conclusion: QT interval duration increases following exercise, although, the degree of change is different for isotonic and isometric exercise.
Keywords: ECG, QTc interval, QT-RR relationship.

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1. Introduction

Physical exercise is a physiological challenge posed to various systems of the body. The cardiovascular system responds to this challenge by bringing about appropriate changes mainly in heart rate. Therefore, the cardiovascular response to exercise can be used as a valuable means to assess its fitness. Physical activity per se is recommended for improving overall cardiovascular health. However, there are reports of adverse cardiac events in the post exercise period. Many such events occur in apparently healthy individuals and remain unexplained, often being attributed to aberrations in cardiac electrical activity. [1] It is apparent that the heart rate changes initiated during exercise require appropriate adjustments in the electrical activity of the heart. These changes are reflected in various segments and intervals of the ECG.

Of the various intervals and segments, QT interval is a significant parameter as it encompasses the entire duration of ventricular electrical activity inclusive of depolarization and repolarization. [2] The normal duration of QT ranges between 0.35 to 0.45 seconds in males. Various studies have reported that an increase or decrease in duration of QT interval predisposes the development of cardiac arrhythmias. [3-5]

The QT duration varies not only in pathological states but in different physiological conditions as well.

Heart rate, relative activity of sympathetic and parasympathetic nervous system, physical exercise, time of the day and gender are some of the physiological factors affecting QT interval duration.

As normal cardiac repolarization adapts to heart rate, it is the predominant factor affecting QT duration. Therefore, various heart rate correction formulas have been used to calculate the corrected QT interval or QTc. Of these Bazzet's formula is the most widely used. Fridericia formula is another correction formula which has shown more consistent results at higher heart rates.[3] However, both formulas have limitations, in that they are best suited for steady state conditions only.[6]

Reports on the effect of physical exercise on QT duration are variable. Some have reported an increase in QT duration while others have reported no change.[2,7] This is possibly due to the fact that physical exercise holds a unique position in that it changes both autonomic tone and heart rate, both of which are known to effect QT duration independently. Hence, the effect of exercise on QT duration is complicated and difficult to explain in a direct cause and effect manner. In a broader sense exercise is characterized by vagal withdrawal and increased sympathetic activity followed by recovery of vago-sympathetic balance in the post exercise period.[2] However, the finer details of the autonomic changes vary depending on the type of exercise, whether isotonic or isometric.

Exercise induced change in QT duration needs to be evaluated as it may throw light on aetiology of post exercise adverse cardiac events. Most of the existing literature on effect of exercise on QT duration, fail to comment on the exact temporal sequence of QT changes if any, following isotonic or isometric exercise. Moreover, they have used rate correction formulas which may not reflect the actual changes. Several reports have suggested that QT dynamics is a better measure of QT dependence on heart rate and seems to be a promising way to assess post exercise QT changes. It is determined by linear regression analysis from which QT/RR slope is calculated. [8-10] An increase in steepness of the slope has been correlated with the risk of death due to arrhythmia. [11,12]

Hence, this study was designed with an aim to assess the temporal sequence of QT interval changes using standard rate correction formulas and QT dynamics following isotonic and isometric exercise.

2. Materials and Methods

The present study was designed as a cross sectional study in the Department of Physiology of a tertiary level hospital in India between 2018 and 2019. 30 healthy male adults were recruited from hospital staff and residents of the hospital. The study protocol was approved by institutional ethical committee (IEC/VMMC/SJH/October/2017-175). Informed consent was taken from all participants. A detailed history of present and past illness was taken and all volunteers underwent a general physical examination. Anthropometric data such as height, weight, waist and hip circumference were also measured. For recording and analysis of QT interval, ML870B80 Exercise Physiology system (A.D instruments) was used. Baseline blood pressure, heart rate and 5 min ECG were obtained. This was followed by Isotonic exercise on day one and isometric exercise on day two.

2.1 Isotonic exercise protocol

Isotonic exercise was performed on Sport top B890 static bicycle ergometry. After 2 minutes of warm up, the work load was increased till the subject reached 70% of his maximum heart rate. The exercise test was terminated 5 minutes after achieving the target heart rate or earlier if the subject reported any discomfort.

2.2 Isometric exercise protocol

On day two, Isometric exercise was performed using a handheld dynamometer. The subjects were asked to hold the hand grip dynamometer in the dominant hand and compress the handle with maximum effort and the tension developed was taken as T1. The procedure was repeated and T2 was recorded. T_{max} was calculated as an average of T1 and T2.Subjects were then asked to perform the exercise at 30% of T_{max} for a period of 5mins.

Post exercise heart rate and blood pressure was recorded at 1, 5 and 15 mins while lead II ECG was continuously recorded up to 15 mins on both days following isotonic and isometric exercise.

2.3 Measurement of QT interval

The ML 870B80 Exercise Physiology system (A.D. Instruments) was used to compute the QT interval before exercise and at 1, 5- and 15-mins post exercise.

The corrected QT interval was calculated using both Bazzet's formula QTc = $(QT/(RR)^{1/2})$ and Fridericia formula (QTc = $QT/(RR)^{1/3}$).[6]

2.4 Measurement of QT dynamics

QT dynamics was calculated by linear regression slope method. This slope determines the percentage of QT interval change per unit of RR interval change. The slope, intercept and r^2 were analyzed from the graph. This was done using GraphPad prism software. The co-ordinates of all QT interval and RR interval are tabulated and a scatter plot was plotted with the RR interval against the X axis and QT interval against the Y axis. Then a linear trendline was drawn over the scatter plot. From the linear trendline, equation of the line was derived in the format y=slope x+ intercept and r^2. [13]

2.5 Statistical methods

Statistical analysis was performed using SPSS version 21.0(SPSS, Inc., Chicago, IL, USA). Quantitative data was summarized as mean, and appropriate measures of dispersion. The data was analysed using paired t-test and

Wilcoxon Signed Rank test based on the assumption of normality of data distribution for statistical comparison of pre and post exercise values for all the parameters. Repeat ANOVA was used to find the significance of parameter change over a period of time and assumption of Sphericity was checked with Mauchly's test. If the assumption of sphericity was violated, then Greenhouse-Geisser or Huynh-Feldt correction tests were used. p value < 0.05 was considered statistically significant.

3. Results

The study was conducted in 30 healthy male subjects. The mean age of the study population was 22.58 ± 3.18 years.

Table 1: The table depicts the anthropometric parameters of all subjects (n=30)

Parameter	Values (Mean±SD)
Age (yrs)	22.58 ± 3.18
Height (cm)	171.01±7.79
Weight (kg)	64.54±7.45
BMI (kg/m^2)	22.09±2.37
WHR	0.90±0.09
BSA(m^2)	1.75±0.12

WHR- Waist Hip Ratio;
BMI- Body Mass Index;
BSA- Body Surface Area

BMI and WHR of all the subjects were within normal limits and none of the subjects were obese.

3.1 ECG Parameters- Isotonic exercise

3.1 a) QT interval changes following isotonic exercise

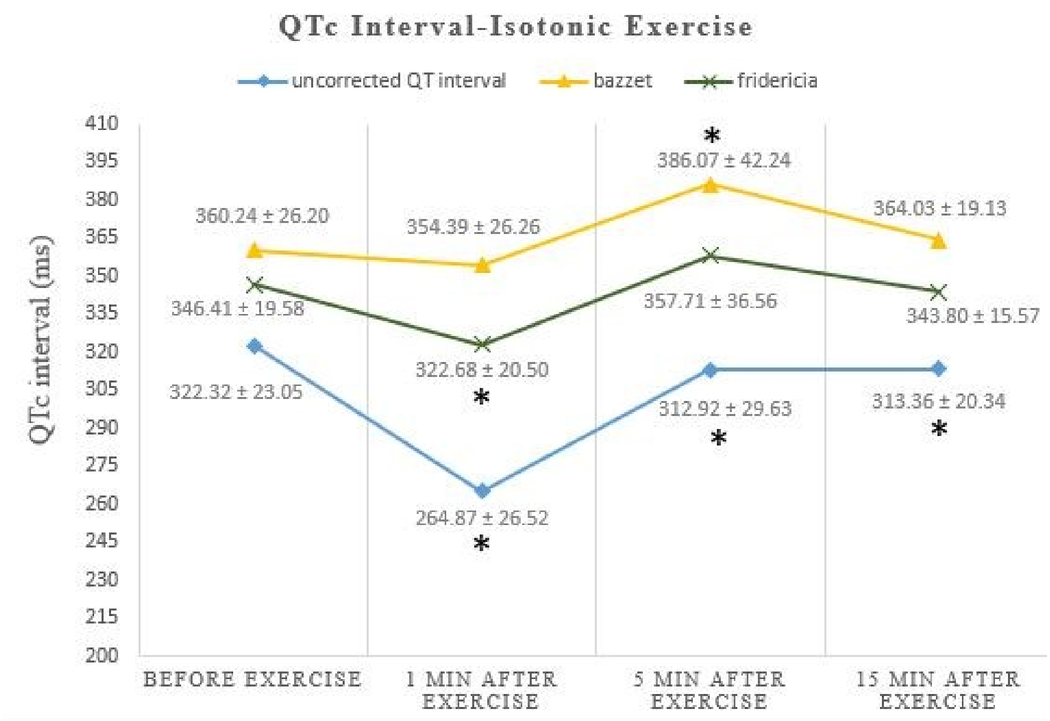


Figure 1: The figure depicts QT and corrected QT interval (QTc) by both Bazzet's and Fridericia method, before and1, 5 and 15min after isotonic exercise

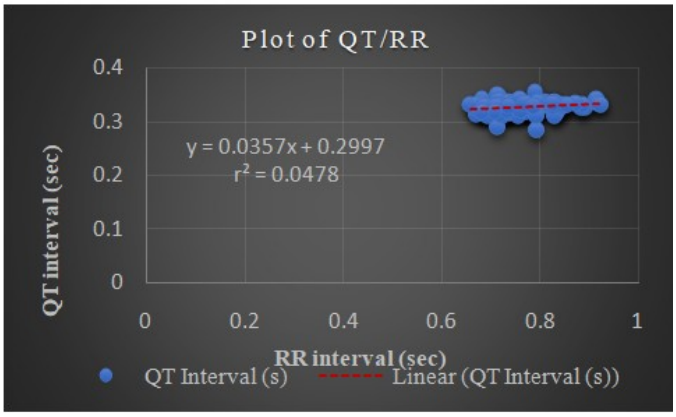
1) All the post exercise values showed statistically significant difference from the baseline in case of uncorrected QT interval.
2) Corrected QT interval (QTc) calculated by Bazzet's formula was statistically significant from the basal value at 5min, post exercise.
3) QTc values obtained by Fridericia formula were statistically significant at 1min, post exercise.

3.1b) QT dynamics following isotonic exercise

Table 2: The table depicts the slope of QT dynamics before and after isotonic exercise

Parameter	Values (Mean±SD)	p Value
QT dynamics slope before exercise	0.0458±0.12	
QT dynamics slope after exercise	0.1284±0.07	p=0.00*

The average value of slope increased from 0.0458±0.12 to 0.1284±0.07 after isotonic exercise and the increase was statistically very significant.

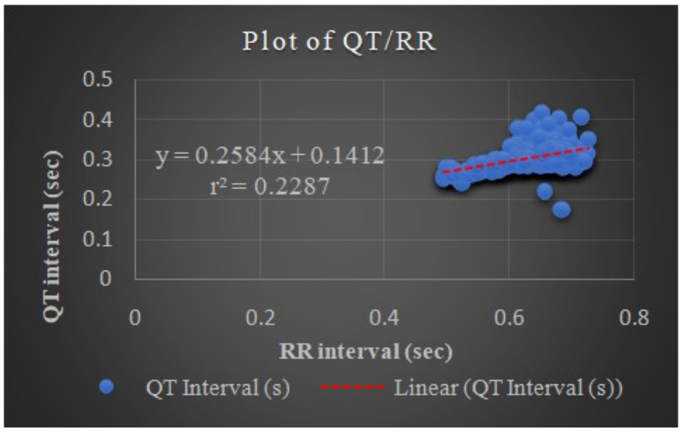


Here the equation is in the format

Y = slope x + y intercept and r^2

Slope value = 0.0375

Figure 2: Representative data for QT dynamics slope in one subject before isotonic exercise



Here the equation is in the format

Y = slope x + y intercept and r^2

Slope value = 0.2584

Figure 3: Representative data for QT dynamics slope of one subject after isotonic exercise

It is evident from the above two figures (Figure 2 and Figure 3) that there is an increase in slope value in that subject and the trendline has become steeper after isotonic exercise.

3.2: ECG Parameters- Isometric exercise

3.2 a) QT interval changes following isometric exercise

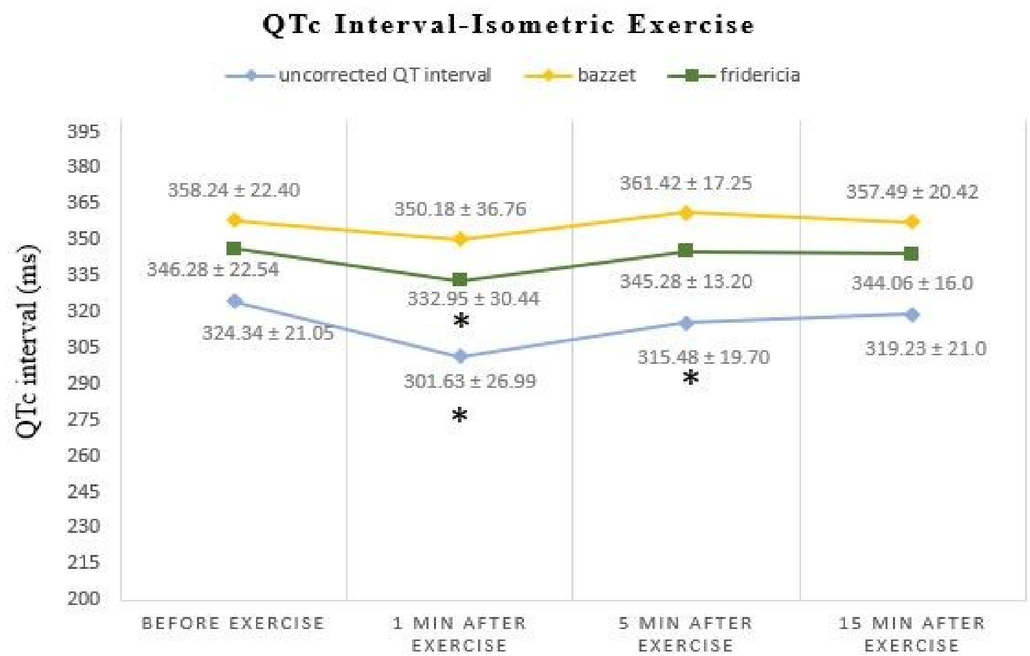


Figure 4: The figure depicts QT and corrected QT interval (QTc) by both Bazzet's and Fridericia method, before and1min, 5min and 15min after isometric exercise

1) The post exercise values at 1 and 5 min showed statistically significant difference from the baseline in case of uncorrected QT interval.
2) Corrected QT interval (QTc) values obtained by Fridericia formula showed statistical significance at 1min post exercise while the ones obtained by Bazzet's formula did not show any statistical significance.

3.2b) QT dynamics changes following isometric exercise

Table 3: The table depicts the slope value of QT dynamics before and after isometric exercise

Parameter	Values (Mean±SD)	p Value
QT dynamics slope before exercise	0.0462 ±0.35	
QT dynamics slope after exercise	0.0538± 0.02	p=0.320

The value of slope increased from 0.0462±0.35 to 0.0538±0.02 after isometric exercise but the increase was not statistically significant.

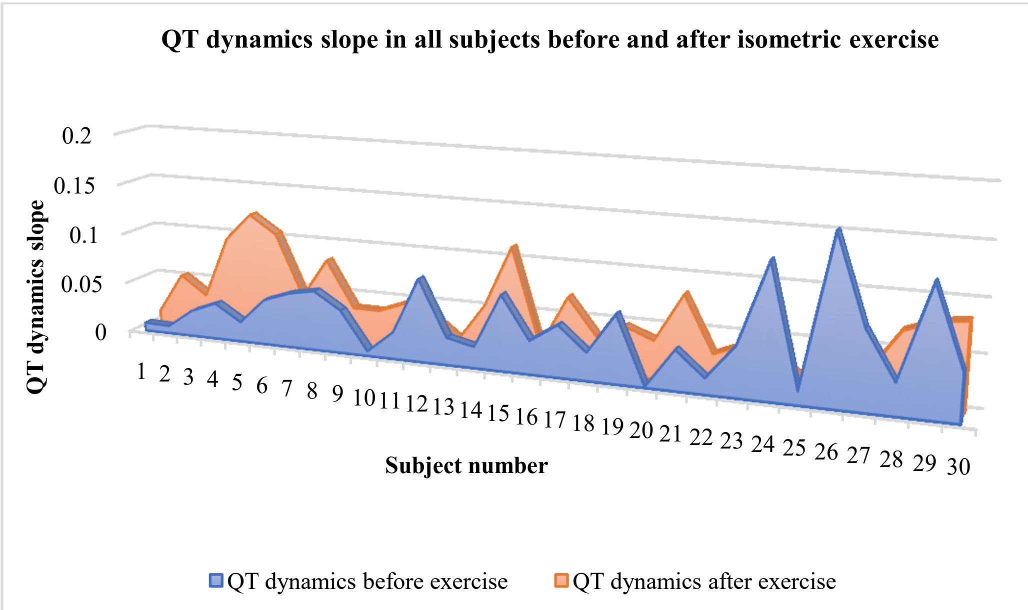


Figure 5: The figure depicts a plot of values of slope in all subjects (n=30) before and after isometric exercise.

The QT dynamics slope increased in almost all subjects after isometric exercise although statistical significance was not obtained.

4. Discussion

The physiological response of the cardiovascular system to either isotonic or isometric is different and can be objectively studied by analysing ECG changes. Of particular interest, is the QT duration which is affected in various pathological and physiological conditions. Any aberration in its duration is a known predisposing factor for arrhythmias. Studying post exercise cardiovascular response to exercise with specific reference to QT duration changes can thus have considerable clinical applicability.

Reports regarding effect of either isotonic or isometric exercise on the QT interval are contradictory. This could be due to the following reasons. First, the current rate correction formulas have limitations and may not be exactly reflective of the actual changes. Second, most of the studies including the one reported from our lab have assessed the entire post exercise period.[2] As a result, the point to point variations in the QT duration have been diluted in the summated or average value. Computing QT interval duration at various time points is likely to yield more information. This study was therefore conceptualized to address the aforementioned issues by evaluating QT interval at various time points after isotonic and isometric exercise. In addition to the temporal sequence of evaluation utilizing two standard rate correction formulas, QT dynamics, a more promising way to assess QT-RR relationship, was also calculated.

Another aspect which need to be mentioned at this juncture is the fact that a number of earlier reports have linked exercise related unexplained adverse cardiac events with abnormalities in the QT interval.[5] Therefore, it was felt that, in addition to determining the physiological variation in QT interval following exercise, this study may also provide insight to a possible causal relationship between exercise and post exercise adverse cardiac events, 30 healthy male adults were recruited for the study. The average age of the subjects was 22.58±3.18 yrs. Only male subjects were chosen because females tend to have a longer baseline QT interval (0.36 to 0.46 seconds) and also exhibit menstrual cycle related variations.

The mean values of height, weight, BSA of the subjects were 171.01±7.79 cm, 64.54±7.45 kgs and 1.75±0.12 m^2, respectively. None of the subjects were obese as revealed by the BMI and W/H ratio. It was important to ensure that none of the subjects were obese as obesity interferes with QT interval values.

4.1 QT interval

The QT interval and QTc utilizing both Bazzet's and Fridericia were computed using the ML 870B80 Exercise Physiology system (A.D. Instruments) before exercise and at 1, 5- and 15-min post exercise. The rationale for using Fridericia formula was the fact that it is a better correction formula at higher heart rates. The QTc values changed significantly in the post exercise period. In order to compare the degree of change in isotonic and isometric exercise on QT interval, repeated ANOVA measures was done. It showed that the observed change in the QT interval over time was statistically significant in both the isotonic and isometric exercise. But the degree of significance differed between isotonic and isometric exercise. QT changes in isotonic exercise showed a greater change ($F=62.64$, df 2.14 and $p<0.05$) than isometric exercise ($F=11.70$, df 1.55 and $p<0.05$).

The temporal sequence analysis revealed that at 1 min following exercise QTc duration was shortened, the duration however increased at 5 min and 15 min post exercise. The lengthening was even more evident in the QTc utilizing Bazzet's formula. However, there was considerable variation in the QTc values obtained by the two formulae the changes being more drastic in the Bazzet's corrected QTc. Nevertheless, the general trend of shortening at 1 min followed by lengthening at 5 min was observed in both types of exercise using the two rate correction formulae. [Figure 1 & 4]

Therefore, when considering the entire post exercise period as done in previous studies, the changing trend of the QTc does not become evident and an overall conclusion of either an increase or decrease in QT duration following exercise is reported. As per the present reports the QT duration fluctuates in the initial post exercise period and reaches near baseline values towards 15 min post exercise. It is important to note that all values of post exercise QT duration fall within its normal range. However, the increase or decrease depending on the exact time point following exercise may act as a risk factor in a predisposed individual.

4.2 QT dynamics

The fact that most of the heart rate correction formulas for QT interval have various limitations becomes evident from the above findings. This happens because various physiological factors influence the QT-RR relationship. Moreover, the hysteresis phenomenon in the QT-RR relationship is not considered in these formulas.[12] QT-RR relationship known as QT dynamics is recently being investigated by various researchers in this field and we decided to use QT dynamics to consolidate our findings.

We plotted individual QT-RR relationship and measured the value of slope by utilizing linear regression analysis. We obtained QT dynamics from a 5 min pre exercise ECG record while the post exercise QT dynamics was obtained from the 15 min ECG record. The average value of the slope obtained by us is different from that reported from QT dynamics for finite periods.[12] We attribute this variation to the difference in ethnicity as the reported values are mainly for the western population.

The average value of the post exercise slope was higher than the pre exercise values. This increase in slope was seen in both the types of exercise but attained statistical significance only in case of isotonic exercise. [Table 2 & 3]

A steep slope indicates greater dependence of QT on RR whereas a flat slope indicates lesser rate dependence. Also, a steeper QT/RR slope has been reported in various diseases and in patients at risk of SCD. It has been reported that the individual QT-RR relationship is more or less constant. Therefore, it is better to characterize the same before studying the effect of interventions as suggested by Sundaram *et al*. [14] However, this was beyond the scope of this study and can be taken up in future studies. Nevertheless, the post exercise slope was definitely steeper in almost all our subjects. [Figure 5]

The QT duration changes obtained by the rate correction formulae were inconclusive and fluctuated in the 15-minute duration. The QT dynamics revealed a more consistent finding, that is, the slope of the QT/RR relation increased in the post exercise period. An exact interpretation of the results in case of isotonic exercise in the study population is that for a unit increase in RR interval, the QT interval duration increased by 0.12 ± 0.07.

In order to comment on the effect of exercise on QT interval, the QT dynamics seems to be a superior choice. These findings may help explain the causation of post exercise adverse cardiac events.

5. Conclusion

In this study, in addition to QT duration we focused on the QT dynamics. The QT duration per se showed inconsistent results. The QT dynamics showed an increase in slope which was statistically significant in case isotonic exercise.

In conclusion, we can say that QT interval duration increases following exercise, as inferred from the study of QT dynamics, though the degree of change is different for isotonic and isometric exercise. This finding is clinically relevant as it may help to better understand post exercise adverse cardiac events.

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