Research article
The effect of mild dynamic exercise on the electromechanical systole of heart in non-athlete, healthy first year medical students of Bengal as a predictive biomarker of arrhythmia

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(Received: December 2021 Revised: May 2022 Accepted: June 2022)
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ABSTRACT

Introduction and Aim: Measurement of Systolic Time Intervals (STIs) is a non-invasive and convenient way of assessing left ventricular electro-mechanical activity. In this study, we assessed effect of mild dynamic exercise on QT, QS₂, QT/QS₂ ratio, QS₂-Index among healthy young first year students at a government medical college of West Bengal, India and compared the same among girls and boys.

Materials and Methods: IX-TA-220 multichannel recorder was used to record Electrocardiogram, Phonocardiogram and Carotid pulse tracing among 180 subjects before and after 1 minute of mild exercise with Harvard's Step of 30 cm height with metronome rhythm of 120 beats per minute. Results were analyzed by Microsoft Excel and comparison of each parameter between boys and girls were done using SPSS software in two hemodynamic states. P-value <0.05 was taken as statistically significant.

Results: Post exercise mean QT and QS₂ shortened and their ratio QT/QS₂ increased. There was a statistically significant difference between pre-exercise and post-exercise mean QT, QT/QS₂ ratio, QS₂ index and significant differences were observed between mean values of the boys and girls.

Conclusion: With hemodynamic changes as in exercise, due to sympathetic stimulation & catecholamine release, both QT and QS₂ should reduce as all the phases of systole shorten but if QT does not reduce in comparison to QS₂ it may lead to arrhythmia in future. Hence QT/QS₂ can be a useful pro-arrhythmic biomarker and may complement ECG and Echocardiography in borderline cases.

Keywords: Systolic Time Intervals; dynamic exercise; arrhythmia; QS₂-index.

INTRODUCTION

Now-a-days, non-invasive tests are prioritised first to evaluate cardiac performance and dynamics. Electro-Mechanical Window (EMW) is one of them. It is the temporal difference between electrical and mechanical events of beating heart through the entire cardiac cycle. Time intervals which indicate systolic cardiac functions are together known as Systolic Time Intervals (STI). It has been suggested that these intervals can be useful parameters to assess the contractile state of the LV myocardium (1-3). The intervals are measured in milliseconds (ms).

Major components of STIs are QT, QS₂, LVET (Left Ventricular Ejection Time) and PEP (Pre-ejection Period). QT=Electrical systole as per electrocardiogram; interval between beginning of Q wave (septal depolarization) to end of T wave (ventricular repolarization) QS₂ = Electromechanical systole = the interval between the beginning of Q wave of ECG to the appearance of the first high frequency vibration of S₂. Here the second heart sound (S₂) indicates closure of Aortic valves. It represents the electrical plus mechanical activity of the entire period of systole which includes Electro-mechanical Lag (EML), QS₁, Isovolumetric contraction time (ICT) and LVET.LVET = Left ventricular ejection time = appearance of carotid pulse to dicrotic notch on pulse transducer recording PEP = Pre-ejection period = (QS₂ - LVET). It is the interval from the onset of ventricular depolarization to the beginning of the left ventricular ejection. PEP/LVET - most sensitive index of ventricular function is normally about 0.35QT/QS₂ with the Electrical systole/Electro-Mechanical systole considered a useful pro-arrhythmic biomarker.

Fig. 1: Electro- Mechanical Window (EMW) of heart
There are remarkable cardiovascular changes during exercise (4). Exercise influences the entire hemodynamics and cardiac response in our body. Exercise causes change in both electrical and mechanical activity of heart by increasing heart rate and contractility. Cardiac diastole is compromised but now intense research proved that cardiac electromechanical systole also changes with exercise.

In this study, we studied the effect of mild dynamic exercise on QT, QS₂, QT/QS₂ and QS₂-Index (QS₂) of 180 healthy first MBBS students of both sexes in a government medical college of West Bengal. We assessed and compared the mean QT, QS₂, QT/QS₂ and QS₂-Index before and immediately after dynamic exercise in sympathetically naive healthy young adults under identical environmental and metabolic conditions and compared the same parameters between the two sexes.

**MATERIALS AND METHODS**

An analytical clinical study of cross-sectional design was done in the Department of Physiology of a tertiary care hospital from 20th March 2019 to 15th February, 2020. 180 non-athlete 1st year MBBS students, weighing between 50-65 kg, height between 150-175 cm, aged between 17 to 19 years of both sexes, participated voluntarily after explaining the procedure.

Students beyond extremes of these anthropometric parameters and/or having a history of hypertension, cardiovascular diseases, respiratory and renal diseases or doing regular physical/athletic activity were excluded from the study. The recording was scheduled at 12 noon every day and 3 hours after the breakfast. The institutional ethical clearance was duly obtained before starting the research. For the recording of STIs, we used IX-TA-220 Recorder which is a multichannel recorder of which following three channels were used for the purpose:

- **Electrocardiograph** - iwire - B3G Bipotential module with A-GC-7165 electrodes to record electrical activities of the heart
- **Phonocardiograph** - a microphone HSM-220 to transduce heart sound to electrical signal
- **Carotid Pulse transducer** (PT-104) for recording the pulse waves of carotid artery.

Subjects were allowed to lie down comfortably on a bed. ECG electrodes were placed in such a manner on the subject that Lead II is recorded where a definite ‘q’ wave is formed. The microphone (phonocardiograph) was placed on the Pulmonary Area on the chest to record second heart sound (S₂). The pulse transducer was placed firmly on the neck over the carotid pulse to record the left ventricular ejection during ventricular systole.

Pre-exercise pulse rate was counted; after a short pre-run, Pre-exercise recording of ECG, PNG and Pulse was done for 30 seconds followed by mild exercise for a minute and recording was repeated immediately after that.

Mild dynamic exercise was done by Harvard Step of 30 cm height on which students were asked to step up and down on alternate foot with the metronome rhythm set at 120 beats per minute.

For calculation of the STIs, good polygraph tracings of at least 10 cardiac cycles were chosen from each recording. Variables for analysis were QT interval, QS₂ interval and QT/QS₂. Duration of QT and QS₂ intervals were automatically produced by Kubios software after manually marking the q wave on ECG and dicrotic notch on the pulse tracing.

The data obtained for the two sexes was compiled on Microsoft Excel and compared. Students ‘t’ test was used to calculate the P-value using SPSS software. P-value <0.05 was considered as statistically significant.

**RESULTS**

A total of 180 participants were involved in this study, 92 of whom were males and 88 females. There was a significant increase (p<0.001) in post-exercise mean heart rate with respect to mean resting heart rate in the study population (Table 1). Mean resting QT of 180 participants was 365 ms and well within normal range of 350-440 ms. Mean post exercise QT was 334 ms and found to be statistically significant (p<0.001; Table 1). Pre-exercise mean QS₂ was lower than the available reference value for both male (546+/−14 ms) and female (549+/−14 ms). There was significant decrease in the QS₂ interval after exercise (p<0.001; Table 1). Mean QT/QS₂ increased significantly (p<0.001) in the post-exercise phase. The value under resting condition should be <1 and considered normal (Table 1). QS₂ Index significantly reduced after exercise (p=0.007; Table 1).

Pre and post exercise Mean QT, QS₂, ratio obtained for male and female participants was compared, and it was observed that apart from QS₂ the other parameters changed significantly in which QT was decreased and the ratio was increased after exercise (Table 2). Mean QS₂/I of male and female found to be statistically significant comparing two sexes only in the pre-exercise state (Table 2). All the parameters were arranged according to sex. In male, after exercise parameters like mean HR (increased), mean QT (decreased), mean QS₂ (decreased), mean QT/QS₂ ratio (increased) showed significant changes in comparison to basal condition. Same changes were observed in females also (Table 3). QS₂-Index (QS₂/I) was calculated separately for male and female participants using Wandermann’s equation (7); the values were...
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523.721ms and 539.277ms for male and female respectively with a highly significant difference between the two sexes (*p=0.001) and in both sexes our observed values were longer than the upper bound of the proposed QS2I by Wandermann (7; Table 2).

Table 1: Comparison of mean values of parameters studied in the study population (n=180) between pre and post-exercise state

| Sl. No | Parameters | Observed Mean +/-SD (Pre-exercise state) (n=180) | Observed Mean +/-SD (Post-exercise state) (n=180) | P value |
|--------|------------|-------------------------------------------------|-------------------------------------------------|---------|
| 1      | HR (bpm)   | 80+/-13                                         | 97+/-14                                         | <0.001* |
| 2      | QT (in ms) | 365+/-33                                        | 334+/-48                                        | <0.001* |
| 3      | QS2 (in ms)| 400+/-38                                        | 356+/-52                                        | <0.001* |
| 4      | QT/QS2     | 0.913+/-0.037                                   | 0.944+/-0.053                                   | <0.001* |
| 5      | QS2-index  | 527.7+/-33                                      | 520.6+/-49                                      | 0.007*  |

Table 2: Mean values of QT, QS2, QT/QS2 in males and females separately in both pre- and post-exercise state

| Parameters | Pre-exercise values | Post-exercise values |
|------------|---------------------|----------------------|
|            | Males (n=92)        | Females (n=88)       | P value | Males (n=92) | Females (n=88) | P value |
| QT (in ms) | 369                 | 360                  | 0.038*  | 343         | 325         | 0.01*  |
| QS2 (in ms)| 401                 | 398                  | 0.624   | 361         | 350         | 0.1    |
| QT/QS2     | 0.918               | 0.907                | 0.023*  | 0.954       | 0.934       | 0.01*  |
| QS2-Index (ms) | 523.721 (ref. value: 489+/-16) | 539.277 (ref. value: 522+/-14) | 0.001*  | 520.7       | 520.5       | 0.9    |

* = statistically significant (p<0.05)

Table 3: Comparison of mean value of pre and post-exercise STI parameters in each sex cohort

| Gender | Parameters | Pre-exercise values | Post-exercise value | P value |
|--------|------------|---------------------|---------------------|---------|
| Male   | Mean HR (bpm) | 77                  | 94                  | <0.001* |
|        | Mean QT (ms)   | 369                 | 343                 | <0.001* |
|        | Mean QS2(ms)   | 402                 | 361                 | <0.001* |
|        | QT/QS2 ratio   | 0.918               | 0.954               | <0.001* |
|        | QS2 Index (ms) | 524.5               | 520.7               | 0.54    |
| Female | Mean HR (bpm) | 83                  | 100                 | <0.001* |
|        | Mean QT (ms)   | 360                 | 325                 | <0.001* |
|        | Mean QS2(ms)   | 398                 | 350                 | <0.001* |
|        | QT/QS2 ratio   | 0.907               | 0.934               | <0.001* |
|        | QS2 Index (ms) | 531                 | 520.5               | 0.1     |

* = statistically significant (p<0.05)
DISCUSSION

The determination of STIs offers a convenient, non-invasive method to study left ventricular performance which was first appreciated by Weissler, Peeler and Roehl (8). By measuring Systolic Time Intervals, we can observe the cardiac function in a single recording in which time is the only variable (1). Both physiological and pathological variations are observed in STIs.

Electrical activity of cardiac myocytes differs between two sexes (9). Normally ECG of a woman’s heart demonstrates a longer QT interval than that of men (which is just the reverse in our study). For meticulous analysis of cardiovascular regulation, STIs are much more important. Alterations in systolic phase duration reflect normal adaptation of the developing heart (10). It has been found that STIs seem to lengthen with age, especially in the elderly with longer QS2 (11). For this we chose healthy young adults between 17 to 19 years of age as our study population.

In normal subject, a physiological diurnal drop of QS2 is noted (12) with an average of 10 ms (13), having maximum effect in between 4 to 8 pm (13). To negate this, we chose the time at 12 noon which is also post-absorptive state after breakfast at around 8.30 or 9 am as food intake has a positive inotropic effect (lowers QS2) and positive chronotropic effect (increases HR).

The sympathetic nervous system shows positive chronotropism, dromotropism, inotropic and bathmotropism by increasing the rate of discharge from SA node and force of contraction, resulting in increase in heart rate, preload, afterload. As sympathetic nervous system is one of the chief regulators of STIs, we chose sympathetically naive young adults as our study population.

Type and severity of Exercise and modulation of cardiovascular response are intensely interrelated. According to a study done by McConahay et al., (14) corrected QS2 did not change significantly after exercise. Our study also corroborates with this fact. Moreover, they found reduction in PEP after exercise that was further balanced by prolongation in corrected LVET of comparable magnitude and for this there was no significant alteration in QS2 (14). In another study by Martens et al., (15) it was observed that LVET and QS2 were shortened after dynamic exercise. So, the former and later study showed 2 different findings. The findings of the later study corroborate with our analysis. This difference is due to many factors like heart rate, conduction velocity, left ventricular end diastolic volume, left ventricular end diastolic pressure, afterload, and inotropic state of myocardium. Agress et al., (16) stated about the influence of different mode, position, and extent of exercise attributing to differences in the outcome in the STI parameters. Data from experiments of Lance et al., (17) and van der Hoeven et al., (18) showed that shortening of QS2 with Heart rate between 60 to 140 bpm had linear relationship that indicates that with the increase of heart rate the QS2 value decreased and vice versa. Hence exercise offers much valuable information about cardiovascular responses.

Systolic time intervals are inversely related to heart rate (1). We also observed the same relation from analysis of our study. Sex specific slight variation seen in STIs (19). Our study also corroborates with this fact. The mean HR at the resting condition were 77 beats per min in males and 83 beats per min in females in the basal state and in the post exercise state mean HR among male and female were 93 bpm and 100 bpm respectively. So, the post-exercise mean HR increased significantly, matching with the sex specific variation (Table 1). Accordingly, we also observed significantly different mean values of QT, QS: I and QT/QS2 for males and females (Table 2).

When heart rate increases QT interval shortens and when heart rate decreases QT interval increases. Both are associated with risk of arrhythmia. Abnormal prolongation may precipitate to ventricular arrhythmia like torsades de pointes whereas short QT may increase occurrence of paroxysmal atrial and ventricular fibrillation or even lead to sudden cardiac arrest (5). The corrected QT interval (QTc) allows comparison of QT values at different heart rates and helps in better detection of arrhythmia. If QTc is > 440ms in men or > 460ms in women it will be called prolonged. There will be increased risk of torsades de pointes if QTc < 500. QTc is termed abnormally short if it is < 350ms. Conventionally, a normal QT should be less than half of the preceding RR interval (5). In our study, mean QT after exercise was 325 ms in female and 343 ms in male both of which come under abnormally short QT (<350ms). Hence both cohorts were prone to arrhythmia more specifically females. Hence, electromechanical Window (EMW) has been proposed as a better predictor of arrhythmia (20) and proper long term follow up is needed for the prediction to be proved in our study population.

QT/QS2: QT/QS2 ratio may represent a reliable index of sympathetic cardiac tone (21). QT should always be less than QS2 at rest and ratio should be < 1. Inversion of this ratio is known as “the QT>QS2 syndrome” which occurs in high catecholamine levels (as in exercise), mitral leaflet prolapses, CAD or diabetes. It is more sensitive and reliable index of pro-arrhythmic danger than traditional QT prolongation. In our study we observed that both the pre and post exercise value of QT/QS2 ratio were < 1 but the post exercise value increased with respect to the pre-exercise value. Henceforth, after exercise all the subjects whose ratio increased much more should be followed up by proper investigation to prevent future incidence of arrhythmia.
De Caprio et al., (21) and Ferro et al., (22) observed that in basal conditions, the QT/QS₂ ratio was less than 1, whereas it increased progressively during the physical exercise (cycle ergometry) and became greater than 1 at peak exercise. These results demonstrate that those stimuli which induce a rise in adrenergic activity may increase the QT/QS₂ ratio. In contrast, the reflex inhibition of the adrenergic activity induced by phenylephrine is accompanied by a reduction in QT/QS₂ ratio. Therefore, the QT/QS₂ ratio might represent a reliable index of sympathetically cardiac control. Our study findings corroborate with the study of De Caprio et al., (21) except the pattern of dynamic exercise being different.

Ferro et al., (22) have showed that both QT and QS₂ had significant correlation with HR and mean QT remained shorter than QS₂ during exercise though both decreased in parallel; but in patients with coronary artery disease QT was longer than QS₂ even at rest and this could be considered a risk factor in CAD patients for ventricular arrhythmia and sudden death.

Singh (23) studied the effect of orthostatic test on STI before and after 70 degrees head up tilt (HUT) in rabbits and found immediate and significant rise in QS₂ though HR dropped and QS₂ remained prolonged even after 10 sec of the tilt. Linde et al., (24) induced Torsades de pointes (TdP) on 8 beagle dogs and then studied for STIs putting them on sling. All dogs were treated with a potent potassium channel (IKs) blocker (JNJ 303; 0.1 mg/kg/min, IV) and after 15 minutes the dogs were triggered with a bolus injection of isoproterenol (0.5 μg/kg, IV) or a mere “natural” stimulus (“fright” with an air brush) to induce a beta-adrenergic stimulation and possible induction of TdP. They concluded that in slinged dogs JNJ 303 prolonged QT, had no effect on QS₂, resulting in an enhanced QT/QS₂ ratio. High QT/QS₂ ratio predicted the induction of TdP after beta-adrenergic stimulation, as observed after isoproterenol, and after a more “natural” stimulus (“fright” with an air brush). This observation proves the importance of QT/QS₂ parameter to unearth a hidden probability of cardiac arrhythmia in an apparently healthy individual when under stress.

CONCLUSION

Left Ventricular STI and Left Ventricular performance are two integral components. Systolic Time Intervals (STI) are influenced by several anthropometric, hemodynamic, and pharmacologic factors during the evaluation of cardiac function. In our study sex specific differences were observed in the variables in the basal condition. Post exercise values of STI parameters also revealed significant sex specific variations. Exercise influenced most of the variables significantly but QS₂ did not show significant changes in both sexes. In both sex QT/QS₂ ratio increased after mild dynamic exercise but remained less than 1. If the ratio is more than 1 then it should be followed up. Hence, QT/QS₂ Ratio and QS2-Index is more important than QS₂ for prediction of arrhythmia.

ACKNOWLEDGEMENT

We express our heartfelt gratitude to Prof. Dr. Ananda Kumar Mukhopadhyay, Head of Department of Physiology, Nil Ratan Sircar Medical College and Hospital, Kolkata for providing laboratory and logistic support. We are thankful to all the participants.

CONFLICT OF INTEREST

Authors declare no conflicts of interest

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DOI: https://doi.org/10.51248/v42i3.1399
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