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The effect of exercise on the ECG criteria for early repolarization pattern

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ABSTRACT

Objective: To determine the effect of exercise and heart rate on the early repolarization (ER) pattern; focusing on the new criteria for identification of ER.

Methods: The ECG measurements on the terminal QRS notch or slur found in early repolarization were quantitated before, during and after exercise; specifically: (i) the amplitude at the onset of the notch (J_o) (ii) the amplitude at the peak of the notch (J_p), (iii) the amplitude at the end of the notch (J_t), (iv) the duration from J_o to J_p (D_1) and (v) the duration from J_o to J_t (D_2).

Results: All individuals ($N = 21$) fulfilling the criteria for ER showed complete disappearance of ER after 3 min of exercise. After 5 min of recovery, 29% of subjects showed return of the ER. The return of ER was dynamic with QRS notching of varying extent, without ST elevation, being evident first. The relationship between heart rate and ER was significant and nonlinear, best fit by a second-order polynomial, suggesting that changes in heart rate with exercise was a factor influencing the presence of the ER pattern and the parameters that define ER.

Conclusion: Each of the newly defined characteristics of the ER are modified and eventually disappear with exercise. The return of ER was dynamic with QRS notching of varying extent being evident first. The changes correlated with variations in heart rate, during both exercise and recovery, suggesting, in part, a role in the underlying mechanism of ER.

Introduction

Searching for ECG findings that identify individuals at high risk of sudden cardiac death is extremely important [1]. Early repolarization pattern characterized by J point or J wave elevation in conjunction with a slurring or notching of the terminal portion of the QRS complex was previous believed to be benign but is now considered to be a predictor of potentially fatal cardiac arrhythmias [2–5]. The association of the early repolarization pattern (ER) with cardiac mortality [6], however is not consistent across studies [7–9]. These discordances in outcomes have been attributed to lack of agreement in the definition of ER [10] or to the presence of different subgroups of ER based on the characteristics of the ER pattern [11,12]. It has been suggested that ST segment elevation alone is not significantly associated with an adverse outcome [12]. These findings refocus the need to define and characterize ER and what factors influence it.

The effect of exercise on the ER pattern has not received much attention [13–18]. The ability of exercise to modify the ER pattern has varied widely in reports from about 50% [15,16] to 100% of cases [13,14]. Almost all of these studies were published before a consensus on defining and characterizing the ER pattern was developed [10]. There is limited data on whether the pattern that is now accepted as ER is in fact modified by exercise and which components of ER might be altered by exercise. Furthermore, early studies did not use standardized testing or relate the levels of exercise with changes in the ER pattern.

The objective of this study was to evaluate the effect of exercise on the ER pattern and to determine which if any of the components of the ER pattern are modified by exercise. We further sought to determine whether any changes in the ER might be attributable to the changes in heart rate with exercise and whether individual ER characteristics were differentially altered with exercise-induced changes in heart rate.

Methods

Subjects

Individuals who were referred for exercise stress testing and had a resting ECG consistent with the ER pattern were included in this study. The resting ECGs were evaluated for the presence of MacFarlane's consensus criteria for ER and two observers had to agree on whether all criteria were met. The collection and analysis of this anonymous data was approved by the Institution's Committee for Research (IRB). Twelve lead ECGs were acquired, at a paper speed of 25 mm/s, prior to and during exercise testing which used the standard Bruce treadmill protocol. ECG measurements were made prior to exercise and at or near completion of each stage of the exercise protocol.

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The inclusion criteria included sinus rhythm on the baseline ECG and sinus rhythm or sinus tachycardia during exercise. The exclusion criteria were the presence of interventricular conduction delay, bundle branch block, significant ST-T changes (≥1 mm of ST depression) at rest or on exercise. The patients with a ST segment elevation that did not have a notch or slur were excluded. ECGs with U waves or T2 complexes that rendered measurements difficult were also excluded. Individuals with positive exercise stress tests i.e. ST segment depression of 1 mm or greater were excluded to minimize the possibility of ST changes secondary to myocardial ischemia.

Terminology

The MacFarlane's consensus criteria used for ER [10] (Fig. 1) are as follows:

1. An end-QRS notch or slur on the down-slope of an R wave in which the notch or the slur was above the baseline, and
2. Jp ≥ 0.1 mV in 2 or more contiguous leads of the 12 lead ECG (excluding V1–V3; to eliminate the possibility of Brugada syndrome) and
3. QRS duration <120 ms

For the notched QRS complex, the nomenclature is (i) the amplitude at the onset of the notch (J_o), (ii) the amplitude at the peak of the notch (J_p), (iii) the amplitude at the end of the notch (J_t), (iv) the duration from J_o to J_p (D_1) and (v) the duration from J_o to J_t (D_2). For the slurred QRS complex, the nomenclature is (i) the amplitude at the onset of the slur (J_p), (ii) the amplitude Jt at end of the slur (J_t) and (iii) the duration from J_p to J_t (D_2).

Data collection

The ECG factors were measured by one observer (HN), to eliminate the inter-observer variability, and were verified by the other observer (SWR). Age, sex, QRS duration, heart rate, condition under which ECG was done (i.e. supine, exercise stage, recovery stage) were recorded. The heart rate and QRS duration were measured manually from the ECG printout. A magnifying glass and pair of calipers were used for all measurements to minimize the intra-observer variability.

If a notch was present, the amplitude at the onset (J_o), peak (J_p) and termination (J_t) of the notch as well as its peak (D_1) and total duration (D_2) were recorded. These measurements were done at the notch with the maximum amplitude if multiple notches were present on the same ECG. All leads containing a notch were recorded. Similarly, if a slur was present, the amplitude at its beginning (J_p) and end of the slur (J_t), its total duration (D_2) and lead numbers were recorded. The ST segment was analyzed to determine if it was horizontal, up or down sloping. This was done based on the amplitude of the ST segment 100 ms from the end point of the notch or the slur to be consistent with the MacFarlane's criteria. The same measurements were made on each ECG. If the ER pattern disappeared with exercise, heart rate and the exercise stage at which it disappeared were recorded.

Data analysis

The mean and standard deviation for notch and slur parameters were calculated. The distribution of leads that showed notched or slurred QRS were evaluated. The data for each ER parameter was compared at each specific stage in exercise and recovery using ANOVA. To evaluate the relationship between changes in heart rate with exercise and ER characteristics, J_p, J_o and J_t parameters, linear and non-linear regression approaches were calculated.

Results

Twenty-one individuals, 16 males and 5 females, mean age 45.6 ± 17.5 years, met the inclusion criteria and the baseline data were recorded (Table 1). The number of leads demonstrating the ER pattern varied between individuals and not everyone showed an elevation in each of the same leads. The ER pattern was present in lead III more than any other lead. Leads II, III, and aVF, demonstrated the ER pattern (82.7%) more than the V4–V6 leads (50.7%). Among the chest leads, V5 showed the ER pattern more than other leads. On the resting ECG, 81% of the patients had an ascending ST segment and 19% had a horizontal ST segment. None of the individuals had a descending ST segment.

Most subjects showed a reduction in the ER characteristics after 3 min of exercise, such that only 29% met the criteria for ER at 3 min of exercise (Fig. 2). By stage 2 of the Bruce protocol, 6 min of exercise, none of the subjects met the criteria for ER. At this time, however, 19% of the subjects demonstrated a notch in only one lead and, thus, only met part of the criteria. In the recovery stage, the ER pattern gradually returned. None of the patients met the criteria for ER by one or 3 min of recovery. At 3 min of recovery, 38% of the participants manifested part of the criteria (one notch). At 5 min of recovery, 29% met the full criteria for ER.

Changes in the individual notch parameters (J_o, J_p, J_t, D_1, and D_2) with the various stages of exercise and in recovery were examined (Fig. 3a & b). At rest, J_p was 0.2 ± 0.08 mV, at 3 min of exercise it was 0.21 ± 0.06 mV and it was zero after that until it reappeared at 5 min of recovery, which was 0.22 ± 0.01 mV (Fig. 3). J_o at rest was 0.13 ± 0.08 mV, at 3 min of exercise it was 0.11 ± 0.04 mV and at 5 min of recovery it was 0.1 ± 0.1 mV. At rest, J_t was 0.07 mV ± 0.05, at 3 min of exercise it was 0.04 mV ± 0.04 and at 5 min of recovery it was 0.03 mV ± 0.0. At rest, D_1 was 16.67 ± 6.67 ms, at 3 min of exercise it

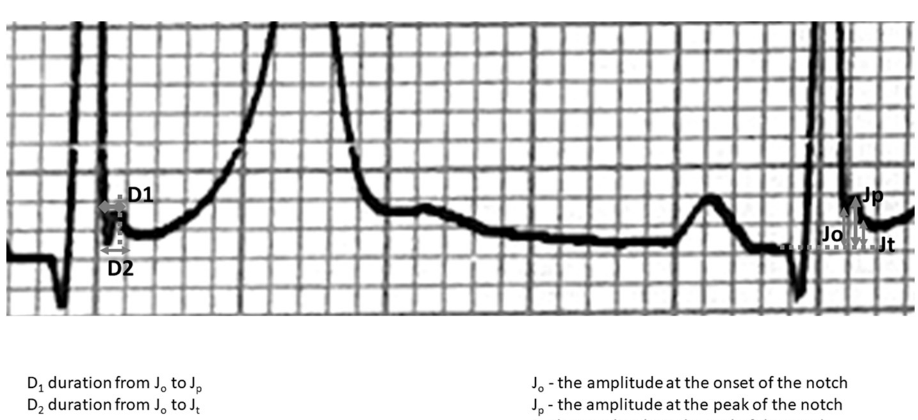

Fig. 1. Shows example of an ECG with the criteria for early repolarization changes and the nomenclature of the criteria specifically for notched QRS complex: (i) J_o – the amplitude at the onset of the notch (ii) J_p – the amplitude at the peak of the notch (iii) J_t – the amplitude at the end of the notch (iv) D_1 – the duration from J_o to J_p (v) D_2 – the duration from J_o to J_t.

Table 1
shows the baseline characteristics of individuals with early repolarization at rest prior to exercise.

Characteristic	Mean	SD
Age (yr.)	45.6	17.5
Heart rate (bpm)	65.1	8.0
QRS duration (ms)	83.3	13.9
J_o (mV)	0.13	0.08
J_p (mV)	0.20	0.08
J_t (mV)	0.07	0.05
D_1 (ms)	16.67	6.67
D_2 (ms)	32.89	6.35
Horizontal ST (%)	19%	
Ascending ST (%)	81%	
Descending ST (%)	0%	
II (%)	81%	
III (%)	86%	
aVF (%)	81%	
V4 (%)	38%	
V5 (%)	71%	
V6 (%)	43%	

For notched QRS complex (i) J_o – the amplitude at the onset of the notch (ii) J_p – the amplitude at the peak of the notch (iii) J_t – the amplitude at the end of the notch (iv) D_1 – the duration from Jo to J_p (v) D_2 – the duration from J_o to J_t.

was 16.0 ± 5.8 ms and at 5 min of recovery it was 15.0 ± 5.0 ms. At rest, D_2 was 32.89 ± 6.35, at 3 min of exercise it was 30.83 ± 8.37 and at 5 min of recovery it was 35.0 ± 5.8 ms.

The changes in the mean J_o, J_p, and J_t with exercise duration and recovery demonstrate the time course of the disappearance of the ER pattern and its slow recovery (Fig. 4). There were highly significant (ANOVA, $p < 0.0001$) changes in each of the three ER parameters from each stage of exercise to the next as well as in recovery. The average of the notch parameters, J_o, J_p, and J_t, measured at 5 min of recovery, however, were similar to those measured at 3 min of exercise.

The notch parameters were averaged for all participants. Those who did not meet the ER criteria were assigned a value of zero for the notch parameters and were included in calculating the mean results. The average values for J_o, J_p and J_t at 5 min of recovery are smaller compared to those at 3 min of exercise (Fig. 4).

We next sought to relate the ER pattern to the heart rate during exercise. The average heart rate for those meeting the ER criteria during stage 1 of exercise was 90.0 ± 8.9 beats per minute (BPM). This was the average heart rate before complete disappearance of the ER. In stage 2 of exercise, the average heart rate was 115.1 ± 21.3 BPM, which corresponds to complete disappearance of ER. During 5 min of recovery, where ER pattern started to reappear, the average heart rate was 84 ± 9.5 BPM. As a point of reference, resting heart rate when ER was evident in all individuals was 65.1 + 8.0 bpm. During exercise, the notch parameters decreased rapidly with increasing heart rate and remained at zero until the recovery period during which return of the notch parameters was gradual. An example of ER parameters and heart rate in one individual and the pattern in the entire cohort are demonstrated (Fig. 5). The changes in one individual are illustrated in the resting ECG (Panel A), ECG with exercise (Panel B) and the ECG at 5 min of exercise (Panel C). The mean values for the ECG criteria for ER, for this individual, at different heart rates indicates that the relationship to heart rate is non-linear (Panel D). The different characteristics of ER according to heart rate are shown for all individuals (Panel E). In the early stage of recovery from exercise, the notch started to reappear but did not meet the ER criteria. A nonlinear relationship was clearly evident. A straight-line relationship (fit) would not be appropriate for the data because it would fail to capture the rapid decrease with increasing heart rate followed by the disappearance of each factor. Considering all subjects, a second-order polynomial, $B_0 + B_1 x + B_2 x^2$, was a better (fit) description of the relationship with heart rate and was statistically significant ($p < 0.05$) for the each of the characteristics of ER.

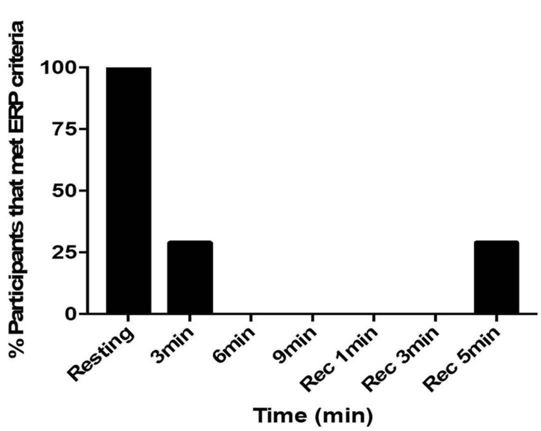

Fig. 2. Shows the percentage of participants meeting ER criteria at various stages of exercise and recovery. There were no (zero) cases after 3 min of exercise and until 5 min of recovery (Rec).

Discussion

We present a comprehensive analysis of the effect of a standardized exercise on each of the newly defined characteristics of the ER pattern. Exercise, at an early stage, reduced the magnitude of each of the ER characteristics and increased exercise duration abolished all ER features. These changes in the ER pattern were significantly related to changes in heart rate with exercise and were clearly not linear but rather appeared to be best fitted by a second-order polynomial. We also demonstrated a slow recovery of the ER pattern after cessation of exercise.

Previous evaluations of the effect of exercise on ER were mainly done in less standardized manners and without an assessment of the ER characteristics. Goldman reported that all of the twenty-five patients who were subjected to a standard Master's exercise test had RS-T segments return to the isoelectric line ‘immediately’ upon commencing exercise [13]. The ECGs shown in the paper were ST elevation without notching or slurring [13]. In contrast, Wasserburg reported only 58% of 24 persons with ER showed resolution of ER with exercise and the other individuals “*continued to exhibit a distinctly elevated S-T segment following exercise and indeed, in two, the segmental elevation became more apparent*” [15]. Chelton & Burchell did an exercise stress test on only 17 of their 100 cases of ER and reported that in each case “immediately after (commencing) exercise the RT segment were at the isoelectric level” [14]. Chapman and Overholt reported on 20 cases of ST elevation and commented that in 45% (9) of the cases the “RST segment returns to the isoelectric line immediately following exercise” [16]. Pearl et al studied 25 healthy black men between 17 and 21 years of age and reported that exercise at a simulated altitude of 4000 m caused a lowering of the J point in several leads and exercise at high altitude, eliminated the appearance of ER [17].

A horizontal or descending ST elevation has been reported to be associated with a worse prognosis than was an ascending ST segment [4,19]. While horizontal or descending ST segments comprised only 20% of our cases with ER, these cases behaved in the same way as upsloping ST segments, specifically exercise produced complete reversal of the ST elevation and abolished the ER pattern. Cay et al reported that subjects with ER had significantly decreased maximum heart rate, heart rate increment and heart rate decrement compared to the control group [20]. This observation did not influence our findings as all subjects attained a heart rate that was associated with the disappearance of the ER pattern.

Production of the typical ER pattern requires regional disparity during repolarization i.e. some regions of the myocardium repolarize earlier than others [21]. Current flow toward the ER region creates positive ST-segment displacement or ST-segment elevation in the ECG leads reflecting electrical activity in that region [21,22]. An early theory to

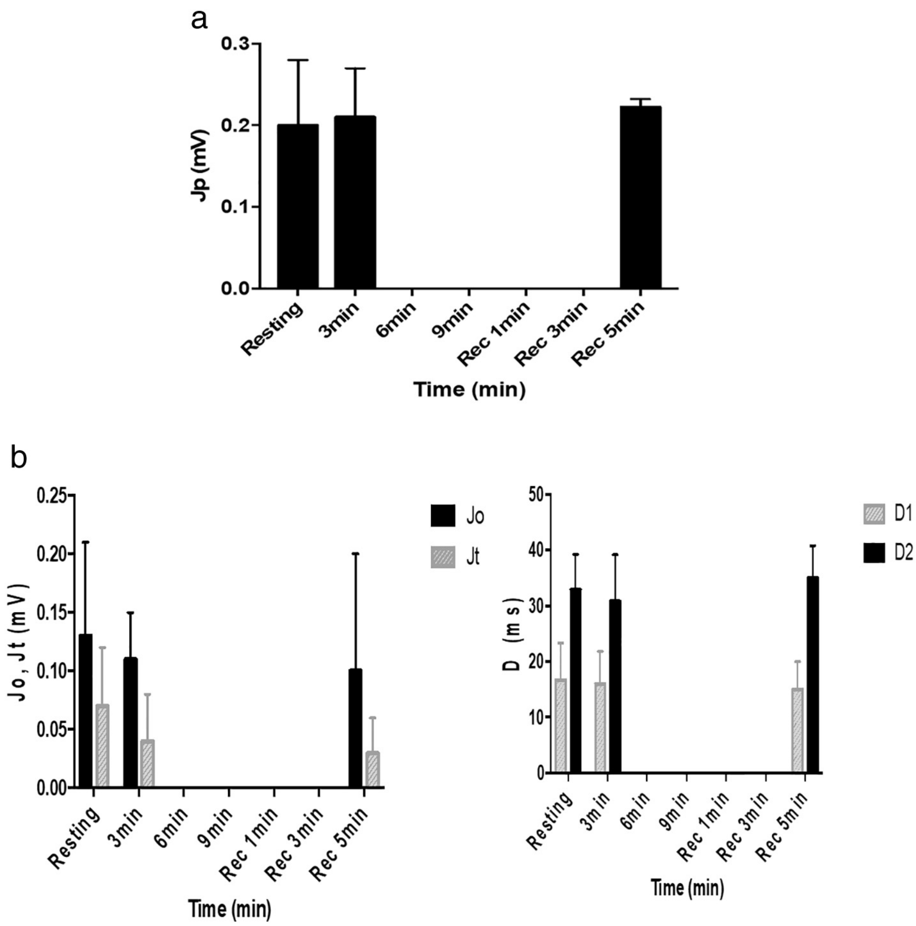

Fig. 3. a. Shows the average J_p for all participants meeting ERP criteria at various stages of exercise and recovery. b. Shows the average J_o and J_t for all participants meeting ERP criteria at various stages of exercise and recovery (Left panel). The average D_1 and D_2 for all participants meeting ERP criteria at various stages of exercise and recovery (Right panel).

explain ER, attributed it to an overlap between the end of depolarization and beginning of repolarization [13,14,23]. More recently, ER has been related to a modification of the time course of repolarization across the ventricular wall secondary to a selective decrease of the epicardial action potential durations or magnitude [24,25]. This drop can be caused by a number of factors including increases in the outward repolarizing currents, such as I_{to}, or decrease in the inward currents such as I_{Na} and I_{Ca}, or both [24,26]. Direct pharmacological inhibition

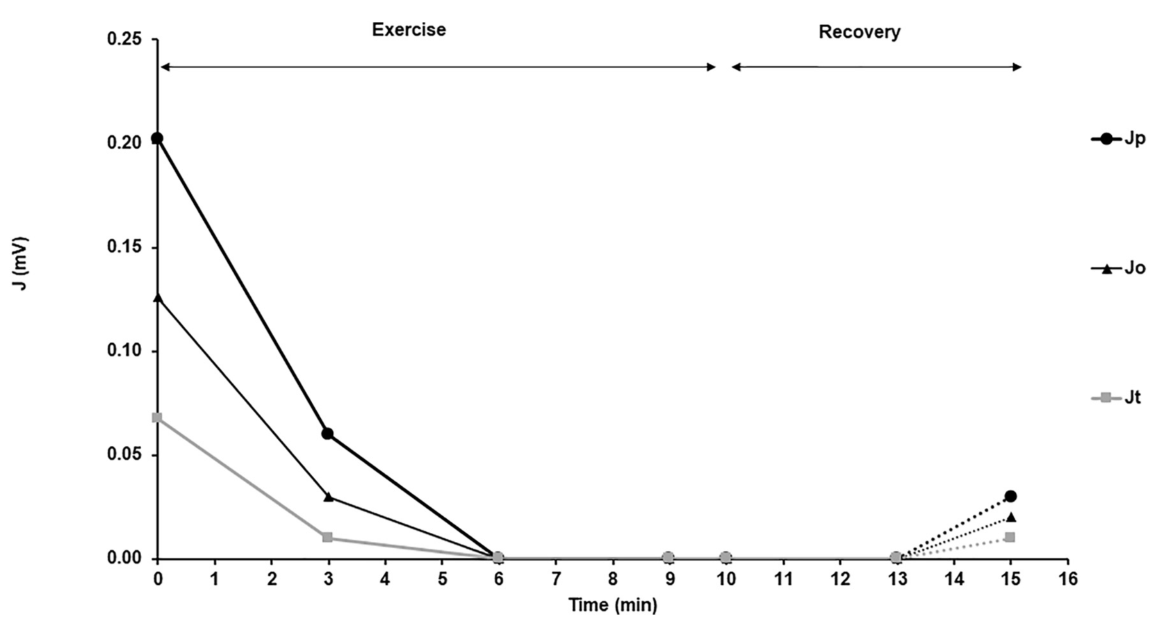

Fig. 4. Shows the average J_p, J_o, and J_t for all participants at various durations (stages) of exercise and recovery.

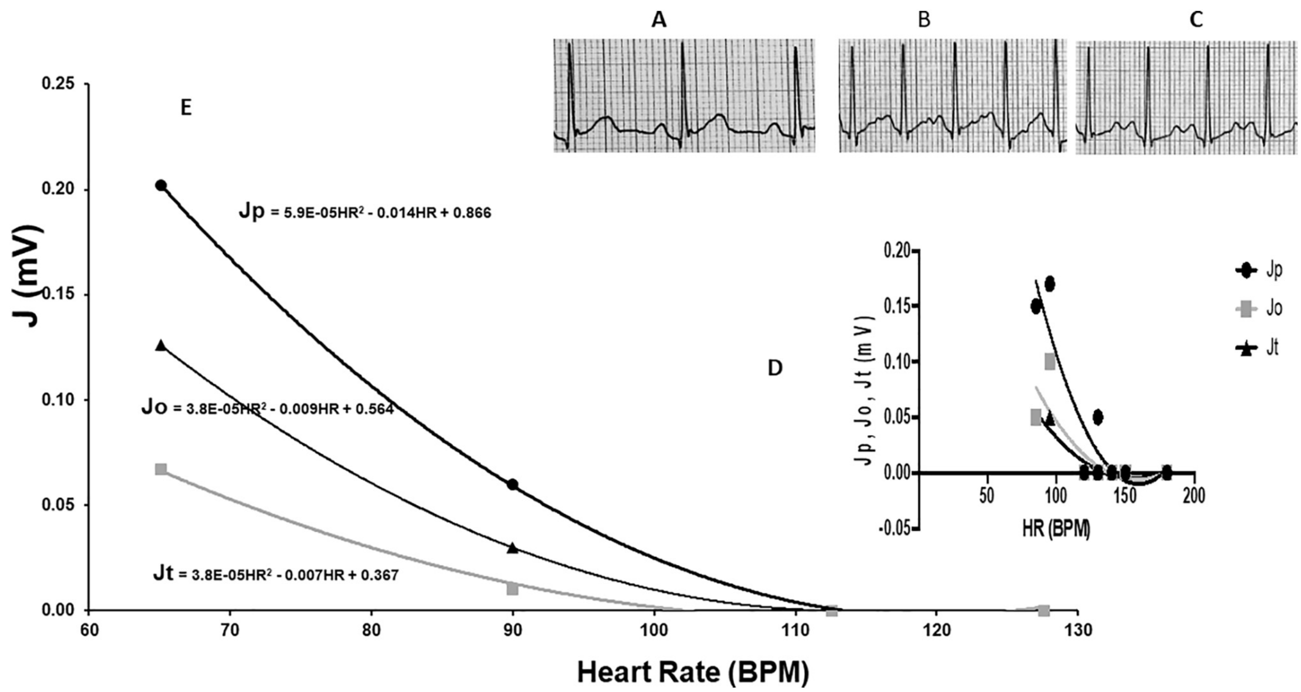

Fig. 5. Shows the early repolarization changes during exercise and recovery in relation to the heart rate. The changes in one individual are illustrative. Repolarization changes are shown in the resting ECG (Panel A), ECG with exercise (Panel B) and the ECG at 5 min of exercise (Panel C). Panel D shows the mean values for the ECG criteria for ER at different heart rates and the nonlinearly of the relationship, in the same individual, is apparent. The relationship of the different characteristics of ER with heart rate are shown for all individuals (N = 21) (Panel E). A nonlinear regression is evident for notch parameters which is a second-order polynomial of best fit for J_p, J_o, and J_t for all participants versus heart rate during exercise. The parameters of the polynomial equations for each relationship is displayed.

of the I_{to} current produced a reduction in the epicardial AP notch and corresponding reduction in the magnitude of the J wave [24]. In recent years, the notch at the end of the QRS complex has been proposed to be due to intraventricular conduction delay [27].

In our study, the average of J_p remained relatively constant as exercise time and heart rate increased. However, J_p was higher during exercise compared to recovery at the same heart rate and in the same individual by an average of 0.2 mV. Thus, it appeared that J_p has a time-dependent component. J_o and J_t showed slightly more variation. Reduction in the ER characteristics were most clearly identified with prolonged stages of exercise. This finding correlates with increased heart rate and a non-linear (second-order polynomial) relationship between heart rate and loss of ER. Similarly, a clear return of the ER pattern was found with increased recovery time. Although heart rates had not completely returned to baseline during the time period of monitoring in recovery, there was a relationship between heart rate reduction and return of ER. Interestingly, close to one third of the individuals demonstrated ER at 3 min of exercise and again at 5 min of recovery.

The dynamic nature of the ER features was demonstrated. In recovery (from exercise) only some of the characteristics re-appeared but there were not enough or at the defined level to fulfill the criteria for ER, e.g. a notch was too small or was not present in contiguous leads. These data suggest that the characteristics of ER maybe dynamic. As a result, an individual may have ER findings under some conditions and not at others.

With the caveat that this study examined exercise which may have multiple effects on cardiac repolarization, it is instructive to consider the possibility that the ER pattern is influenced by exercise-induced increases in heart rate. While this study did not examine the molecular mechanisms responsible for ER, their consideration can be helpful to explain our findings. The effect of heart rate may be attributed to the effect of heart rate on the slow component of I_{to} current, which decrease with faster heart rates [24]. This is followed by the attenuation of the magnitude of the notch in phase 1 [25]. Notch attenuation and restoration of epicardial repolarization with elevated heart rates may eliminate the ER pattern [28]. Reduction in ST segment elevation has been attributed to reduced availability of I_{to} at faster heart rates due to slower recovery of the current from inactivation [29]. Increase in parasympathetic modulation may account for the J waves in athletes [30]. This finding may explain why exercise and increased heart rate are associated with disappearance of the ER pattern in individuals following completion of a race [31]. It has been hypothesized that increased vagal tone, lower heart rate, and higher cardiovascular fitness are factors responsible for the increased prevalence of ER in younger adults [21] and lower prevalence in older individuals [32]. To the extent that this is a valid mechanism, the withdrawal of vagal tone during exercise may be another factor accounting for the disappearance of ER with exercise.

Several limitations of the study should be discussed. First, we studied a relatively small number of individuals. However, the abolition of the ER pattern with exercise was uniform and was found in 100% of individuals suggesting that there was no ambiguity or requirement for a larger sample size to define the effect. Furthermore the number of individuals evaluated was similar to or larger than previous studies on the effect of exercise on ER [13–17]. Second, the recovery generally did not go beyond 5 min for the majority of the patients as per the exercise protocol. Had we collected more data, we could perhaps identify the time after which all participants would show the reappearance of their ER pattern. Third, the heart rate data for our study was collected from ECG measurements at set intervals of 3 min during exercise. If we had access to continuous heart rate monitoring and ECG data, we could monitor the ER parameters continuously. While this would have permitted a more precise timing of ER disappearance it would not have altered the overall high proportion of cases that demonstrated the disappearance of ER with exercise. Lastly the conclusion about heart rate must be viewed in the context that changes in heart rate were produced by exercise which itself may be associated with other effects on cardiac repolarization.

Conclusion

Each of the newly defined characteristics of ER is modified and indeed can be completely abolished with exercise. These changes correlated with increases in heart rate that likely influence the mechanism of ER. Importantly clinicians should be aware that the individual characteristics of ER are dynamic and recognize the potential heart rate dependency of the ER pattern.

Acknowledgements/Statement of competing interests

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