Increased Dispersion of Ventricular Repolarization during Recovery from Exercise

HHM Draisma, B Hooft van Huysduynen, CA Swenne, AC Maan,
EE van der Wall, MJ Schalij

Leiden University Medical Center, Leiden, The Netherlands

Abstract

In a recent study, frequent ectopy during recovery from exercise was reported to bear an increased risk for death, whereas frequent ectopy during exercise did not. We compared exercise- and recovery ECGs to corroborate the hypothesis that dispersion of ventricular repolarization is augmented during recovery. In healthy male subjects spanning a large range of fitness, we analyzed all 10-s ECGs recorded during maximal oxygen consumption tests. We selected for every recovery ECG the best heart rate-matched exercise ECG in the same subject, and compared several ECG parameters between the matched ECGs. The observed recovery-exercise differences in these parameters indicate that dispersion of ventricular repolarization increases early during recovery, particularly due to increased action potential duration heterogeneity. Increased vagal tone during recovery may be the cause of this potential threat, apparently most outspoken in highly fit subjects.

1. Introduction

It has not been established whether the risk of death increases due to strenuous exercise, however, results from a recent study conducted on a general hospital population suggest, that ventricular ectopy during recovery from exercise bears an independent mortality risk [1].

In the last decade, assessment of dispersion of ventricular repolarization (DOR) from the ECG to quantify the vulnerability of the heart to re-entrant arrhythmias, has gained interest. In the light of a possibly increased arrhythmia risk during recovery, we hypothesized that DOR might be augmented during the recovery phase, with respect to actual exercise. Here we present the preliminary results of a study in which we sought to further establish the concept of electrophysiological hysteresis [2] in the setting of maximal exercise tests.

2. Methods

The study population consisted of 57 healthy male subjects (aged 33±11 years), spanning a large range of fitness. Bicycle ergometry began with a load of 40 watts (W). This load was increased by 20W per minute until maximal exercise was reached. Ten-second ECG recordings were intermittently recorded on an exercise electrocardiograph during rest, exercise and recovery (up to 5 minutes after maximal exercise). Later, these recordings were downloaded to a personal computer for subsequent analysis.

Within the study group, two subgroups of unfit and highly fit subjects were defined on the basis of their maximal oxygen consumption (VO_{2max}), baroreflex sensitivity (BRS), left ventricular mass (LVM) and resting heart rate (HR).

For each subject, the ECG with the highest HR, separating exercise and recovery, was identified. Subsequently, we composed exercise–recovery ECG pairs on the basis of the closest matching HR. Each thus matched ECG pair was assigned its corresponding recovery time (RCT, time after peak exercise) and percentage of the heart rate reserve (HRR; the difference between the HRs during maximal exercise and during supine rest). Figure 1 illustrates this procedure for a typical subject.

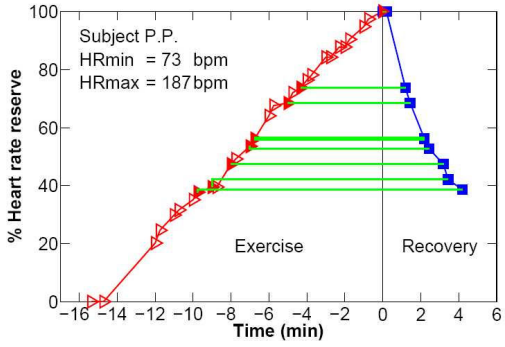

Figure 1. Symptom-limited exercise test in a normal subject. Triangles: exercise; squares: recovery. Exercise–recovery ECG pairs are indicated by solid markers and connected by horizontal lines. QRST vector magnitude signals in the ECG pair connected by the thick horizontal line are shown in Figure 2. HRmin, HRmax: resting HR (0 %HRR) and maximal HR (100 %HRR), in bpm.

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We used our MATLAB research-oriented ECG/VCG analysis program LEADS (Leiden ECG Analysis & Decomposition Software) for analysis of the ECGs. This system is described in detail elsewhere in this issue [3]. In brief, LEADS calculates a vectorcardiogram from the ECG using the inverse Dower matrix and detects the QRST complexes using the spatial velocity signal. After coherent averaging of selected beats, the program assesses the end of the QRS complex and computes the end of the T wave with the steepest tangent method. In a final interactive procedure, the operator reviews and edits the end of QRS estimate in the averaged beat.

Six parameters, derived from the averaged beat by the LEADS program, were used to characterize a given ECG: QRS duration, QT_{peak}, QT_{end}, T-wave area symmetry ratio (SR_{area}), maximal T wave magnitude (maxT), and ventricular gradient magnitude (VG). QT_{peak}, QT_{end}, SR_{area} and maxT were computed in the vector magnitude signal. SR_{area} was calculated as the ratio of the early T wave area (from the end of the QRS complex to the apex of the T wave) to the late T wave area (from the apex to the end of the T wave). VG, which is considered to be a measure for action potential duration (APD) heterogeneity [4] was computed by vectorially adding the QRST areas in the scalar X-Y-Z leads.

Exercise and recovery values of these six parameters were compared in the total study group (N = 57), in the subgroup of unfit subjects (N = 10) and in the subgroup of highly fit subjects (N = 8). Data was pooled in %HRR and in RCT bins, 10% and 1 minute wide, respectively. There were data in six RCT bins (centered around 0, 1, …, 5 minutes post peak-exercise) and nine %HRR bins (centered around 20, 30, …, 100 %HRR). Presence of exercise–recovery hysteresis was tested in the total study group and in the unfit and highly fit subgroups by comparing the exercise and recovery contents of each %HRR and RCT bin, using paired t-tests at the 5% level. The amount of hysteresis in a given ECG parameter in a given bin was expressed as a fraction (the difference between the recovery and the exercise value, divided by the exercise value). Finally, differences between the unfit and highly fit subgroups were tested in a similar way, this time using unpaired t-tests at the 5% significance level.

3. Results

At similar heart rates during exercise and recovery, QT_{peak}, QT_{end} and SR_{area} were smaller during recovery, while maxT and VG were larger (see Figure 2 for a typical example). QRS durations during exercise and recovery were not significantly different.

Significant exercise–recovery hysteresis was detectable for each ECG parameter, irrespective of whether the data was distributed over %HRR bins or over RCT bins. Maximal hysteresis in QT_{peak} and in QT_{end} occurred after 1 minute RCT or 20–60% HRR; recovery values differed 5.6–8.6% from exercise values. Maximal hysteresis in maxT and in VG occurred after 2 minutes RCT or 60% HRR; recovery values differed 52–89% from exercise values. Maximal hysteresis in SR_{area} occurred after 1 minute RCT or at 30% HRR; recovery values differed 20% from exercise values. As an example, a summary of the measured VG values in all subjects and a statistical exercise–recovery comparison is provided in Figure 3.

The amplitude of the hysteresis is larger in highly fit than in unfit subjects (see Table 1). VG and maxT roughly assume the double value after 1 minute RCT or at 60% or 40% HRR, respectively.

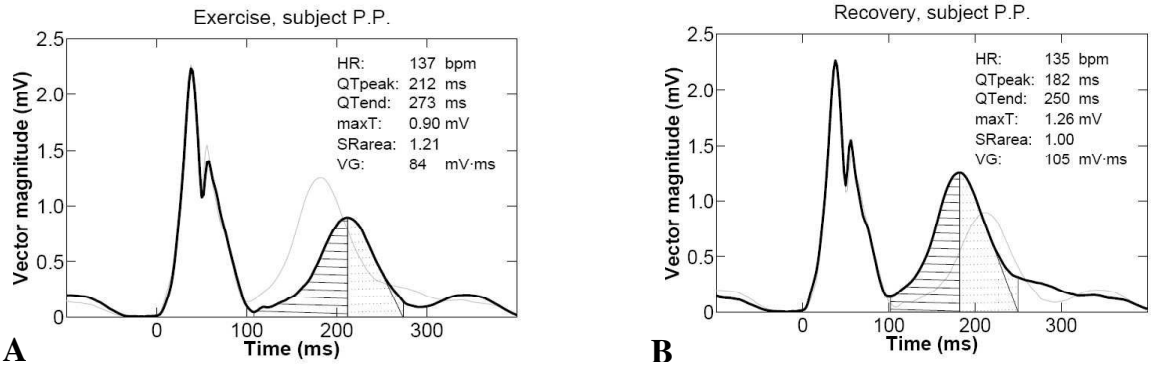

Figure 2. Vector magnitude of the averaged QRST complexes obtained from the exercise–recovery ECG pair highlighted in Figure 1. In panel A the exercise ECG is displayed in black; the recovery ECG is displayed in grey for visual comparison. Panel B displays the recovery ECG in black, and the exercise ECG in grey. All parameter values in panel A relate to the exercise ECG, and in panel B to the recovery ECG. Left hatched area: area under the curve between end-of-QRS and peak T. Right hatched area: area under the curve between peak T and end-of-T.

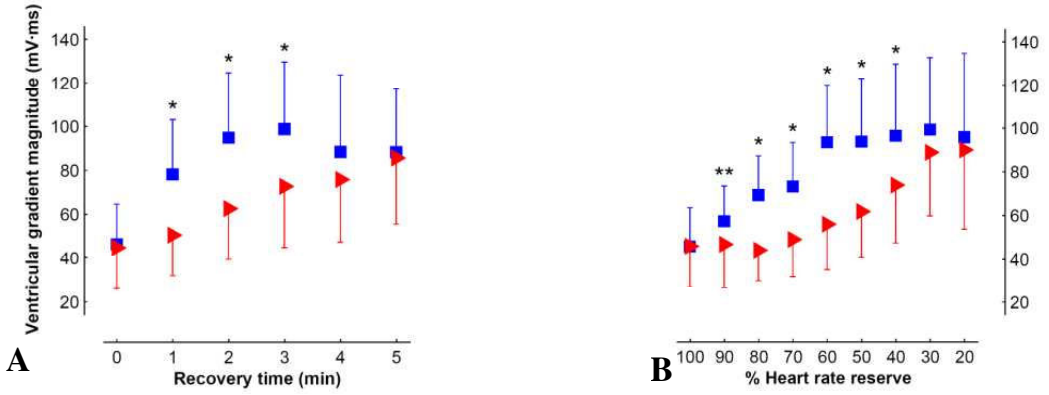

Figure 3. Ventricular gradient magnitude in heart rate-matched ECGs recorded during exercise (triangles) and recovery (squares) in all subjects, ordered according to RCT (Panel A) and %HRR (Panel B). Significant recovery-exercise differences are indicated by single (P<0.05) and double (P<0.01) asterisks. Error bars: standard deviations from the mean.

Parameter	RCT (min)	Unfit hysteresis	Highly fit hysteresis	% Diff.
QT_{peak}	2	–9.3 ms	–24 ms	+160
QT_{end}	1	–7.5 ms	–27 ms	+255
maxT	1	+290 µV	+570 µV	+96
SR_{area}(NS)	2	–0.23	–0.25	+8
VG	1	+24 mV·ms	+41 mV·ms	+71

Table 1. Maximal exercise-recovery hysteresis differences between highly fit and unfit subjects, related to the unfit hysteresis value, and ordered according to RCT. NS: nonsignificant.

4. Discussion and conclusions

DOR is a physiological phenomenon that is caused by the added effect of heterogeneity in activation time and heterogeneity in APD in the ventricles. For example, epicardial action potentials are shorter than endocardial action potentials. As a consequence, the epicardium, while being activated last, repolarizes first [5]. Net electrical forces in the heart, giving rise to a non-zero heart vector, occur only when there are momentary regional differences in transmembrane potentials. Hence, T wave generation rests on DOR [4].

Notwithstanding its possible mechanistic link with cardiac mechanical activity, DOR is currently most often thought of as a condition facilitating reentrant activity. Tacitly assuming that DOR is closely linked to dispersion of refractoriness [6], an increase would widen the time window during which an extrasystole could initiate a tachyarrhythmia [7]. We conducted the current study because increased DOR might constitute a risk factor in subjects with triggering events (ectopic activity). Our study demonstrates that, in heart rate-matched ECGs, QT_{peak} and QT_{end} intervals are briefer, the T wave is more symmetric, and maxT and VG are larger during recovery from exercise than during actual exercise. These ECG changes are consistent with the hypothesis that during recovery from exercise the repolarization heterogeneity is enhanced due to enhanced APD heterogeneity. This can be concluded from the following four arguments:

1. Shorter APD during recovery. The decreases in QT_{peak} and QT_{end} during recovery are suggestive of a generalized APD shortening shortly after exercise. This APD shortening is likely caused by the increased adrenergic influences during recovery from exercise: norepinephrine and epinephrine levels, increasing during exercise, continue to increase further after exercise [8]. Parasympathetic outflow, which is very little during actual exercise, resumes during recovery [9], which creates a situation of both enhanced adrenergic and cholinergic influences during recovery from exercise in comparison to during actual exercise. However, the study by Inoue and Zipes has shown that, at identical heart rates, the ventricular effective refractory period (and, hence, likely, APD) is smaller under combined elevated sympathetic and parasympathetic stimulation [10]. The latter may account for the observed QT_{peak} and QT_{end} shortening.

2. Increased DOR during recovery. The more symmetrical T wave in combination with the increased T wave amplitude during recovery from exercise, indicate [11] increased DOR with respect to actual exercise.

3. Similar depolarization. The absence of exercise–recovery hysteresis in QRS duration suggests that ventricular depolarization did not dramatically change (compare panels A and B in Figure 2 for a visual impression). Therefore, it is not very likely that the

observed T wave changes were secondary changes, that is, they were caused by altered intraventricular conduction. This leaves primary changes (APD changes) as the more likely cause of the modified T wave morphology.

4. Increased APD heterogeneity. The increase in VG during recovery signifies an increased APD dispersion during recovery. This is likely to occur because APD alterations in response to a given combination of sympathetic and parasympathetic stimulation differ regionally. For example, at the endocardium, there is no independent parasympathetic effect on APD; parasympathetic stimulation mainly reduces sympathetically induced APD shortening [12]. However, stimulation of the epicardium by acetylcholine has an independent effect, and can slightly increase, but, at higher concentrations, also reduce action potential duration.

Our data demonstrates furthermore that SR_{area}, maxT and VG have a much larger hysteresis in highly fit than in unfit subjects. A possible cause for this is the stronger parasympathetic reactivation during recovery in highly fit subjects, as demonstrated by Imai and colleagues [13], in combination with the increased DOR as associated with hypertrophied hearts.

In conclusion, our study provides strong supportive evidence of increased DOR during recovery from maximal exercise in normal male persons of any fitness level. Moreover, the results suggest that repolarization heterogeneity during recovery is increased despite generally shorter cycle lengths, and that this increase is due mainly to augmented action potential duration heterogeneity. We also demonstrated that, after maximal exercise, highly fit persons have a much larger hysteresis than unfit subjects. Obviously, an explicit exercise–recovery hysteresis such as observed in our study will not exist to this extent at lower peak exercise intensity levels. It should be further investigated whether this effect renders individuals more susceptible to arrhythmia induction (e.g., by a triggering ventricular extrasystole) during recovery from exercise.

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Address for correspondence:

Cees A. Swenne, PhD
Cardiology Department
Leiden University Medical Center
PO Box 9600
2300 RC Leiden
The Netherlands
E-mail: c.a.swenne@lumc.nl