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The importance of ST elevation in $V_{2–4}$ ECG leads in athletes

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Background: Early repolarization in the anterior ECG leads ($ERV_{2–4}$) is considered to be a sign of right ventricular (RV) remodeling, but its etiology and importance are unclear. *Methods:* A total of 243 top-level endurance-trained athletes (ETA; 183 men and 60 women, weekly training hours: 15–20) and 120 leisure-time athletes (LTA; 71 men and 49 women, weekly training hours: 5–6) were investigated. The $ERV_{2–4}$ sign was evaluated concerning type of sport, gender, transthoracic echocardiographic parameters, and ECG changes, which can indicate elevated RV systolic pressure [left atrium enlargement (LAE), right atrium enlargement (RAE), RV conduction defect (RVcd)]. *Results:* Stroke volume and left ventricular mass were higher in ETAs vs. LTAs in both genders ($p < 0.01$). Prevalence of the $ERV_{2–4}$ sign was significantly higher in men than in women [$p = 0.000$, odds ratio (OR) = 36.4] and in ETAs than in LTAs ($p = 0.000$). The highest $ERV_{2–4}$ prevalence appeared in the most highly trained triathlonists and canoe and kayak paddlers (OR = 13.8 and 5.2, respectively). Within the ETA group, the post-exercise LAE, RAE, and RVcd changes developed more frequently in cases with than without $ERV_{2–4}$ (LAE: men: $p < 0.05$, females: $p < 0.005$; RAE: men: $p < 0.05$, females: $p < 0.005$; RVcd: N.S.). These post-exercise appearing LAE, RAE, and RVcd are associated with the $ERV_{2–4}$ sign (OR = 4.0, 3.7, and 3.8, respectively). *Conclusions:* According to these results, $ERV_{2–4}$ develops mainly in male ETAs due to long-lasting and repeated endurance training. The $ERV_{2–4}$ sign indicates RV's adaptation to maintain higher compensatory pulmonary pressure and flow during exercise but its danger regarding malignant arrhythmias is unclear.

Keywords: pulmonary artery pressure, early repolarization, exercise ECG, endurance athletes, right ventricular adaptation

Introduction

Early repolarization (ER) – a concave-shaped ST elevation – is a frequently described ECG change. It has been known for 50 years; nevertheless, its significance has not been clarified yet. ER may have anterolateral and/or inferolateral manifestation (1, 33), but in athletes, it appears most frequently in the $V_{2–4}$ anterior precordial leads ($ERV_{2–4}$). The prevalence of $ERV_{2–4}$ in athletes ranges from 35% to 91% depending on its definition (12, 16). The etiology of $ERV_{2–4}$ is unclear. The role of exercise is unquestionable, but impact of drugs (e.g., cocaine) was also presumed (16). Cardiac magnetic resonance examinations proved that there is no ischemic mechanism in the manifestation of ER (29).

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Some experts assume that (1) $ERV_{2–4}$ is a harmless ECG alteration; (2) however, others agree that $ERV_{2–4}$ may reflect right ventricular (RV) remodeling and may have causal role in malignant arrhythmias.

(1) Studies dealing with ECG changes in athletes considered $ERV_{2–4}$ (and some other ECG changes) as a physiological phenomenon depending on gender (they were less frequent in women), type of sports, and level as well as duration of training. These ECG changes were explained by increased parasympathetic tone, RV, septum and left ventricular (LV) hypertrophy, right atrium enlargement (RAE), and left atrium enlargement (LAE) (5, 16, 36). The prevalence of $ERV_{2–4}$ also depends on the total burden of exercise; therefore, data vary considerably (22, 35).

(2) $ERV_{2–4}$ may also be dangerous because of its close relationship with Brugada syndrome and arrhythmogenic RV cardiomyopathy (ARVC). It is well-known that Brugada syndrome may cause life-threatening ventricular tachyarrhythmias. Both $ERV_{2–4}$ and Brugada syndrome respond similarly to pharmacologic agents, neuromodulation, and exercise (15, 17). A similar mechanism is supposed for $ERV_{2–4}$ and Brugada ECG abnormalities, i.e., the plateau of epicardial action potential is lower than that of the endocardium leading to ST-segment elevation on the electrocardiogram (37). ARVC is another syndrome with predilection to malignant arrhythmias and it has been found to be part of the cause of sudden cardiac death (SCD) of athletes (3, 24).

The role of RV alteration in the etiology of athletes' SCD has just recently been identified. ARVC-like histological alterations (RV dysplasia and remodeling) may be developed by endurance sports (18–20, 30, 38). RV dilatation has also been demonstrated in endurance-trained male athletes (6, 21). RV and right atrium dimensions were significantly greater in endurance-trained athletes than in strength-trained athletes and controls (8). The underlying cause of the morphological alterations of the RV may be the elevation of pulmonary artery pressure (PAP) during exercise. This elevation of PAP correlates with the time spent with highly intensive training (7, 31). During exercise, the mean PAP (mPAP) depends primarily on the blood flow (Q), but also on pulmonary vascular resistance (PVR) and left atrium pressure (LAP): $mPAP = (PVR \times Q) + LAP$ (8, 20, 26, 32). Among transthoracal echocardiography (TTE) parameters, the LV stroke volume (SV) correlates best with systolic PAP (7, 8). It has been demonstrated that during exercise the systolic PAP can be significantly increased even up to 80 mmHg accompanied by temporary enlargement of the RV. It has also been proven that elevated PAP and RV diameters return to the basic state some minutes after the termination of the exercise (6, 19, 26).

SCD of athletes is a rare clinical event (0.5–1/100,000 athletes/year), but it is 2–4 times more frequent than in the sedentary members of the corresponding age group (14).

It is interesting that the prevalence of SCD in female athletes is 5–20 times rarer than in male ones (2, 14, 23). The cause of this difference is unclear; one of the supposed causes may be milder LV hypertrophy due to the regulatory effect of estrogens in women (9, 28).

All publications dealing with ER agree that $ERV_{2–4}$ needs further investigation to clarify its predilection to malignant arrhythmias just like its origin and hemodynamic importance (12, 16).

We intended to find an explanation for the etiology and hemodynamic impact of the $ERV_{2–4}$ phenomenon. For this reason, the prevalence of $ERV_{2–4}$ has been studied in different endurance sports in male and female athletes separately. We analyzed the relationship of the $ERV_{2–4}$ sign with other ECG changes and TTE parameters indicating elevated PAP.

Materials and Methods

The 12-lead ECG, exercise ECG and TTE records of 243 top-level Caucasian endurance-trained athletes (ETA; weekly training: 15–20 h) and 120 Caucasian leisure-time athletes (LTA; weekly training: 5–6 h) were investigated. The following ETAs participated in the study: triathletes (54 men/18–35 years, mean age: 25 years and 22 women/18–33 years, mean age: 20 years), canoe and kayak paddlers (79 men/18–35 years, mean age: 24 years and 18 women /18–30 years, mean age: 21 years), soccer players (35 men/18–32 years, mean age: 24 years), handball players (15 men/20–35 years, mean age: 28 years), and water polo players (20 women /18–30 years, mean age: 22 years). LTAs: 71 men/18–35 years, mean age: 29 years and 49 women/18–35 years, mean age: 27 years. From the above athletes, only triathletes practice a typical endurance-type sport, but the other investigated sports also involved high levels of endurance.

ECGs were implemented by a Cardiosys H-01 recorder (Experimetria Ltd., Budapest, Hungary) in supine position. ECG changes at rest (1 day after last training) and following exercise (using Bruce protocol) were matched. The age-predicted maximal heart rate (HR) was targeted. For standardization of the interpretation, exercise ECGs were analyzed when the HR fell between 100 and 120 bpm.

TTE examinations were conducted using a Philips HD15 ultrasound (Amsterdam, Netherlands) equipment with a 2.5–3.5 MHz-s transducer (Bothell, WA, USA) on the day of exercise ECG. Apical four-chamber and parasternal long-axis views were acquired according to the guidelines of the American Society of Echocardiography.

ECG and TTE examinations were carried out at Semmelweis University, Faculty of Physical Education and Sport Sciences between 2009 and 2014.

The ECG and TTE characteristics analyzed had earlier been described as potential signs of ARVC, elevated PAP, parasympathetic activity, malignant arrhythmias, or LV hypertrophy (7).

ECG alterations were defined in this study as follows:

ERV $_{2–4}$: ST elevation exceeding 2 mm at least in two adjacent leads of $V_{2–4}$ was accepted (in the literature, ST elevation exceeding 0.1 mV is already defined as ER) (4).
RAE – (= P pulmonale): sign of right atrium pressure and/or volume overload. It was accepted when the positive P wave was higher than 2.5 mV in leads II–III–aVF.
LAE – (= P terminal force): sign of LAP and/or volume overload: the P wave in lead V_1 was wider than 0.04 s and more negative than 0.1 mV.
RVcd –: it should be highlighted that the presence of terminal r′ restricted only to lead V_1 was defined as slow RV conduction without any block. The term of incomplete Right Bundle Branch Block was used if r′ was present in leads V_1 and V_2, and r′ exceeded 0.2 mV, and the duration of QRS was less than 0.12 s (25).
Right-axis deviation: if the amplitude of the R wave in lead III is greater than that in lead II.
QTc: QT corrected to HR according to Bazett's formula.
HR abnormalities: sinus bradycardia, bradyarrhythmias (e.g., conduction abnormalities, sino-auricular, and atrio-ventricular blocks), and tachyarrhythmias.
Resting ECG with sign of $ERV_{2–4}$ and post-exercise ECG with signs of RAE, LAE, and RVcd of a 20-year-old first-class male kayak paddler are demonstrated in Fig. 1.

TTE alterations analyzed:

SV_c: corrected LV SV to body surface area.
LVMc: LV mass (LVM) corrected to body surface area (LVMc = LVM/body surface area$^{3/2}$) (27).

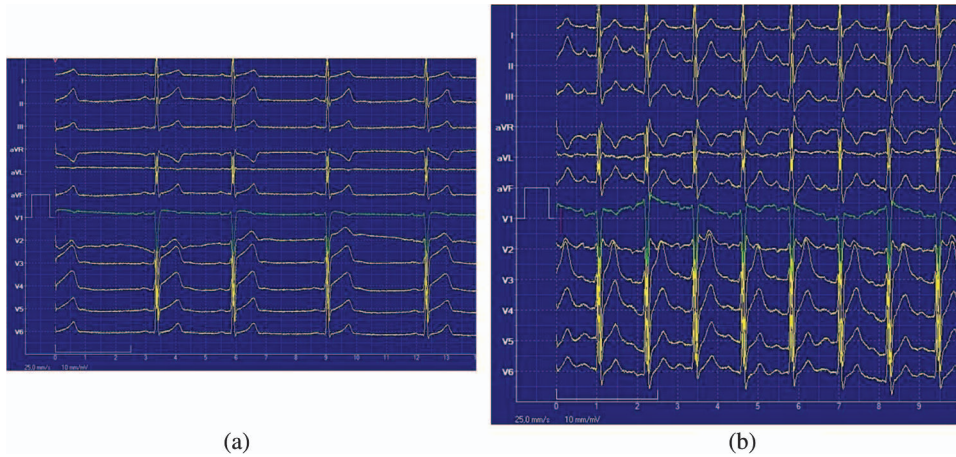

Fig. 1. Resting ECG record (a) with sinus brady-arrhythmia and ST elevation in $V_{2–4}$ and post-exercise ECG record (b) with signs of RAE, LAE, and RVcd of a 20-year-old first-class male kayak paddler

E/A ratio: the ratio between the peak velocities of the early and late phases of the diastolic filling.
EF: ejection fraction assessed by the modified Simpson's rule formula.

Statistical analysis

Statistical analysis was carried out using SigmaStat 2.03 and SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA). The relationship between $ERV_{2–4}$ and types of sport, ECG, and exercise ECG signs as well as TTE parameters was investigated by logistic regression, χ^2 test, and analysis of variance.

Results and Discussion

The results are summarized in Tables I–III.

Table I demonstrates the appearance of $ERV_{2–4}$ in different ETA groups and in the LTA group. The LV hypertrophy of these groups is characterized by LVM_c. SV_c is associated with systolic PAP.

The SV_c and LVM_c were significantly higher in ETAs than in LTAs both in men ($p < 0.01$ and $p < 0.01$, respectively) and in women ($p < 0.01$ and $p < 0.01$, respectively).

The prevalence of $ERV_{2–4}$ was significantly higher in ETAs than in LTAs ($p = 0.000$). The highest prevalence appeared in triathlonists [odds ratio (OR) = 13.8, pertaining confidence interval (CI) = 2.5–75.8; $p = 0.002$] and canoe and kayak paddlers (OR = 5.2, CI = 1.5–18.1; $p = 0.009$).

The prevalence of $ERV_{2–4}$ was significantly higher in male ETAs + LTAs than in female ETAs + LTAs (OR = 36.4, CI = 8.8–149; $p = 0.000$).

Table II demonstrates LV TTE parameters and exercise-induced ECG signs (which can indicate elevated PAP) as a function of the presence of the $ERV_{2–4}$ sign.

ETAs with $ERV_{2–4}$ sign compared to LTAs was linked to significantly higher LV parameters (LVM_c: in both genders $p < 0.01$; SV_c: males $p < 0.001$, females $p < 0.05$) and

Table I. ST elevation (early repolarization) in ECG leads $V_{2–4}$ ($ERV_{2–4}$) in various sports

Sports	Gender	Training hours	Height (cm)	Weight (kg)	*N*	TTE		ECG
						SVc (ml/m^2)	LVMc (g/m^2)	$ERV_{2–4}$ (%)
Kayaker–canoeists	Male	18 ± 5	184 ± 6	84 ± 7	79	55 ± 10	96 ± 18	89
	Female	19 ± 5	169 ± 4	66 ± 7	18	48 ± 7	88 ± 12	22
Triathletes	Male	18 ± 7	179 ± 7	68 ± 10	54	54 ± 8	97 ± 16	89
	Female	15 ± 7	171 ± 7	55 ± 5	22	42 ± 7	81 ± 15	45
Handball players	Male	20 ± 2	193 ± 6	102 ± 8	15	52 ± 5	86 ± 8	73
	Female	–	–	–	0	–	–	–
Soccer players	Male	16 ± 2	182 ± 7	79 ± 9	35	47 ± 7	84 ± 12	71
	Female	–	–	–	0	–	–	–
Water polo players	Male	–	–	–	0	–	–	–
	Female	18 ± 6	176 ± 6	72 ± 9	20	45 ± 6	79 ± 11	25
All ETAs mean/sum	Male	18 ± 4	183 ± 6	80 ± 8	183	52 ± 8	93 ± 14	84
	Female	17 ± 6	172 ± 6	64 ± 7	60	45 ± 6	82 ± 12	32
LTA	Male	6 ± 3	177 ± 8	74 ± 13	71	42	82 ± 14	17
	Female	5 ± 3	167 ± 6	68 ± 9	49	35	68 ± 9	2

TTE: transthoracic echocardiographic; *N*: number of cases; SVc: left ventricular stroke volume corrected to body surface area; LVMc: left ventricular muscle mass corrected to body surface area; ETA: endurance-trained athletes; LTA: leisure-time athletes

Table II. Transthoracic echocardiographic (TTE) parameters and ECG changes in the function of the presence of ERV_{2-4} sign

	Gender	Training hours	*N*	TTE		Resting ECG				Post-exercise ECG		
				SVc (ml/m^2)	LVMc (g/m^2)	HR (bpm)	LAE (%)	RAE (%)	RVcd (%)	LAE (%)	RAE (%)	RVcd (%)
ETA with ERV_{2-4}	Male	17 ± 4	154	50	135	54	5	1	31	58	60	33
	Female	17 ± 3	19	47	111	63	32	0	53	63	74	11
ETA without ERV_{2-4}	Male	16 ± 4	29	48	131	53	3	0	17	24	21	14
	Female	17 ± 2	41	42	107	57	2	2	17	24	27	5
LTA without ERV_{2-4}	Male	6 ± 3	59	39	105	66	10	3	20	10	10	5
	Female	5 ± 3	48	36	88	70	6	0	17	25	17	2

ETA: endurance-trained athlete; LTA: leisure-time athlete; N: number of cases; SVc: left ventricular stroke volume corrected to body surface area; LVMc: left ventricular muscle mass corrected to body surface area; ERV_{2-4}: ST elevation in leads V_{2-4}; HR: heart rate; LAE: left atrial enlargement; RAE: right atrial enlargement, RVcd: right ventricular conduction disturbances

Table III. Relationships (OR) between $ERV_{2–4}$ and post-exercise ECG changes indicating elevated pulmonary artery pressure

Post-exercise ECG parameters	*p* level	OR (CI)
LAE	0.000	3.970 [2.147–7.341]
RAE	0.000	3.730 [2.004–6.942]
RVcd	0.000	3.846 [1.774–8.336]
RAE + RVcd	0.000	4.525 [2.484–8.245]
RAE + RVcd + LAE	0.000	5.066 [2.778–9.238]

LAE: left atrial enlargement; RAE: right atrial enlargement, RVcd: right ventricular conduction disturbances; OR: odds ratio; CI: confidence interval

higher rate of exercise-induced ECG alterations (LAE: in males $p < 0.005$, in females N.S.; RAE: in males $p < 0.005$, in females $p < 0.05$; RVcd: in males $p < 0.05$, in females: N.S.).

Within ETA individuals, LVM_c and SV_c did not differ significantly between groups with or without $ERV_{2–4}$, but the rate of exercise-induced ECG alterations was higher in the $ERV_{2–4}$ group vs. the group without $ERV_{2–4}$ (LAE: in males $p < 0.05$, in females $p < 0.005$; RAE: in males $p < 0.05$, in females $p < 0.005$; Rvcd: N.S.).

Table III demonstrates the statistical relationships between $ERV_{2–4}$ and exercise-induced ECG alterations indicating elevated PAP during exercise.

The results of some observations are not demonstrated in the previous tables, but they are worth mentioning.

ER in the inferior-lateral leads exceeding 0.2 mV ST-segment elevation occurred only in 12 subjects vs. 173 subjects presenting $ERV_{2–4}$ in this study population.

Right-axis deviation was observed in eight cases, whereas left-axis deviation above 0°developed in six cases. R/S wave ratio in lead V_1 could not be evaluated owing to small R-wave amplitudes, which depended on the position of the V_1 electrode.

Negative T-waves were seen in leads $V_{2–4}$ in 10 athletes (2 kayaker-canoeists/1 man; 8 triathletes/7 men). These negative T-wave alterations were mentioned in the literature mostly in Afro-American athletes. Their 13% incidence was not considered pathological (10, 34). In our 10 cases showing this morphology, positive but not tall T-waves were apparent during exercise. The value of QTc was not pathologic either at rest or during exercise in this population. The resting HR was significantly lower (47 vs. 55/min) and the LV hypertrophy was slightly more pronounced in our 10 cases with negative T-waves vs. all ETA cases. The "not pathological" attribution of this ECG alteration is not entirely correct in our opinion; rather, it is more appropriate to state that no evidence has been found to date for negative consequences in athletes having this ECG alteration.

Arrhythmias were also present in this study population. Premature ventricular contractions (PVCs) appeared during exercise only in subjects with $ERV_{2–4}$ (6 cases). PVCs were always of RV origin. Repetitive non-sustained (4–16 beats) ventricular runs with left bundle branch block morphology (i.e., with RV origin) developed following exercise in one triathlonist woman.

Bradyarrhythmias like SA-block, 1st or 2nd degree AV block showed up in 14 cases at rest.

QTc was always in normal range, and there was no difference in its value either among different sports or according to the presence of $ERV_{2–4}$.

There was no difference in blood pressure between groups of various sports.

Systolic and diastolic function (EF, E/A) determined at rest have been found to be normal in all groups, and there was no significant difference between groups of various sports.

Many researchers reported frequent occurrence of $ERV_{2–4}$, RAE, LAE, and RVcd in ETAs (5, 11, 12, 31, 36). RVcd and RAE are directly related to high RV pressure and may be associated with RV and atrium wall strain. LAE indirectly refers to elevated PAP, whereas PAP also involves LAP. It is due to that under extreme endurance exercise, LV hypertrophy may lead to temporary relative compliance failure and elevated LV end diastolic pressure indicated by LAE. Although the sensitivity of these ECG alterations is not high and their occurrence in athletes is regarded not pathological, their appearance during exercise may indicate elevated PAP. In this study, it was shown that ECG signs of elevated PAP occur more frequently in those ETAs whose $ERV_{2–4}$ persists.

The physiological mechanism of the $ERV_{2–4}$ sign and its relationship with exercise were not clear and its clinical relevance was still debated in the relevant publications. According to this study, $ERV_{2–4}$ could be the consequence of repetitive and sustained PAP elevation due to endurance sports. The causes of PAP elevation during exercise are increased systemic blood flow (which exceeds the decrease of PVR), as well as increasing left atrial pressure, i.e., PAP elevation is a compensatory response during exercise (20, 26). This is due to the prevalence of the $ERV_{2–4}$ alteration is high particularly in male endurance athletes (it is rare in women athletes and in non-athletes), in whom LV hypertrophy is much more explicit (characterized by greater LVM_c and SV_c) compared to women and non-athletes. The role of LV hypertrophy in elevated PAP may be twofold: on the one hand, males are able to reach higher exercise levels generating greater blood flow; on the other hand, LV hypertrophy may lead to higher LAP and consequently to higher pulmonary post-capillary pressure.

Our interpretation for the earlier supposed $ERV_{2–4}$ etiologies is the followings:

The role of parasympathetic tone has been suggested (16). According to our opinion, the parasympathetic tone does not explain the $ERV_{2–4}$, because in ETA individuals, the low HR (indicating parasympathetic tone) does not differ between groups with or without $ERV_{2–4}$.

Interventricular septum hypertrophy has also been mentioned as the possible etiology of the $ERV_{2–4}$ (16). Our interpretation is the following: although high-level physical exercise could result in both septal hypertrophy and $ERV_{2–4}$, nevertheless, septal hypertrophy in asymmetric septum hypertrophy disease does not cause $ERV_{2–4}$ (13).

The role of cocaine has also been brought up (16). We did not investigate the effect of cocaine, but we agree with this idea, since cocaine may constrict small vessels, thus promoting the elevation of PAP. Therefore, the use of cocaine for endurance athletes means an increased risk.

Our examinations highlight the fact that the ECG parameters of elevated PAP persist for different periods. LAE and RAE rapidly regress. They are found on the resting ECG only rarely in ETAs in contrast with their high occurrence rate during exercise. These data prove that RAE and LAE ECG signs can develop due to atrium wall strain without atrium enlargement. The RVcd persists longer. About half of RVcd was also shown at rest 1 day after the last training. $ERV_{2–4}$ is also reversible, but it persists for weeks. We did not see $ERV_{2–4}$ even in ETAs who had stopped sport activity some months earlier. This study

confirms the regression capability of these parameters. They are related to temporary pressure overload and wall strain.

In conclusion, we found that $ERV_{2–4}$ alteration and some post-exercise ECG parameters (LAE, RAE, and RVcd) were more frequent in ETAs (mainly in the highest trained triathlonists and canoe and kayak paddlers) and males than in LTAs and women. The higher level of LV hypertrophy in the ETA population (proved by higher LVM_c on TTE) can result in greater blood flow and can contribute to elevated PAP. We concluded that $ERV_{2–4}$ may develop due to long lasting and repetitive elevated PAP, and the increase of PAP during exercise is more frequent in case of $ERV_{2–4}$. Therefore, the $ERV_{2–4}$ indicates that the RV is able to maintain the greater compensatory pulmonary flow during exercise with higher PAP.

We can hypothesize that athletes during exercise without RV remodeling and $ERV_{2–4}$ are not able to reach high PAP, and they are threatened by acute RV failure during extreme exercise (e.g., marathon).

On the other hand, publications suppose that $ERV_{2–4}$ (as a sign of RV remodeling) can mean a higher risk of malignant arrhythmias because of more morphological and electrophysiological similarities with Brugada syndrome and ARVC. It may be the cause why SCD in athletes is 2–4 times more frequent than in the corresponding age group. We found $ERV_{2–4}$ less frequent in women, which may explain the lower prevalence of SCD in female athletes.

Limitation of the study

We did not perform TTE examination during physical exercise.

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