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Is Early Repolarization Syndrome a Risk for Sudden Cardiac Death in Young Athletes?

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Abstract

Purpose of review To review data available in medical literature on the prognostic implications of the detection of an "early repolarization" (ER) pattern at standard electrocardiogram (ECG) in athletes, with particular reference to a possible increased risk of sudden death.

Recent findings In 2010, a case–control study of patients with vs. without idiopathic ventricular fibrillation in athletes found a higher prevalence of infero-lateral slurring J wave in cases than controls (28.6% vs. 7.6%; $p = 0.006$). Subsequently, a few studies assessed the prognostic value of the ER pattern (J point/ST-segment elevation with a typical ascending morphology and/or J wave with a notched morphology or with slurred QRS) in populations of athletes. Overall, a number of 3882 athletes were included in 5 studies, 1330 of whom (34.3%) had some evidence of ER pattern. No case of sudden death, as well as no increased risk of cardiovascular events, was reported in these studies.

Summary Our revision of population studies involving athletes in medical literature failed to find any apparent increase of the arrhythmic risk associated with ER/J wave, which, therefore, should be continued to be considered as benign findings on standard ECG.

Opinion statement

While the "early repolarization" (ER) pattern has for many years be considered as a benign electrocardiographic pattern, in recent years, some studies challenged this view by showing an increased rate of arrhythmic events, as well as cardiovascular events, associated with this pattern, in particular with prominent J wave (either notched or slurred). The potential arrhythmogenic effect of ER/J wave pattern may raise even more concern in athletes, due the higher prevalence of the finding in these subjects compared to non-athlete subjects. The revision of population studies involving athletes in medical literature, however, fails to find any apparent increase of the arrhythmic risk associated with ER/J wave. Thus, the detection of typical ER pattern at standard ECG should be continued to be considered as a benign finding in athletes as in the general population.

Introduction

The "early repolarization" (ER) pattern at the electrocardiogram (ECG) was first described in 1935 and traditionally consists of J-point/ST-segment elevation (STE) with a typical concave ST morphology [1]. This finding is often associated with notching or slurring of the terminal part of the QRS complex (usually defined as notched/slurred J wave) and broad and upright T waves. ER is mainly recorded in mid-to-left precordial leads (from V2 to V5–V6), but it can be found also in inferior leads [2]. Furthermore, ER is more prevalent in young male subjects and black people and is favored by lower heart rates, while disappears during exercise and other conditions associated with decreased vagal activity and increased adrenergic activity [1–3].

The ER pattern has for a long time been considered a "normal variant" with a benign prognosis [1–5]. In 2008, however, Haissaguerre et al. challenged this view by reporting a higher rate of "ER" among 206 patients with cardiac arrest due to idiopathic ventricular fibrillation compared to 412 healthy controls (31.3% vs. 5.1%, respectively; $p<0.001$) [6]. Subsequently, other case–control studies reported increased rates of "ER" among patients with idiopathic ventricular fibrillation or sudden death compared to control groups, thus suggesting that the ER pattern could actually be associated with an increased risk of sudden death [7, 8].

Furthermore, some population studies confirmed the increased arrhythmic risk associated with ER [9–12], also reporting an increased risk of total and cardiovascular mortality associated with ER [9, 13–16]. Thus, Tikkanen et al. in a population of 10,864 subjects, 630 of whom (5.8%) had the ER pattern, found that J-point elevation of ≥ 0.1 mV in inferior leads was associated with an increased risk of cardiac death (adjusted relative risk [RR], 1.28; 95% confidence interval [CI], 1.04–1.59; $p=0.03$) [9]. Notably, subjects with J-point elevation > 0.2 mV in inferior leads had a markedly elevated risk of both cardiac death (adjusted RR, 2.98; 95% CI, 1.85–4.92; $p<0.001$) and arrhythmic death (adjusted RR, 2.92; 95% CI, 1.45–5.89; $p=0.01$), despite this finding was present in 36 subjects (0.3%) only.

On the whole, population studies, however, often showed some discordant results. Some of them, indeed, suggested that the increased risk might actually be related to the presence of prominent J waves (either

notched or slurred) rather than the typical ST-segment elevation of ER [13–15]; others showed a significant association with clinical events of notched, but not slurred, J wave, and of inferior, rather than antero-lateral, J wave location [16]; others found a prognostic role for ER/J wave in subgroups of individuals only (e.g., women and white) [10, 17]. Several other studies, finally, failed to find any prognostic value for ER/J wave in apparently healthy subjects [18–23]. All these discordant data left the question of the risk associated with ER/J wave in the population unresolved.

ECG definitions

One of the possible reasons for the heterogeneous results reported in medical literature may rely on the variability in the definition and diagnosis of ER on the ECG [24–26]. While the ER pattern considered a benign finding in routine ECG assessment has clearly been described and classically includes a typical ascending ST-segment elevation, the term ER was more recently used to indicate different ECG findings, mainly focused on prominent notched J wave and/or slurring of the terminal part of the QRS (slurred J wave), independently of ST elevation or even in presence of convex or horizontal ST elevation [27].

This led various authors to include in the "ER groups" subjects with very anomalous "J wave" and/or widening of QRS and/or ST segment changes, which might hardly been interpreted as a benign typical ER during routine ECG reading [27], as it appears from several ECGs included as examples of ER in articles reporting an association between "ER" and arrhythmic events [6–8].

A further potential bias, concerning population studies, is that the assessment of ER pattern was done retrospectively, i.e., by knowing the clinical outcome of subjects, although ECG tracings were usually reassessed in a blind way.

For this reason, we conducted a fully prospective long-term study of 4,176 consecutive subjects without any apparent history of cardiovascular disease who underwent a routing ECG for a check-up or pre-operative assessment for non-cardiac surgery [28]. The ECGs were collected and analyzed on enrolment according to well pre-specified criteria finalized to identify the presence of an ER pattern and/or J wave. The diagnosis of "ER" had to include a typical J point/ST-segment elevation > 1 mm, with or without any J wave/QRS slurring in at least 2 contiguous inferior (DII-DIII-aVF), limb lateral (DI-aVL), and/or left precordial (V_4–V_6) leads. A "J wave" was diagnosed when the terminal part of the QRS (before the J point) showed a notch (notched J wave) or a widening (slurred QRS/J wave) ≥ 0.1 mV in at least 2 contiguous leads (Fig. 1).

In our study, no increase in all-cause or cardiovascular death was recorded both during an intermediate average follow-up of 6 years and after a longer term average follow-up of 10 years [29, 30•]. Importantly, only one case of sudden death was recorded in this population, occurring in a subject without any component of the ER/J wave pattern. Thus, our data suggest a poor arrhythmogenic potential for the ECG finding.

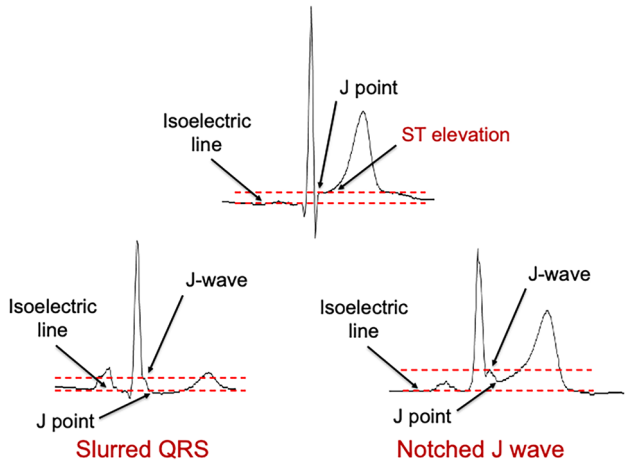

Fig. 1 Methods for measurement of ST-segment elevation and notched/slurred J wave. (Used with permission of Elsevier, from Lanza GA et al. J Electrocardiol 2012;45:404-410, permission conveyed through Copyright Clearance Center, Inc.) [28].

Potential implication for sudden death of ER in athletes

Cardiac arrest/sudden death is a rare event in athletes, widely ranging in the medical literature from < 0.1 to 38 per 100,000 person-years, with a large higher prevalence in men compared to women [31, 32]. The occurrence of sudden death, however, is particularly dramatic in athletes, as it often occurs in young or adult people who apparently are in excellent clinical conditions.

Autopsy studies have shown that cardiac arrest/sudden death usually occurs in athletes with some evidence of structural heart abnormalities, which mainly include obstructive coronary artery disease in subjects older than 35 years and hypertrophic or arrhythmogenic cardiomyopathy in younger subjects [33]. However, a subset of these subjects does not present any structural cardiac abnormality in the clinical history or at autopsy. In these subjects, some form of cardiac ion channel disease or other electrical disorder is probably often involved, which might include the ER pattern.

The issue of the clinical implications of ER/J wave in athletes might be more relevant than in the general population; when considering that in subjects performing sport activities or even engaging intense physical efforts, the pattern of ER/J wave is expected to be more frequently found at the ECG compared to untrained subjects. The higher parasympathetic tone and, therefore, the lower heart rate, typical of trained subjects, are indeed major determinants of the pattern [1–5, 28, 34]. Thus, if ER is a potential cause of arrhythmic events, the number of subjects at risk might be higher in trained individuals than in the general population.

The higher prevalence of ER pattern in athletes has been confirmed in a few studies directly comparing athletes with untrained healthy subjects. Bianco et al. [35] compared the ECGs of 155 male athletes (mean age 30.9 years) and 50 sedentary male controls (mean age 25.3 years), reporting a typical ST-segment elevation of ER in 139 (89%) and 18 (36%; $p = 0.025$) subjects, respectively. Claessen et al. [36•] assessed the presence of ER, defined as

an end-QRS notch or slur with elevation of J point ≥ 0.1 mV, in 2090 athletes and 151 non-athlete subjects, reporting ER in 502 (24%) and 26 (17%) athletes and controls, respectively (adjusted odds ratio 1.5; 95% CI 1.0–2.4). In a large retrospective study, Muramoto et al. [37] compared the ECG findings of 1114 multi-ethnic athletes (age 19.2 ± 1.6 years, 56.7% males) and 4041 ambulatory older healthy subjects (age 57.3 ± 13.5, 89.9% males). Any ER pattern was more frequently found in athletes than controls, both in inferior leads (13.1 vs. 10.3%, respectively, $p = 0.009$) and lateral leads (24.7 vs. 8.8%, respectively, $p < 0.001$). McClean et al. [38] in a meta-analysis of studies comparing ECG findings of pediatric athletes and pediatric non-athletic controls reported an average prevalence of ER in 37.1% and 29.2% in the 2 groups, respectively. At variance with these studies, Brosnan et al. [39] reported a similar prevalence of ER pattern in 726 young Australian male athletes (mean age 20 years) compared to a slightly older group of 170 young untrained male controls (mean age 28 years). However, a lower heart rate (HR), together with non-Caucasian ethnicity, a higher QRS voltage, and a shorter QRS duration, was a significant predictor of ER on the ECG, suggesting that some selection bias might have precluded the evidence of a significant association of physical activity with ER in this study.

Notably, the importance of physical activity in the appearance of ER is also confirmed by the increased appearance of the ER pattern on the ECG after periods of training [40] and its frequent regression after periods of detraining [41].

Outcome studies of ER pattern in athletes

The possibility that the presence of ER/J wave at the ECG in athletes might be associated with SCD/CA was first suggested by Cappato et al. [42]. These authors analyzed the ECGs of 21 athletes (mean age, 27 ± 8 years; 76% men) recorded before or immediately after cardiac arrest or before sudden death and compared the results with the ECGs of 365 healthy control athletes (age 28 ± 8 years; 90% males) eligible for competitive sport activities. The presence of a J wave (notched) in any lead, with or without QRS slurring or ST-segment elevation, did not differ significantly between cases (10 patients, or 47.6%) and controls (108 subjects, or 29.5%; $p = 0.09$). However, a J wave and/or QRS slurring together in inferior (II, III, aVF) and lateral leads (V4 to V6) were more frequently found in cases than control athletes (28.6% versus 7.9%, $p = 0.007$). Furthermore, QRS slurring in any lead was also present in 28.6% of cases but in only 7.6% of controls ($p = 0.006$). Interestingly, ST elevation in any lead was observed in 9.5% of cases only ($n = 2$) but in 21.6% of controls ($n = 79$; $p = 0.27$). Importantly, during a median follow-up period of 36 months, recurrences of VF/sustained ventricular tachycardia among the 19 cases resuscitated from cardiac arrest did not differ between patients with vs. those without J wave/QRS slurring, occurring in 5 out of 10 patients with and 8 out of 9 patients without J wave/QRS slurring.

After this first case–control study, the prognostic role of ER/J wave in athletes was retrospectively assessed in some observational population studies. The main characteristics and results of these studies are summarized in Table 1. They, on the whole, involved 3882 athletes, 1330 (34.3%) of whom were found to have some evidence of ER pattern.

Noseworthy et al. [40] reported no cardiovascular events during an average follow-up of 21 months (range 7–50) in 879 athletes, 221 of whom (25.1%) had some type of ER pattern.

In the large retrospective study by Muramoto et al. [37], after a mean follow-up of 36 months in athletes and 7 years in ambulatory untrained subjects, no single component or combination of ER components, including those often considered associated with the highest risk (such as J wave in inferior leads and/or horizontal/downsloping STE ≥ 0.1 mV) [43, 44], was associated with an increased risk of cardiovascular death (CVD).

Quattrini et al. [45] studied 704 highly trained healthy Italian athletes (age 25 ± 5 years, 62% males). The ER pattern was defined as J wave and/or QRS slurring, irrespective of ST elevation, and was found in 102 subjects (14,5%), with QRS slurring present in 32 (4% of the whole population). ST elevation was a frequent finding in this cohort, being found in 461 subjects (65.5%), and was more frequently found in subjects with compared to those without J wave/QRS slurring (84 vs. 62%). Male sex, endurance sport, higher body surface area (BSA), Sokolow-Lyon criteria for left ventricular hypertrophy (LVH), lower HR, and presence of ST elevation were predictors of ER pattern (J wave/QRS slurring). No adverse cardiovascular events were recorded during an average follow-up of 6 years (maximum 18 years). J wave in this study showed also no association with ventricular arrhythmias detected at 24-h ECG Holter monitoring.

Serra-Grima et al. [41] performed clinical follow-up of 299 elite athletes (age 20.2 ± 6.4 years, 65.9% males). An ER pattern at basal ECG was present in 94 subjects (31.4%) and was located in inferior leads in 6 subjects (2%), in lateral leads in 54 (18,1%), and in infero-lateral leads in 34 (11.4%). Almost all subjects with ER (97.5%) showed J point elevation between 1 and 2 mm with upsloping ST elevation. Male sex, sinus bradycardia, Sokolow-Lyon criteria for LVH, and longer QRS duration were predictors of ER pattern. There were no deaths or cardiac arrests during an average follow-up of 24 ± 7.6 years. In this study, the presence of ER at the ECG was reassessed at follow-up. Only 51 of 94 subjects with ER at baseline (54.3%) still showed ER at follow-up, while 12 subjects (5.9% of non-ER subjects at baseline) showed a de novo ER pattern at the follow-up ECG.

Halasz et al. [46•] prospectively enrolled 886 white healthy pediatric athletes (age 11.7 ± 2.5 years, 72.5% male). Overall, an ER pattern was present in 117 (13.2%) subjects and was located in infero-lateral leads in 63 (53,8%), in inferior leads only in 45 (38.5%), and in lateral leads only in 9 (7,7%). In this pediatric population, older age, lower HR, longer PR interval, shorter QRS duration, Sokolow-Lyon criteria for LVH, and increased precordial and limb R-wave voltages were predictors of ER pattern. No cardiovascular events, including arrhythmic events, occurred during an average follow-up of 4.2 years. Also in this study, the presence of ER at the ECG was reassessed at follow-up. ER persisted in 80.3% of ER subjects, although 28% of them showed a change in ER localization and/or J-wave morphology. A de novo ER at the ECG, on the other hand, was found at follow-up in 2.3% of non-ER subjects at baseline.

Table 1. Main characteristics of population studies assessing the prognostic implications of early repolarization pattern in athletes. No arrhythmic events or cardiovascular events were reported in any of the studies

Author	No. athletes	Age (years)	Male sex (%)	ER pattern (%)						ER pattern predictors	Mean follow-up (years)
				Any ER	Any ER		J wave (notched)	QRS slurring	STE		
					Lat	Inf					
Noseworthy et al. [40]	879	18.4 ± 0.8	62.0	25.1	22.6	3.8	13.2	1.6	11.7	Male sex, Afro-American ethnicity, increased QRS voltages, lower HR	1.75
Muramoto et al. [37]	1114	19.2 ± 1.6	56.7	37.8	30.2	18.6	8.7	10.4	21.9	Male sex, Afro-American ethnicity, athletic status	3.0
Quattrini et al. [45]	704	25.0 ± 5.0	62.0	67.8	14.1	10.8	14.5[b]	4.5	65.5	Male sex, endurance sport BSA, Sokolow criteria for LVH, lower HR	6.0 (548 athletes)
Serra-Grima et al. [41]	299	20.0 ± 6.4	65.9	31.4	29.4	13.4	2.7[c]	9.0	13.0	Male sex, sinus bradycardia, Sokolow criteria for LVH, longer QRS duration	24.0
Halasz et al. [46•]	886[a]	11.7 ± 2.5	72.5	13.2	8.3	11.1	10.3	2.9	13.7	Older age, lower HR, longer PR interval, shorter QRS duration, Sokolow criteria for LVH increased R wave voltages	4.2

BSA body surface area, *ER* early repolarization, *HR* heart rate, *Inf* inferior leads (DII, DIII, aVF), *Lat* lateral leads [DI-aVL, V_4-V_5-V_6], *LVH* left ventricular hypertrophy, *STE* ST-segment elevation

[a]Pediatric population

[b]J wave and/or QRS slurring

[c]J wave ≥ 0.2 mV

Comments

The data available in medical literature indicate that the detection of the "ER pattern" at standard ECG is not associated with an increase of arrhythmic risk, as well as of cardiovascular events, in athletic people.

When excluding the initial, small case–control study by Cappato et al., who suggested some prognostic implication for the ER pattern [42], no population study reported any evidence of an increase of arrhythmic events in athletes with, as compared to those without, the presence of an ER pattern at the ECG. No cases of arrhythmic events or sudden death, in fact, occurred in all available outcome studies of athlete populations, including, on the whole, 3882 athletes followed for a variable period of 7 months to 32 years. The lack of any evidence of arrhythmic risk concerned both the typical definition of ER, which includes the presence of an ascending ST-segment elevation, and the presence of notched J wave and/or slurred QRS at the ECG.

Of note, although in the study by Cappato et al., a diffused J wave and/or QRS slurring, but not typical ST elevation, were more frequently found in athletes with sudden death/cardiac arrest than in control athletes, the recurrence of ventricular fibrillation was not predicted by any J wave/QRS slurring, thus questioning the increased arrhythmogenic risk associated with these ECG findings [42].

The lack of any evidence of increased arrhythmic risk in athletes with ER in population studies is in keeping with our recent prospective studies [29, 30•], as well as several retrospective population studies, of untrained subjects, that failed to find a significant prognostic implication of any ER pattern, both as far as arrhythmic events and global or cardiovascular mortality are concerned [18–23].

It should be observed, however, that the occurrence of fatal or life-threatening arrhythmic events in athletes are very rare, whereas the number of subjects included in the published studies is limited compared to the wide population of athletes in the world. Thus, it is not possible to exclude that some residual increased risk, detectable only in studies including several hundred thousand athletes with adequate follow-up, might exist with some component of the ER pattern. However, available data strongly suggest that, if any, this risk would be so low that it might hardly have practical consequences in the assessment of the cardiovascular risk in athletes, particularly considering the significant prevalence that the various components of the ER pattern have in these subjects, as well as in the general population of healthy people.

Of note, the assessment of the predictive value of ER over long term follow-up times might be challenging when considering that a significant proportion of subjects may show changes or disappearance of the pattern over the time, while a small proportion may also show a new ER pattern on the ECG [41, 46•].

Conclusions

In conclusion, the data available in medical literature consistently show that the ER pattern, in any of its components (J point/ST segment elevation, J wave, and slurred QRS), is not associated with any evidence of increased arrhythmic risk or worse clinical outcome and should therefore be considered a benign ECG finding in athletes.

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Compliance with Ethical Standards

Conflict of Interest
Saverio Tremamunno declares no conflict of interest. Gaetano Antonio Lanza declares no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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