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# Long-term Follow-up of Early Repolarization Pattern in Elite Athletes $\stackrel{\star}{\sim}$

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#### ABSTRACT

**BACKGROUND:** Early repolarization pattern (ERP) is considered a benign variant of the electrocardiogram (ECG), more frequent in athletes. However, prospective studies suggested that ERP is associated with an increased risk of sudden cardiac death (SCD). The purpose of this study is to determine the prevalence, clinical characteristics, and long-term outcome of ERP in elite athletes during professional activity and after retirement. **METHODS AND RESULTS:** A cohort of 299 white elite athletes recruited between 1960 and 1999 was retrospectively analyzed. Athletes were eligible if they had participated for at least 6 consecutive months in high competition and retired for a minimum of 5 years before inclusion. Clinical data and ECG were abstracted from the clinical records using a questionnaire, and outcomes after a mean follow-up of 24 years were registered. Among the 299 athletes, 66% were men with a mean age of 20 (SD 6.4) years. ERP was found in 31.4% of participants, and it was located in lateral ECG leads in 57.4% of cases, in inferior leads in 6.4%, and in both leads in the remaining 36.2%. After retirement, ERP still persisted in 53.4% of athletes. Predictive factors for the persistence were: left ventricular hypertrophy signs at the baseline ECG (odds ratio [OR] 4.35; 95% confidence interval [CI], 1.43-13.24; P = .010), sinus bradycardia after retirement (OR 2.56; 95% CI, 1.09-5.99; P = .031), and presence of ERP during the sportive career (OR 20.35; 95% CI, 8.54-48.51; P < .001). After a mean follow-up of 24 years, no episodes of SCD occurred.

**CONCLUSIONS:** A third of elite athletes presented ERP, and this persisted in 53.4% of cases after retirement. After a long follow-up period, no difference in outcome of SCD was seen.

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**KEYWORDS:** Athletes; Early repolarization pattern; Electrocardiogram; Sudden cardiac death

Early repolarization pattern is defined as a broad positive deflection originating from an elevated J-point in inferior or lateral electrocardiogram (ECG) leads.<sup>1</sup> This ECG pattern has been historically considered a normal variant in the general population,<sup>2</sup> being more prevalent in males, Blacks, and in young trained athletes, especially those

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engaged in endurance disciplines.<sup>3,4</sup> However, emerging data from case-control<sup>5,6</sup> and prospective cohort<sup>7</sup> studies suggest that early repolarization pattern in the inferior ECG leads is associated with an increased risk of sudden cardiac death. Although sudden cardiac death is relatively rare in athletes, an association between early repolarization pattern in inferior leads and sudden cardiac death has been recently reported.<sup>8</sup> Moreover, recent refined analyses of the morphology of ST segment following the early repolarization waveforms have afforded new light in the stratification of individuals at higher risk of arrhythmic death. Indeed, ascending/upsloping ST segments identified individuals with benign prognosis, whereas horizontal/descending ST variant was associated with a high risk of arrhythmic death.<sup>9-11</sup> Although in almost 50% of cases of sudden cardiac death in athletes there was not an identifiable cardiac disorder,<sup>12</sup> studies in patients with

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acute myocardial infarction have shown that the presence of horizontal/descending ST segment in the ECG recorded before the ischemic event increased the risk for occurrence of ventricular fibrillation.<sup>13,14</sup> The magnitude of early repolarization pattern and the intensity of the training are closely related,<sup>15</sup> but the factors determining the persistence

of early repolarization pattern in athletes after cessation of highlevel training are not well known. Therefore, the aim of our study was to analyze the prevalence and clinical characteristics of early repolarization pattern in active athletes and the very long-term prognosis after their retirement.

#### METHODS

#### Study Population

This is a retrospective longitudinal study that included white, highlevel competition athletes ascribed to the Health and Sport Unit of

Consell Català de l'Esport of Barcelona City, Medical Service of Barcelona Football Club, and High Performance Center at Sant Cugat del Vallés, Barcelona, between 1960 and 1999. Athletes were included if they fulfilled the following criteria: 1) participation in elite competitions defined according to the criteria of the Study Group of Sports Cardiology of the European Society of Cardiology<sup>16</sup>; 2) maintenance of a high level of competition training for at least 6 consecutive months; and 3) retirement from intensive training for a minimum of 5 years before inclusion in the study. The total number of athletes eligible was 302. We finally enrolled 299 because 3 subjects were lost during the follow-up (without early repolarization pattern in baseline ECG). This study was approved by our institutional review committee, and written consent was obtained from all participants.

### **Clinical Variables**

Demographic and clinical baseline information was abstracted from the clinical records using a structured questionnaire. This included the type of sport performed, the number of hours of weekly training during competition periods, and the number of years participating in high-level competition. The level of training during the high competition period was classified dichotomously according to a 12-weekly-hours training cut-off. A resting 12-lead ECG was obtained during the baseline visit.

In the follow-up visit, we recorded a complete clinical history, ECG, cardiovascular events (sudden cardiac death, myocardial infarction, and stroke), number of years since retirement from high competition, and information on current physical activity categorized as high, >5 hours a week; low, <5 hours a week. Follow-up period was calculated as the time (years) elapsed between the baseline and the follow-up visit.

#### **ECG Variables**

The presence of early repolarization pattern and its morphologic characteristics were stated according to the work of Tikkanen et al.<sup>9</sup> Early repolarization pattern is defined by upright deviation of the J-point of at least 1 mm (0.1 mV) from baseline, appearing either as QRS complex slurring (a

smooth transition from the QRS

to the ST segment), QRS complex

notching (a positive J deflection

inscribed on the S wave), or as

discrete QRS complex contour

(early repolarization pattern after

signal return to baseline). These

patterns could be observed in the

inferior ECG leads (II, III, and

aVF), lateral leads (I and aVL, V4-

V6), or in both groups of leads.

ST-segment patterns after the J

point were coded as: 1) horizontal/ descending or 2) upsloping/rapidly

ascending. The upsloping/rapidly

ascending ST segment was defined

as  $\geq$  0.1 mV elevation of ST

# CLINICAL SIGNIFICANCE

- One-third of elite athletes presented the benign early repolarization pattern (upsloping ST-segment), whereas the one related to sudden cardiac death risk (rectified/descending ST-segment) was rare.
- Early repolarization pattern persisted in half of athletes after professional sport retirement, and no episodes of sudden cardiac death were observed after 24 years of follow-up.

segment within 100 ms after the J point or a persistently elevated ST segment of  $\geq 0.1$  mV throughout the ST segment. Horizontal/descending type was defined as < 0.1mV elevation of the ST segment within 100 ms after the J point. The baseline was defined as the level between 2 T-P intervals. Sinus bradycardia was categorized as: light (51-60 beats per minute), moderate (41-50 beats per minute), and severe ( $\leq 40$  beats per minute).<sup>17</sup> QT-interval duration was corrected according to the Bazett formula. Left bundle branch block was defined by a prolonged QRS duration of 120 ms or more associated with broad, notched R wave without q waves in leads I, aVL, and V6, and an rS pattern in lead V1. Right bundle branch block was characterized by prolonged QRS duration of 120 ms or more associated with an R, rSR', or qR wave in lead V1; wide, slurred S waves in leads I, aVL, V5, and V6; and a wide terminal r wave in aVR. The presence of left ventricular hypertrophy on the ECG was defined by a Sokolov-Lyon index<sup>18</sup>: (S wave in lead V1) + (R wave in lead V5 or R wave in lead V6) > 35 mm; (R wave in lead V5) or (R wave in lead V6) > 26 mm. Any of the above 2 conditions being positive was taken as left ventricular hypertrophy.

# **Echocardiographic Variables**

Because echocardiographic examination was not feasible at the beginning of the inclusion period (1960) and was not routinely performed in athletes thereafter, we include in this study only the recordings obtained in 64% of participants during the follow-up visit.

# **Data Analysis**

Descriptive analyses were performed at the first step. Categorical variables were described by frequencies and percentages. Statistical differences were analyzed using a  $2 \times 2$  table test and the  $\chi^2$  test. Continuous variables were described by the mean and standard deviation, and statistical differences were analyzed using the Student's t test in the case of a normal distribution. To identify independent predictors of early repolarization pattern in the follow-up visit, a multivariable logistic regression model was constructed, adjusting for the covariates statistically significant at the univariate analysis (P value < .20 as a criterion of entry into multivariate analysis). Additionally, the final model was adjusted for those variables categorized as clinically relevant. Significant predictors of early repolarization pattern were expressed in terms of odds ratio (OR) and 95% confidence intervals (CI). To assess the predictive ability of our model, we calculated the area under the receiver operating characteristics curve (receiver operating characteristic) after a nonparametric distribution assumption. A P value of < .05 was considered statistically significant. Data were analyzed using the statistical package SPSS for Windows (SPSS Statistics, 21 version; IBM, Armonk, NY).

# RESULTS

#### **Clinical Characteristics**

Among the 299 elite athletes included in the study, 94 (31.4%) presented early repolarization pattern on admission. As shown in **Table 1**, athletes with and without early repolarization pattern showed comparable demographic profile except for a higher incidence of males in the former group. Likewise, both groups of athletes showed comparable distribution of competition categories and similar volume of physical training. Our study participants had been in the elite sport over 3 years on average and most of them trained more than 12 hours a week. The

sports spectrum was very broad, but athletics were practiced by about 45% of participants.

#### ECG

As shown in Table 2, the presence of early repolarization pattern was significantly associated with sinus bradycardia, criteria of left ventricular hypertrophy, and a longer QRS complex duration. However, there were not differences in the corrected QTc interval and the presence of right bundle branch block. The early repolarization pattern was observed in lateral leads in 57.4% of cases, in inferior leads in 6.4%, and in both regions in 36.2%. The large majority of cases (97.5%) presented an ascending/ upsloping ST segment with a J-point elevation between 0.1 and 0.2 mV from baseline. In the group of early repolarization pattern, the pattern of the QRS morphology was discrete in 41.2% of cases, and slurred and notched in about 30%. There were 2 cases of horizontal/descending ST segment, more apparent in the inferior leads. Figure 1 illustrates 4 cases of ascending/upsloping ST-segment type of early repolarization pattern recorded in 4 elite athletes.

#### Follow-up

The mean follow-up was 24 years (SD 7.6), with a minimum and a maximum of 10 and 47 years, respectively. Mean age of participants at the second visit was 45 years (SD 9.3, interquartile range 24-75). After competition retirement, 30% of individuals of the non-early-repolarization pattern group and 50% of those with early repolarization pattern continued to maintain a significant level of training (>5 hours/week) (28.5% vs 47.6%, P = .004). As shown in **Table 3**, the prevalence of cardiovascular risk factors and cardiovascular events in our series was very low. Nonfatal

 Table 1
 Demographic and Sportive Characteristics of 299 Elite Athletes with and without Early Repolarization Pattern at Study Inclusion

				ECG Localization of ERP			
	No ERP (n $=$ 205)	ERP (n = 94)	P-Value	Inferior (6)	Lateral (54)	Inferolateral (34)	P-Value
Age, years	20.1 ± 6.4	$\textbf{20.5} \pm \textbf{6.4}$	ns	$\textbf{21.3} \pm \textbf{9.2}$	$\textbf{20.3} \pm \textbf{6.5}$	20.7 ± 5.8	ns
Male, %	60.5	77.7	.004	66.7	75.9	82.4	.027
Weight, Kg	$\textbf{63.7} \pm \textbf{12.8}$	$\textbf{61.9} \pm \textbf{10.9}$	ns	56.2 $\pm$ 9.9	$\textbf{61.0} \pm \textbf{10.7}$	$\textbf{64.4} \pm \textbf{10.9}$	ns
Height, cm	$170.7\pm11.1$	170.1 $\pm$ 9.2	ns	166.2 $\pm$ 11.8	$\textbf{170.1} \pm \textbf{9.3}$	$171.0\pm8.7$	Ns
BMI, Kg/m²	$\textbf{21.1} \pm \textbf{2.6}$	$\textbf{21.0} \pm \textbf{2.2}$	ns	$\textbf{19.8} \pm \textbf{1.7}$	$\textbf{20.8} \pm \textbf{2.2}$	$\textbf{21.5} \pm \textbf{2.3}$	Ns
Sportive category			ns				ns
Athletics, %	45.4	44.7		50.0	50.0	35.3	
Swimming, %	13.2	16.0		16.7	9.3	26.5	
Basketball, %	6.8	4.3		0.0	5.6	2.9	
Others, %	34.6	35.1		33.3	35.2	35.3	
Volume of training							
High (>12 h/w), %	79.5	84.9	ns	100	86	80.6	ns
Low (<12 h/w), %	20.5	15.1		0	14	19.6	
Time on high-level competition, y	$\textbf{3.5} \pm \textbf{5.1}$	$\textbf{3.8} \pm \textbf{4.8}$	ns	$\textbf{6.3} \pm \textbf{9.9}$	$\textbf{3.0} \pm \textbf{4.2}$	$\textbf{4.6} \pm \textbf{4.4}$	ns

Abbreviations: BMI = body mass index; BSA = body surface area; ECG = electrocardiogram; ERP = early repolarization pattern; h = hour; Kgs = kilograms; m = meters; ns = no significance; w = week; y = year.

				ECG Localization of ERP			
	No ERP (205)	ERP (94)	P-Value	Inferior (6)	Lateral (54)	Inferolateral (34)	<i>P</i> -Value
HR, beats per minute	$\textbf{50.5} \pm \textbf{24.8}$	$\textbf{47.0} \pm \textbf{19.5}$	ns	$\textbf{42.7} \pm \textbf{21.7}$	$\textbf{46.8} \pm \textbf{20.6}$	$\textbf{47.9} \pm \textbf{17.9}$	ns
Sinus bradycardia, %	63.9	87.2	<.001	66.7	85.2	94.1	<.001
Light	38.6	39.5		33.3	34.1	48.4	
Moderate	36.4	43.2		50	50	32.3	
Severe	25	17.3		16.7	15.9	19.4	
Any J-point $\geq$ 0.2 mV, %	_	8.2	_	0	6.3	12.9	<.001
QRS pattern, %	_	41.2	_	50	47.9	29	
Discrete	_	29.4		33.3	22.9	38.7	<.001
Slurred		29.4		16.7	29.2	32.3	
Notched							
QRS duration, ms	$82\pm8$	92 $\pm$ 8	<.001	$90 \pm 6$	$91\pm8$	$95\pm8$	ns
ST-segment pattern, %							
Ascending/upsloping	_	97.5	_	83.3	97.7	100	.059
Horizontal/descending	_	2.5		16.7	2.3	0	
Sokolov-Lyon $>3.5$ mV, $\%$	10.2	40.5	<.001	33.3	38.3	45.2	<.001
QT, ms	$\textbf{336.8} \pm \textbf{145.1}$	$\textbf{260.9} \pm \textbf{136.4}$	ns	$\textbf{348.3} \pm \textbf{171.4}$	$\textbf{352.9} \pm \textbf{143.0}$	$\textbf{375.3} \pm \textbf{121.9}$	ns
QTc, ms	$\textbf{331.3} \pm \textbf{142.5}$	$\textbf{337.1} \pm \textbf{126.8}$	ns	$\textbf{320.3} \pm \textbf{157.1}$	$\textbf{331.9} \pm \textbf{134.1}$	$\textbf{348.2} \pm \textbf{112.2}$	ns
RBBB, %	4.4	6.4	ns	0	7.4	5.9	ns

branch block.

myocardial infarction occurred in 2 athletes and none of the participants died. We observed a prevalence of the early repolarization pattern in 63 of 299 athletes (21.1%), mainly located at the lateral (50.8%) and inferior-lateral ECG leads (47.6%). The presence of bradycardia was significantly higher in the early repolarization group (71.4% vs 41.9%, P < .001). Among the 63 athletes who presented early repolarization pattern in the follow-up, 51 already showed this pattern at the time of enrollment (54.3%, "persistent early repolarization pattern"), while in 12 of them this pattern appeared de novo. Supplementary Table 1 summarizes the demographic, clinical, and electrocardiographic characteristics of athletes with these 3 early repolarization pattern forms.

The echocardiographic examination was performed in 64% of cases during the follow-up visit. Athletes with or without early repolarization pattern showed comparable left ventricular ejection fraction (74  $\pm$  10 vs 71  $\pm$  9%), thickness of left ventricular septum (9  $\pm$  1 vs 9  $\pm$  2 mm), thickness of posterior left ventricular wall (9  $\pm$  1 vs 8  $\pm$ 2 mm), and left atrial diameter (33  $\pm$  5 vs 32  $\pm$  6 mm). Although in both groups the left ventricular diameter was within normal limits, this parameter was larger in the early repolarization group (50  $\pm$  6 vs 48  $\pm$  5 mm, P < .05).

The multivariate analysis showed that the predictors of current early repolarization pattern were left ventricular hypertrophy at the baseline ECG (OR 4.35; 95% CI, 1.43-13.24; P = .010), sinus bradycardia after retirement (OR 2.56; 95% CI, 1.09-5.99, P = .031), and early repolarization pattern during elite activity (OR 20.35; 95% CI, 8.54-48.51; P < .001). However, male sex and the volume of training either during high-level competition or after retirement was not a significant predictor. Figure 2 shows the receiver operating characteristic curve of the model to predict the presence of early repolarization pattern in the follow-up ECG (area under the curve 0.89; 95% CI, 0.85-0.94, P < .001).

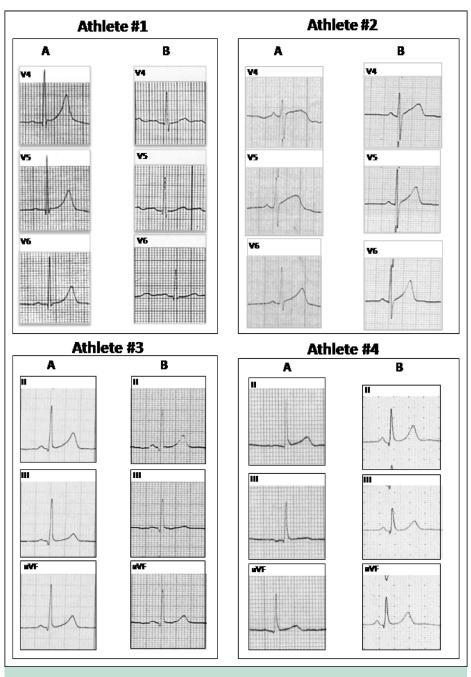
# DISCUSSION

#### Main Findings

This study shows that one-third of elite athletes presented early repolarization pattern during their active competition life. In 97.5% of cases, the early repolarization pattern was characterized by ascending/upsloping ST segment, and only 2.5% presented horizontal/descending ST-segment pattern. Moreover, the study showed that the early repolarization pattern persisted after professional retirement in 54.3% of cases.

# Prevalence of Early Repolarization Pattern and **Related Factors**

The prevalence of early repolarization pattern in the general population is largely variable, as it is influenced by, among others, race, age, level of physical activity, characteristics of the QRS complex, and by the definition of early repolarization pattern itself.<sup>19</sup> In a recent meta-analysis based on 7 prospective observational cohort studies and on 3 casecontrol studies, the prevalence of early repolarization pattern varied from 0.9% to 31%.<sup>20</sup> Applying strict criteria, the prevalence of early repolarization pattern was 18.6% in



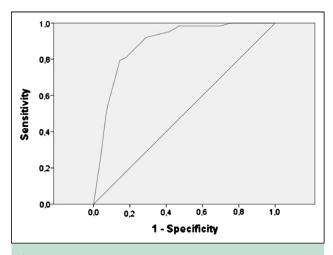
**Figure 1** Illustrative cases of ascending/upsloping ST segment type of early repolarization pattern recorded in 4 elite athletes. Athlete #1: Disappearance of the early repolarization pattern in lateral leads in a marathon runner after a follow-up of 17 years. (A) Electrocardiogram (ECG) recorded in 1983. (B) ECG recorded 5 years after sport competition retirement. Athlete #2: Persistence of the repolarization pattern in lateral leads in a footballer after a follow-up of 20 years. (A) ECG recorded in 1991. (B) ECG recorded 6 years after sport cessation. Athlete #3: Disappearance of early repolarization pattern in inferior leads in a tennis player after a follow-up of 24 years. (A) ECG recorded in 1980. (B) ECG recorded 9 years after retirement. Athlete #4: Persistence of early repolarization pattern in inferior leads in a swimmer after a follow-up of 28 years. (A) ECG recorded in 1977. (B) ECG recorded 11 years after competition retirement.

a series of 5069 participants of the CARDIA cohort who had a mean age of 25 years, and 40% were of black race.<sup>21</sup> The prevalence of early repolarization pattern among athletes is higher than that observed in the general population. In our elite athletes, the early repolarization pattern was present in 31% of cases, and this prevalence was similar to that

				ECG Localization of ERP			
	ERP (n = 63)	No ERP (n =236)	P-Value	Inferior (1)	Lateral (32)	Inferolateral (30)	P-Value
Age, years	$\textbf{43.7} \pm \textbf{9.75}$	45.0 ± 7.5	ns	55.00	$\textbf{43.12} \pm \textbf{7.64}$	43.87 ± 7.28	ns
Male, %	87.3	60.2	ns	100	84.4	90.0	ns
Weight, Kg	$\textbf{73.7} \pm \textbf{72.1}$	$\textbf{72.1} \pm \textbf{14.4}$	ns	55.00	$\textbf{73.91} \pm \textbf{10.95}$	$\textbf{74.10} \pm \textbf{10.32}$	ns
BMI, Kg/m²	$\textbf{23.5} \pm \textbf{2.8}$	$\textbf{23.5} \pm \textbf{3.5}$	ns	19.00	$\textbf{23.31} \pm \textbf{3.05}$	$\textbf{23.93} \pm \textbf{2.53}$	ns
Sinus bradycardia %	71.4	41.9	.000	100	68.8	73.3	ns
Sportive category %							ns
Athletics	46	45.3	ns	100	50.0	40.0	
Swimming	14.3	13.6		0.0	15.6	13.3	
Basketball	3.2	6.8		0.0	6.2	3.2	
Others	36.5	34.3		0.0	341.4	40.0	
Volume of training %							
High (>5 h/w)	47.6	28.5	.004	100	46.9	46.7	ns
Low (<5 h/w)	52.4	71.5		0	53.1	53.3	
Smoker, %	3.2	17.5	.041	0.00	6.2	0.00	ns
High blood pressure, %	1.6	8.9	.048	0.00	0.00	3.3	ns
Dyslipidemia, %	17.5	12.3	ns	0.00	18.8	16.7	ns
Diabetes, %	0.0	0.9	ns	0.00	0.00	0.00	ns
CV events %							
Myocardial infarction	0.0	0.9	ns	0.00	0.00	0.00	ns
Stroke	0.0	0.9	ns	0.00	0.00	0.00	ns
NSMVT	3.2	1.7	ns	0.00	3.1	3.3	ns
Time on high-level	13.9 $\pm$ 5.7	11.9 $\pm$ 5.9	.022	$\textbf{22.0}\pm\textbf{0.0}$	12.9 $\pm$ 5.4	14.6 $\pm$ 5.9	ns
competition, y							
Leaving high level	13.2 $\pm$ 6.4	16.5 $\pm$ 8.5	.004	$\textbf{16.0}\pm\textbf{0.0}$	13.2 $\pm$ 6.6	$\textbf{13.1} \pm \textbf{6.4}$	ns
competition, y							
Study follow-up, y	$\textbf{22.4} \pm \textbf{6.2}$	$\textbf{24.7} \pm \textbf{7.9}$	.030	$\textbf{32.0}\pm\textbf{0.0}$	$\textbf{22.1} \pm \textbf{6.7}$	$\textbf{23.4} \pm \textbf{5.6}$	ns

<b>Table 3</b> Clinical and Sportive Characteristics of 299 Elite Athletes after a Mean Follow-up	up of 24 Years
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Abbreviations: BMI = body mass index; CV = cardiovascular; ECG = electrocardiogram; ERP = early repolarization pattern; h = hour; HR = heart rate; Kgs = kilograms; m = meters; ms = milliseconds; NSMVT = non-sustained monomorphic ventricular tachycardia; <math>w = week; y = years.



**Figure 2** Receiver operating characteristics curve of the model. The graphic shows the receiver operating characteristic curve of the model predicting the presence of early repolarization pattern in the follow-up electrocardiogram (ECG; area under the curve 0.89; 95% confidence interval, 0.85-0.94; P < .001). The model includes left ventricular hypertrophy at the baseline ECG, sinus bradycardia after retirement, and early repolarization pattern during elite activity.

observed in a cohort of 503 athletes recruited between 2000 and 2010 at the University of Miami,<sup>3</sup> and was also comparable with a study on 879 college athletes registered between 2006 and 2010 at Harvard University.<sup>15</sup> In the multivariate analysis, the predictive factors for the presence of early repolarization pattern after competition retirement were left ventricular hypertrophy at the baseline ECG, sinus bradycardia, and presence of early repolarization pattern during the sporting career. The most common type of sportive activity associated with early repolarization pattern in our series was athletics (45%). However, this association was not statistically significant because of the wide spectrum of modalities, intensity of training, and physiological characteristics of the exercise (isovolumetric or isotonic) performed by our athletes.

The mechanism by which intensive physical training could favor the development of early repolarization pattern is apparently related to a concomitant increased vagal tone. Indeed, it has been extensively documented that sinus bradycardia is one of the most prevailing electrophysiological features in active athletes,<sup>22</sup> and that the degree of sinus bradycardia depends on intensity of physical training.<sup>23</sup> Parasympathetic modulation increases regional electrophysiological differences and repolarization

dispersion, which might result in an elevation of the ST and J point and prominent T waves.<sup>24</sup> Experimental studies in dogs have raised the hypothesis that early repolarization pattern is caused by a transmural voltage gradient created by a spike-and-dome action potential, which is present in the epicardium but absent in the endocardium.<sup>25</sup> The latter is mediated by transitory outward potassium current. This hypothesis is supported by the observation of mutations affecting the potassium currents in patients with early repolarization pattern suffering ventricular arrhythmias.<sup>26,27</sup>

# **Prognosis of Early Repolarization Pattern**

Studies conducted in the general population have reported cases of sudden cardiac death secondary to idiopathic ventricular fibrillation in individuals with early repolarization pattern.<sup>5,6</sup> More recently, a meta-analysis based on 7 prospective observational cohort studies and on 2 case-control studies showed that early repolarization pattern was associated with increased risk and a low intermediate absolute incidence rate of arrhythmia death.<sup>20</sup> In these reports, the presence of J-point elevation > 0.1 mV in the inferior leads and the notching configuration was associated with an increased risk for arrhythmia death.

The estimated annual incidence of sudden cardiac death in athletes is very low (1/75,000 to 1/200,000).<sup>28-30</sup> In a case-control study including 21 athletes with sudden cardiac death and 365 healthy athletes with previous ECG screening, the J wave or QRS slurring was found more frequently among athletes with sudden cardiac death than in controls.<sup>8</sup> However, in a prospective study in a cohort of 503 athletes with a 30% early repolarization pattern prevalence, there were no cases of family history of sudden cardiac death, and there were no cases of sudden cardiac death or symptomatic ventricular tachyarrhythmia during the 10year period of ECG screening.<sup>3</sup> Likewise, in a crosssectional cohort of 879 newly matriculated student athletes with early repolarization pattern mainly of the inferior subtype, there were no cases of sudden cardiac death and unexplained syncope or hospitalization for cardiovascular causes after a mean follow-up of about 21 months.<sup>15</sup> In these series, the incidence of early repolarization pattern increased after a load period of intensive physical training. A major contribution in risk stratification in subjects with early repolarization pattern was the observation of an association between the morphology of the ST segment and the hazard ratio of arrhythmic death.<sup>9</sup> Indeed, young athletes with horizontal/descending ST segment had an increased hazard ratio of arrhythmic death compared with subjects with ascending/upsloping ST-segment pattern. These findings were later confirmed in case-control series in the general population.<sup>10,11</sup> Our study supports that early repolarization pattern is a common finding in elite athletes and, after the largest follow-up period ever reported (mean follow-up of 24 years), the long-term prognosis of ERP in athletes remains to be clarified.

In summary, this retrospective cohort of 299 elite athletes of white ethnicity shows that early repolarization pattern was present in one-third of the participants and that this ECG pattern was not associated with fatal events after a mean follow-up of about 24 years. In 97.5% of cases, the early repolarization pattern was associated with ascending/ upsloping ST segment, and only 2.5% presented horizontal/descending ST-segment pattern. The early repolarization pattern persisted in 54.3% of cases after sportive retirement and was highly associated with sinus bradycardia. The predictive factors for the presence of early repolarization pattern after retirement were left ventricular hypertrophy at the baseline ECG, current sinus bradycardia, and presence of early repolarization pattern during the elite activity.

# **Study Limitations**

The sample size of our cohort was relatively modest, but the strength of the data presented here is founded by the very long follow-up period of the study. All of our participants were of white ethnicity, thus, present data cannot be extrapolated to other races because a higher association of early repolarization pattern with African ethnicity has been recognized.<sup>3,4</sup>

Echocardiographic studies were not feasible at the early beginning of the inclusion period, and were not routinely performed thereafter. However, the recordings obtained during the follow-up visit in 64% of athletes suggested that the early repolarization pattern is not associated with underlying structural heart disease, as has been previously recognized.<sup>15</sup>

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#### References

- 1. Shipley R, Hallaran W. The four lead electrocardiogram in 200 normal men and women. *Am Heart J.* 1936;11:325-345.
- 2. Wasserburguer RH, Alt WJ. The normal RS-T segment elevation variant. *Am J Cardiol*. 1961;8:184-192.
- **3.** Junttila MJ, Sager SJ, Freiser M, et al. Inferolateral early repolarization in athletes. *J Interv Card Electrophysiol.* 2011;31:33-38.
- 4. Higgins JP. Normal resting electrocardiographic variants in young athletes. *Phys Sportsmed*. 2008;36:69-75.
- Haïssaguerre M, Derval N, Sacher F, et al. Sudden cardiac arrest associated with early repolarization. N Engl J Med. 2008;358: 2016-2023.
- Rosso R, Kogan E, Belhassen B, et al. J-point elevation in survivors of primary ventricular fibrillation and matched control subjects: incidence and clinical significance. J Am Coll Cardiol. 2008;52:1231-1238.
- Tikkanen JT, Anttonen O, Junttila MJ, et al. Long-term outcome associated with early repolarization on electrocardiography. *N Engl J Med.* 2009;361:2529-2537.
- Cappato R, Furlanello F, Giovinazzo V, et al. J wave, QRS slurring, and ST elevation in athletes with cardiac arrest in the absence of heart disease: marker of risk or innocent bystander? *Circ Arrhythm Electrophysiol.* 2010;3:305-311.

- **9.** Tikkanen JT, Junttila MJ, Anttonen O, et al. Early repolarization: electrocardiographic phenotypes associated with favorable long-term outcome. *Circulation.* 2011;123:2666-2673.
- Rosso R, Glikson E, Belhassen B, et al. Distinguishing "benign" from "malignant early repolarization": the value of the ST-segment morphology. *Heart Rhythm.* 2012;9:225-229.
- Kim SH, Kim DY, Kim H-J, et al. Early repolarization with horizontal ST segment may be associated with aborted sudden cardiac arrest: a retrospective case control study. BMC Cardiovasc Disord. 2012;12:122.
- Maron BJ, Doerer JJ, Haas TS, et al. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980-2006. *Circulation*. 2009;119:1085-1092.
- Tikkanen JT, Wichmann V, Junttila MJ, et al. Association of early repolarization and sudden cardiac death during an acute coronary event. *Circ Arrhythm Electrophysiol.* 2012;5:714-718.
- Naruse Y, Tada H, Harimura Y, et al. Early repolarization is an independent predictor of occurrences of ventricular fibrillation in the very early phase of acute myocardial infarction. *Circ Arrhythm Electrophysiol.* 2012;5:506-513.
- **15.** Noseworthy PA, Weiner R, Kim J, et al. Early repolarization pattern in competitive athletes: clinical correlates and the effects of exercise training. *Circ Arrhythm Electrophysiol*. 2011;4:432-440.
- 16. Corrado D, Pelliccia A, Bjørnstad HH, et al. Cardiovascular preparticipation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol. Consensus Statement of the Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. *Eur Heart J.* 2005;26:516-524.
- Strauss HC, Bigger JT, Saroff AL, Giardina EG. Electrophysiologic evaluation of sinus node function in patients with sinus node dysfunction. *Circulation*. 1976;53:763-776.
- Sokolov M, Lyon T. The ventricular complex in left ventricular hypertrophy as obtained by unipolar precordial and limb leads. *Am Heart J.* 1949;37:161-186.

- Rosso R, Halkin A, Viskin S. J waves and early repolarization: do not confuse me with the facts! *Heart Rhythm.* 2012;9: 1603-1604.
- Wu S-H, Lin X-X, Cheng Y-J, et al. Early repolarization pattern and risk for arrhythmia death: a meta-analysis. *J Am Coll Cardiol*. 2013;61: 645-650.
- Walsh JA, Ilkhanoff L, Soliman EZ, et al. Natural history of the early repolarization pattern in a biracial cohort: CARDIA (Coronary Artery Risk Development in Young Adults) Study. J Am Coll Cardiol. 2013;61:863-869.
- Viitasalo MT, Kala R, Eisalo A. Ambulatory electrocardiographic recording in endurance athletes. *Br Heart J.* 1982;47:213-220.
- Serra-Grima R, Puig T, Doñate M, et al. Long-term follow-up of bradycardia in elite athletes. *Int J Sports Med.* 2008;29:934-937.
- Barbosa EC, Bomfim Ade S, Benchimol-Barbosa PR, Ginefra P. Ionic mechanisms and vectorial model of early repolarization pattern in the surface electrocardiogram of the athlete. *Ann Noninvasive Electrocardiol.* 2008;13:301-307.
- Yan GX, Antzelevitch C. Cellular basis for the electrocardiographic J wave. *Circulation*. 1996;93:372-379.
- Haïssaguerre M, Chatel S, Sacher F, et al. Ventricular fibrillation with prominent early repolarization associated with a rare variant of KCNJ8/KATP channel. J Cardiovasc Electrophysiol. 2009;20: 93-98.
- Medeiros-Domingo A, Tan B-H, Crotti L, et al. Gain-of-function mutation S422L in the KCNJ8-encoded cardiac K(ATP) channel Kir6.
   1 as a pathogenic substrate for J-wave syndromes. *Heart Rhythm.* 2010;7:1466-1471.
- Corrado D, Basso C, Schiavon M, Thiene G. Screening for hypertrophic cardiomyopathy in young athletes. N Engl J Med. 1998;339: 364-369.
- 29. Maron BJ. Sudden death in young athletes. N Engl J Med. 2003;349: 1064-1075.
- Viskin S, Rosso R, Halkin A. Making sense of early repolarization. *Heart Rhythm.* 2012;9:566-568.

	Persistent ERP (n = 51)	Nonpersistent ERP ( $n = 43$ )	De Novo ERP (n = 12)	P-Value
Age, y	43.7 ± 7.0	41.2 ± 8.9	$\textbf{43.7} \pm \textbf{6.9}$	ns
Male, %	86.3	67.4	91.7	.043
Weight, Kg	73.5 $\pm$ 11.0	$\textbf{67.7} \pm \textbf{13.4}$	74.5 $\pm$ 10.2	.043
BMI, Kg/m2	$\texttt{23.6}\pm\texttt{3.0}$	$\textbf{22.5} \pm \textbf{2.9}$	$\textbf{22.9} \pm \textbf{1.9}$	ns
Sinus bradycardia, %	68.6	46.5	83.3	.023
Sportive category %				
Athletics	43.1	46.5	50.0	
Swimming	17.6	14.0	8.3	ns
Basketball	3.9	44.7	0.0	
Others	35.3	34.9	41.7	
Volume of training, %				
High $>5$ h/w	41.2	31.0	75.0	.024
Low < 5 h/w	58.8	69.0	25.0	
Smoker, %	23.5	31.0	25.0	ns
High blood pressure, %	2.0	7.1	0.0	.048
Dyslipidemia, %	21.6	16.7	0.0	ns
Diabetes, %	0.0	0.0	0.0	ns
CV events %				
Myocardial infarction	0.0	0.0	0.0	ns
Stroke	0.0	0.0	0.0	ns
NSVTM	3.9	4.7	0.0	ns
Time on high-level competition, y	13.8 $\pm$ 5.9	11.9 $\pm$ 5.8	$14.8\pm5.5$	ns
Leaving high-level competition, y	13.4 $\pm$ 6.3	12.8 $\pm$ 6.8	$\textbf{12.1} \pm \textbf{7.0}$	ns
Study follow-up, y	$\textbf{22.6} \pm \textbf{6.2}$	20.9 $\pm$ 6.2	$\textbf{21.3} \pm \textbf{6.3}$	ns
ERP location, %				
Inferior	2	_	0.0	
Lateral	49	—	51.3	<.01
Inferolateral	49	_	48.7	
Any J-point $>$ 0.2 mV, %	0.0	0.0	8.3	<.01
QRS pattern, %				
Discrete	38.6	97.1	55.6	
Slurred	19.5	2.9	22.2	<.01
Notched	31.8	0.0	22.2	
QRS duration, ms	92.9 $\pm$ 8.5	90.6 $\pm$ 12.1	$\textbf{95.4} \pm \textbf{12.1}$	ns
ST-segment deviation, %				
Ascending/upsloping	90.7	66.7	100	ns
Horizontal/descending	9.3	33.3	0.0	
Sokolov-Lyon index $>$ 3.5 mV, %	21.4	5.7	40.0	.025

**Supplementary Table 1** Demographic, Clinical, and Electrocardiographic Characteristics of Athletes with Persistent, Nonpersistent, and De Novo Early Repolarization Pattern after a Follow-up Period of 24 Years

Abbreviations: BMI = body mass index; CV = cardiovascular; ERP = early repolarization pattern; h = hour; kg = kilograms; m = meters; mm = millimeters; ms = milliseconds; mV = millivolts; ns = no significance; NSMVT = nonsustained monomorphic ventricular tachycardia; w = week; y = year.