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Does early repolarization in the athlete have analogies with the Brugada syndrome?

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Aim To re-examine the prevalence and presentation of early repolarization in athletes and to compare it with electrocardiographic abnormalities observed in patients with the Brugada syndrome.

Methods Electrocardiograms of 155 male athletes and 50 sedentary controls were studied. Early repolarization was considered present if at least two adjacent precordial leads showed elevation of the ST segment ≥ 1 mm. Amplitude and morphology of ST elevation, the leads where it was present and the lead in which it showed its maximum value were analysed together with QRS duration, the presence of right ventricular activation delay, QT and QTc duration. Data were compared with those obtained by electrocardiograms of 23 patients with the Brugada syndrome.

Results Early repolarization was found in 139 athletes (89%) and 18 controls (36%, $P \leq 0{\cdot}025$), being limited to right precordial leads in 42 (30%) athletes and 13 (72%) controls ($P \leq 0{\cdot}001$). Only 12 (8·6%) athletes and one control (5·5%) with early repolarization had an ST elevation 'convex toward the top' in right precordial leads, similar to that seen in the Brugada syndrome. In athletes the maximum ST elevation was greater ($2{\cdot}3 \pm 0{\cdot}6$ mm) than in the controls ($1{\cdot}2 \pm 0{\cdot}8$ mm; $P \leq 0{\cdot}004$) but significantly lower than in patients with the Brugada syndrome ($4{\cdot}4 \pm 0{\cdot}7$ mm; $P \leq 0{\cdot}0001$). Patients with the Brugada syndrome also had a greater QRS duration ($0{\cdot}11 \pm 0{\cdot}02$ s) than athletes ($0{\cdot}090 \pm 0{\cdot}011$ s; $P \leq 0{\cdot}0001$) with early repolarization.

Conclusions Early repolarization is almost always the rule in athletes but it is also frequent in sedentary males. Tracings somewhat simulating the Brugada syndrome were observed in only 8% of athletes without a history of syncope or familial sudden death. Significant differences exist between athletes with early repolarization and patients with the Brugada syndrome as regards the amplitude of ST elevation and QRS duration.
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Key Words: Early repolarization, athletes, Brugada's syndrome, sudden death.

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Introduction

The electrocardiogram (ECG) of athletes at rest, especially in those that are endurance-trained, frequently shows ST-segment elevation, mainly in precordial leads. This condition, named early repolarization, is considered a benign electrocardiographic change due to athletic conditioning[1–4]. Renewed interest in early repolarization arose after the discovery by Brugada and Brugada[1] of a new syndrome, characterized by ST elevation in right precordial leads (V_1–V_3), with or without a delay in right ventricular activation. The Brugada syndrome is now recognized as a primary, genetically determined[5], electrical disease with a high risk of sudden cardiac death. The prevalence of ventricular fibrillation in such patients has been estimated as high as 40–60%[6].

The aims of this study were: (1) to re-examine the prevalence and patterns of ST elevation in athletes with early repolarization; (2) to compare this type of ST elevation with that observed in patients with the Brugada syndrome.

Methods

We studied the ECG tracings at rest of 155 top-ranking male Caucasian athletes (age $30{\cdot}9 \pm 10{\cdot}1$ years), 83 of whom were distance runners, 38 professional soccer players and 34 cyclists, and those of 50 male Caucasian sedentary students (age $25{\cdot}3 \pm 3{\cdot}5$ years). All those who entered this study came to our centre for scientific reasons only and had no evidence of organic heart

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disease as judged from clinical history, physical and echocardiographic examination.

Early repolarization was considered present when at least two adjacent precordial leads showed an elevation ≥ 1 mm of the ST segment. The ST elevation was accurately analysed by considering its morphology, the number of precordial leads in which it was present, its maximum amplitude (mm) and the lead where this maximum was located. We also measured: heart rate, the Sokolov index (sum of the S wave in V_1 + the higher R wave in V_5 or V_6, mm); the duration of the QRS complex (s) and the duration of QT (s) and QTc (s), according to Bazett's formula, the presence of delay in right ventricular activation; the presence of positive or negative giant T waves (≥ 10 mm) and, when present their maximum amplitude (mm).

Furthermore, we made a meta-analysis of 23 ECGs of patients with the Brugada syndrome, published in the literature[3–13] and considered suitable for a detailed examination. Tracings were magnified with the help of graphic software for a better analysis of their characteristics, and we considered the correct conversion factor, for time and amplitude, in measuring the above described parameters.

Statistical analysis

Student's t-test for independent samples and the chi-squared test were used when appropriate comparing two different groups. When we considered more than two groups, Newman–Keuls–Student's test was used. The Mann–Whitney U test was used to verify the presence of differences in the distribution on precordial leads of ST elevation and of positive giant T waves between athletes and controls. A difference was considered significant when P was $\leq 0{\cdot}05$. Statistical analysis was performed using STATISTICA version 4.1 software by Statsoft.

Results

Heart rate, Sokolov index and QRS duration

As expected, athletes had lower heart rate ($50{\cdot}8 \pm 6{\cdot}9$ vs $73{\cdot}7 \pm 11{\cdot}2$ beats . min^{-1}; $P \leq 0{\cdot}0001$), greater Sokolov index ($46{\cdot}5 \pm 11{\cdot}6$ vs $33{\cdot}2 \pm 8{\cdot}2$ mm; $P \leq 0{\cdot}0001$), and a slightly but significantly longer QRS duration ($0{\cdot}095 \pm 0{\cdot}011$ vs $0{\cdot}088 \pm 0{\cdot}010$ s; $P \leq 0{\cdot}0001$) than the controls.

Prevalence and pattern of early repolarization in athletes and controls

Early repolarization was found in 139 of the 155 athletes (89%) and in 18 of the 50 controls (36%) ($P \leq 0{\cdot}025$). Among athletes, early repolarization was observed in 87·9% of distance runners, 94·7% of professional soccer players and 88·2% of cyclists.

The amplitude of maximum ST elevation was higher in athletes ($2{\cdot}3 \pm 0{\cdot}6$ mm) than in controls ($1{\cdot}2 \pm 0{\cdot}8$ mm; $P \leq 0{\cdot}04$); among athletes, the amplitude was lower in soccer players than in cyclists ($1{\cdot}95 \pm 0{\cdot}44$ mm vs $2{\cdot}55 \pm 0{\cdot}76$, $P \leq 0{\cdot}001$) and in distance runners ($1{\cdot}95 \pm 0{\cdot}44$ vs $2{\cdot}35 \pm 0{\cdot}81$ mm; $P \leq 0{\cdot}02$).

The amplitude of maximum ST elevation was located 'more at left' in precordial leads, i.e. toward V_3 and V_4, in athletes than in controls ($P \leq 0{\cdot}008$) (Fig. 1A). In subjects with early repolarization, 42 of 139 athletes (30·2%) and 13 of 18 controls (72·1%) had ST elevation in right precordial leads ($P \leq 0{\cdot}001$); the amplitude of maximum ST elevation in these individuals was $2{\cdot}0 \pm 0{\cdot}62$ mm in the 42 athletes and $1{\cdot}8 \pm 0{\cdot}52$ mm in the 13 controls (ns). However, only 12 athletes, i.e. 8·6% of those with early repolarization and 28·5% of those with early repolarization located only in right precordial leads, had a 'convex toward the top' ST elevation morphology, which could be considered similar to that observed in most patients with the Brugada syndrome (Fig. 1B). Only one control had early repolarization located only in right precordial leads with a 'convex toward the top' ST elevation morphology.

QRS duration, right ventricular conduction delay, QT duration and T wave

The duration of the complex QRS was greater in athletes than in controls ($0{\cdot}095 \pm 0{\cdot}011$ vs $0{\cdot}088 \pm 0{\cdot}010$ s; $P \leq 0{\cdot}0001$), with no difference when only subjects with early repolarization were considered. Forty-two of the 155 athletes (27%) and nine of the 50 controls (18%) had a minor right ventricular conduction delay (Fig. 1A); only one athlete (0·6%) had a complete right bundle branch block. All 42 athletes with minor right ventricular conduction delay and the one with right bundle block had early repolarization, while only four out of the nine controls with minor right ventricular conduction delay had early repolarization.

The duration of the QT was longer in athletes than in controls ($0{\cdot}423 \pm 0{\cdot}039$ vs $0{\cdot}364 \pm 0{\cdot}031$ s; $P \leq 0{\cdot}0001$), but no difference was observed when the QT was corrected for heart rate (QTc: $0{\cdot}388 \pm 0{\cdot}031$ s for athletes, $0{\cdot}379 \pm 0{\cdot}0283$ s for controls).

No athletes or controls had giant (≥ 10 mm) negative T waves. One soccer player with early repolarization had biphasic-negative T waves in leads V_4–V_6. Positive giant T waves were seen in 86 of the 155 athletes (55·4%) (Fig. 1C), all with early repolarization, and in nine of the 50 controls (18%) ($P \leq 0{\cdot}0001$), six of them also having early repolarization.

Electrocardiograms of patients with the Brugada syndrome

Patients with the Brugada syndrome (Fig. 2) showed a higher heart rate ($76{\cdot}9 \pm 19{\cdot}3$ vs $50{\cdot}8 \pm 6{\cdot}9$ beats . min^{-1}; $P \leq 0{\cdot}0001$), a greater amplitude of

the maximum ST elevation (4·4 ± 1·9 vs 2·3 ± 0·6 mm; $P \leq 0{\cdot}0001$), a longer QRS duration (0·116 ± 0·019 vs 0·095 ± 0·011 s; $P \leq 0{\cdot}0001$) and a lower Sokolov index (23·3 ± 8·2 vs 46·7 ± 11·8 mm; $P \leq 0{\cdot}0001$) than the 139 athletes with early repolarization (Table 1). Similar results were obtained comparing patients with the Brugada syndrome with the 42 athletes having ST elevation limited to right precordial leads (maximum ST elevation: 1·9 ± 0·6 mm, QRS duration: 0·09 ± 0·010 s and Sokolov index: 44·5 ± 10·8 mm, all with a $P \leq 0{\cdot}0001$).

Comparing patients with the Brugada syndrome and athletes with early repolarization in right precordial leads, a cut-off value of 2 mm for the maximum ST elevation had a 95% sensitivity, 74% specificity and 66% positive and 97% negative predictive values for the presence of the disease. A cut-off value of 3 mm had a 56% sensitivity, 95% specificity and 87% positive and 80% negative predictive values. A cut-off value of 0·11 s for QRS duration had a 56% sensitivity, 93% specificity and 81% positive and 79% negative predictive values. When the two parameters are considered together, cut-off values, respectively, of 2 mm for the maximum ST elevation and 0·11 s for QRS duration had a 56% sensitivity, 100% specificity and 100% positive and 80% negative predictive values (Fig. 3).

All patients with the Brugada syndrome had a QT interval within normal limits, and it was lower than in all athletes with early repolarization (0·378 ± 0·043 vs 0·427 ± 0·038 s; $P \leq 0{\cdot}0001$) and in those with early repolarization limited to right precordial leads (0·378 ± 0·043 vs 0·413 ± 0·035 s; $P \leq 0{\cdot}0001$). However, when correction for heart rate was made, patients with the Brugada syndrome had a significantly longer QTc than all athletes with early repolarization (0·424 ± 0·049 vs 0·39 ± 0·031 s; $P \leq 0{\cdot}0001$) and athletes with early repolarization limited to right precordial leads (0·424 ± 0·049 vs 0·38 ± 0·028 s; $P \leq 0{\cdot}0001$).

Only two of the 23 patients with the Brugada syndrome (8·6%) had giant positive T waves in precordial leads: a 44-year-old man with an autonomic disorder[11] and a 47-year-old man with hypertension[3].

Discussion

An 'abnormal' ECG tracing at rest is the rule in top-ranking endurance-trained athletes[1,3,14]. ECG abnormalities belong to three main groups: (1) physiological changes, such as sinus bradycardia and high QRS and T wave voltages, which are the result of training; (2) borderline changes, such as negative T waves, which may be correlated with training but also due to concealed heart disease; and (3) abnormal or clearly pathological changes[15].

ST elevation, the so-called early repolarization, is one of the most common ECG 'abnormalities' in athletes. Its prevalence varies from 10% in the general athletic population to 100% in selected groups of endurance-trained subjects[1–3,16]. The underlying mechanism of early repolarization is not yet well understood. In the past, it was attributed to an enhanced activity of right cardiac sympathetic nerves[4], or to an enhanced vagal tone[15,17]. Nevertheless, it is reasonable to suppose that the autonomic nervous system plays an important role because ST elevation is reduced or abolished by exercise and beta-stimulating agents, such as isoproterenol, and increased by beta-blocking drugs[5,7,17].

Renewed interest in early repolarization occurred after the discovery of the Brugada syndrome, a primary electrical disease of the heart, characterized by ST elevation in right precordial leads and a high risk of sudden death by ventricular fibrillation in subjects without apparent organic heart disease[5]. Several studies have been performed to assess mechanisms of ST elevation and life-threatening arrhythmias in this syndrome, the most plausible being a dispersion of repolarization between the two ventricles[8] and/or between the epicardial and endocardial layer of the right ventricle[9]. This mechanism has many analogies with that proposed for early repolarization[4,9]. Also, the effects of drugs are analogous, since in patients with the Brugada syndrome the ST elevation increases with beta-blocking agents and diminishes with isoproterenol[7]. In some patients, the ST elevation may be transient and reproduced only by administrating sodium-channel blockers such as ajmaline[18]. Although programmed ventricular stimulation can also precipitate malignant tachyarrhythmias in patients with transient 'normalization' of the ECG, the inducibility of ventricular fibrillation and the risk of sudden death seem to be higher when ST elevation in right precordial leads reaches its maximal value[19,20].

Prevalence and significance of early repolarization in athletes

As has been documented in the sports medicine literature, early repolarization is a functional and benign phenomenon which usually disappears by interrupting

Figure 1 **Representative tracings of athletes with early repolarization: A. Electrocardiogram of a 39-year-old marathon runner showing marked bradycardia with sinus arrhythmia (32–37 beats . min^{-1}), high QRS voltages, minor delay in right ventricular activation (rSr′ in V_1), concave ST elevation from V_3 to V_6 and giant positive T waves. B. Electrocardiogram of a 27-year-old cyclist showing moderate sinus bradycardia (44 beats . min^{-1}), high QRS voltages, a minor delay in right ventricular activation (rsr′ in V_1), diffuse ST elevation in precordial leads with a convex shape in V_2 and V_3 and giant positive T waves. C. Electrocardiogram of a 31-year-old marathon runner showing marked sinus bradycardia (39 beats . min^{-1}), high QRS voltages, ST elevation in leads V_2 and V_3 with a 'convex toward the top' morphology resembling that seen in most patients with the Brugada syndrome. (Paper speed 25 mm . s^{-1}, 1 cm=1 mV).**

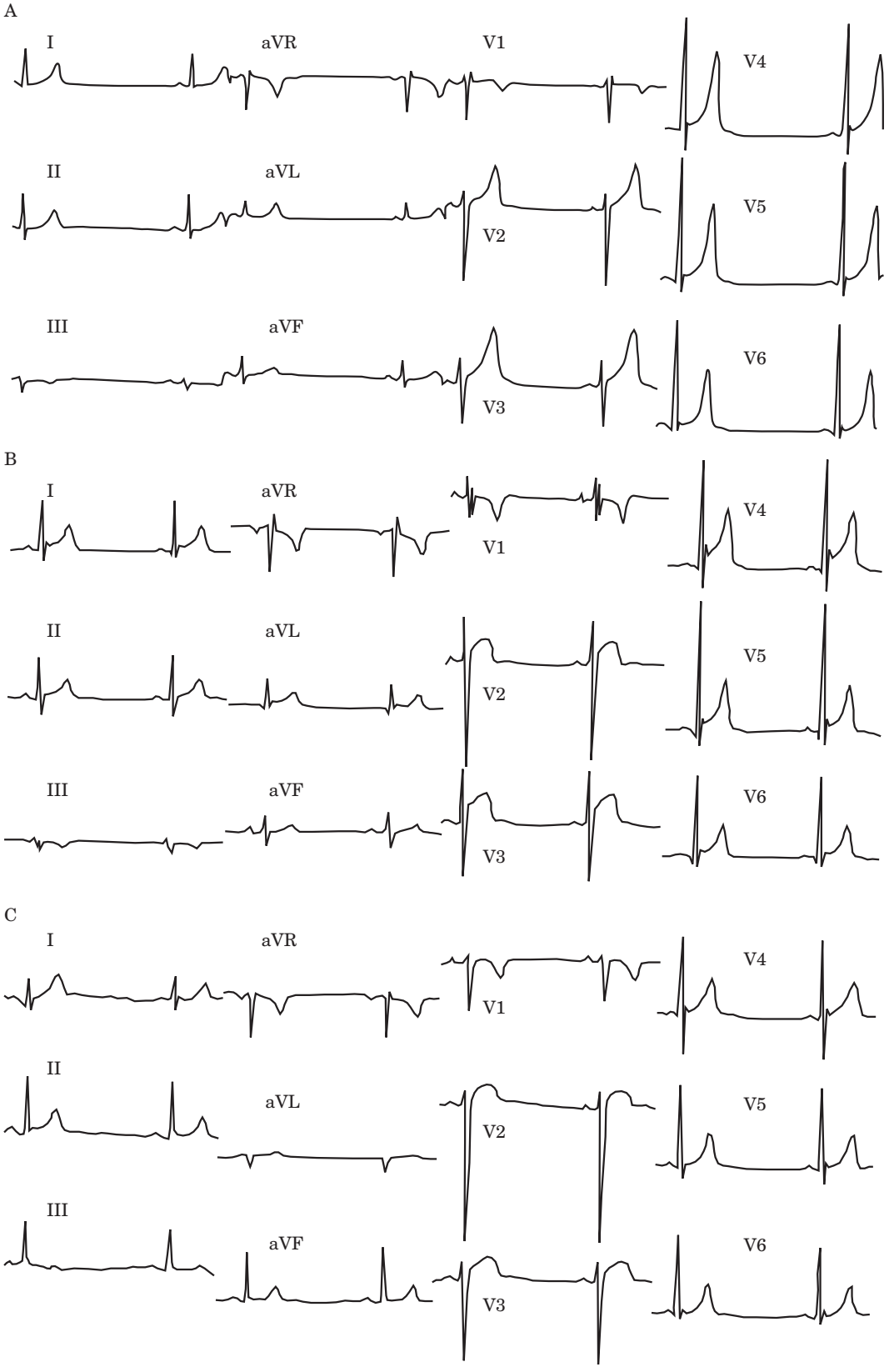
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Table 1 Differences between 139 athletes with early repolarization and 23 patients with the Brugada syndrome

	Athletes with early repolarization	Patients with Brugada syndrome
Subjects	139	23
Heart rate (beats . min^{-1})	50·8 ± 6·9	76·9 ± 19·3*
Sokolov index (mm)	46·5 ± 11·6	23·3 ± 8·2*
QRS duration (s)	0·095 ± 0·011	0·116 ± 0·019*
ST elevation (mm)	2·3 ± 0·6	4·4 ± 1·9*
QT (s)	0·427 ± 0·038	0·378 ± 0·043*
QTc (s)	0·39 ± 0·031	0·424 ± 0·049*

*$P \leq 0{\cdot}001$.

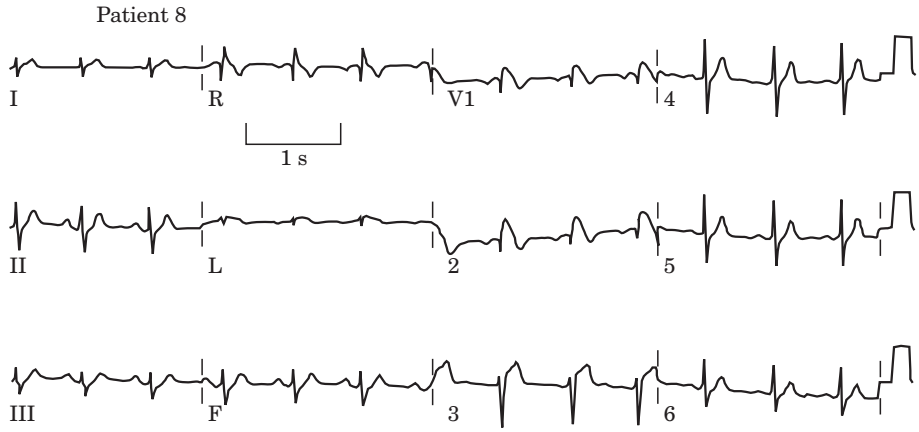

Figure 2 **Electrocardiogram of a patient with the Brugada syndrome showing marked ST elevation in leads V_1 trough V_3 with a 'convex toward the top' morphology, particularly in leads V_1 and V_2. Reproduced with the permission of P. Brugada[1].**

training. From this point of view, our paper has simply confirmed that early repolarization is almost always the rule in top-ranking athletes. Although it can also be observed in sedentary young controls, there were significant differences between the two groups. In athletes, the amplitude of the maximum ST elevation was greater, 'shifted to the left' in precordial leads and very frequently associated with higher QRS and T wave voltages, producing an electrocardiographic pattern, representative of the so-called 'athlete's heart', which cannot be confused with the ECG of patients with the Brugada syndrome.

Athletes with a Brugada-like ST elevation

Our paper shows that a more accurate differential diagnosis is necessary only in a few athletes (about 8%), i.e. those with ST elevation limited to right precordial leads showing a 'convex toward the top morphology'. An 8% prevalence was four times greater than that found in the general population[13]. However, our athletes with a Brugada syndrome-like pattern had no familial history of sudden cardiac death and were completely asymptomatic in spite of a long career including a very large number of intense training sessions and competitions. We considered whether these athletes should undergo invasive and expensive instrumental investigations, such as an electrophysiological study, genetic analysis and so on.

We think that a first step in decision-taking about further investigations can come from an accurate analysis of the ECG. Patients with the Brugada syndrome showed significant differences in respect of athletes: the amplitude of maximum ST elevation is greater, the QRS duration longer and the Sokolov index lower. Furthermore, ST elevation does not usually extend beyond lead V_4 and is rarely associated with giant positive T waves. The simultaneous presence of a QRS duration greater than 0·11 s and maximum ST elevation in right precordial leads greater than 2 mm have 100% positive and 80% negative predictive values, respectively, for the presence of a Brugada syndrome. In our study group, the only athlete with QRS duration >0·11 s had a right bundle branch block and a maximum ST elevation of 1·5 mm in V_1–V_2.

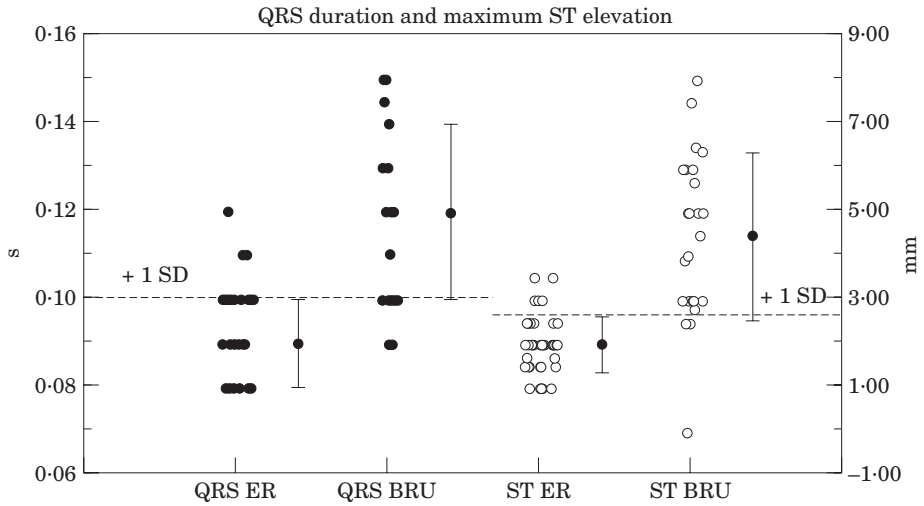

Figure 3 **QRS duration (s) and maximum ST elevation (mm) in athletes with early repolarization limited to right precordial leads (n=42) and in patients with the Brugada syndrome (n=23). The means of the two groups are significantly different. Cut-off values, respectively, of 2 mm for maximum ST elevation and 0·11 s for QRS duration considered together had 100% positive and 80% negative predictive value for the presence of the Brugada syndrome.**

Conclusions

We confirmed that 'early repolarization' is almost always the rule in athletes, although it can also be found in normal people, and it represents one of the elements which characterize the typical athlete's ECG. Only about 8% of athletes have an ST elevation with upward-convexity in right precordial leads that could recall that observed in most patients with the Brugada syndrome. However, they have a lower ST elevation and QRS duration than patients with the Brugada syndrome.

For these reasons, we think that invasive and expensive instrumental investigations, such as an invasive electrophysiological study, are very rarely justified in athletes with early repolarization, providing that they are asymptomatic, have a negative familial history for sudden cardiac death, and an accurate analysis of the ECG is made.

We are indebted to Professor Pedro Brugada for his helpful suggestions and friendly collaboration.

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