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Marked Ventricular Repolarization Abnormalities in Highly Trained Athletes' Electrocardiograms: Clinical and Prognostic Implications

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OBJECTIVE We sought to study the functional, clinical and prognostic implications of marked repolarization abnormalities (MRA) sometimes seen in athletes' electrocardiograms (ECGs).

BACKGROUND The clinical meaning of ECG MRA in athletes is unknown. No relationship has been drawn between either training intensity or any particular type of sport and MRA. Athletes are usually symptom free and do not show any decrease in their physical performance. It is as yet unclear whether MRA may have a negative effect on the performance of such athletes in competitive sports.

METHODS We studied 26 athletes with MRA (negative T waves ≥2 mm in three or more ECG leads at rest). No athletes presented clinical symptoms of cardiac disease or decrease in their physical performance. Clinical and physical examinations, ECG at rest, exercise test and echocardiographic and antimyosin studies were performed in all athletes. Rest/exercise myocardial perfusion single-photon emission computed tomography studies were performed in 17 athletes. The follow-up ranged from 4 to 20 years (mean 6.7 years).

RESULTS Four athletes were excluded due to hypertrophic cardiomyopathy. Echocardiographic studies showed right and left normal ventricular dimensions for highly conditioned athletes. In the exercise test, heart rate was 166 ± 12.4 beats/min, and exercise tolerance was 15.2 ± 2.7 metabolic equivalents of the task. All athletes had ECG at rest simulating myocardial ischemia or "pseudoischemia" with a tendency to normalize during exercise. Myocardial perfusion studies were normal in the studied athletes. Antimyosin studies showed mild and diffuse myocardial radiotracer uptake in 15 athletes (68%). No adverse clinical events were observed in the follow-up.

CONCLUSIONS These results suggest that MRA have no clinical or pathological implications in athletes and should, therefore, not preclude physical training or participation in sporting events. (J Am Coll Cardiol 2000;36:1310–6) © 2000 by the American College of Cardiology

Physical training with dynamic exercise predominance produces changes both in heart structure and in the electrocardiogram (ECG). The most common changes in the structure of the heart are an increase in ventricular wall thickness and the diameter of the left ventricle (LV), both evidenced in echocardiographic studies. In the ECG, the most frequent changes are sinus bradycardia, first degree heart block, second degree Mobitz I (Wenckeback) and repolarization alterations. Sinus bradycardia is almost constant and can be below 30 beats per minute, especially during the night. These ECG changes are more frequent in trained athletes than they are in sedentary people (1–6).

Changes in ventricular repolarization are normally slight. Marked repolarization abnormalities (MRA) are not common and suggest the presence of heart disease (Fig. 1). They do not bear any apparent relation to training intensity or any particular type of sport. Athletes are generally symptom-free and do not show any decrease in their physical performance.

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The purpose of this study was to assess the clinical significance and prognosis of changes in ventricular repolarization in athletes with an ECG showing MRA. For this purpose, we studied athletes with MRA by means of echocardiography, exercise test, rest/exercise myocardial perfusion single-photon emission computed tomography and antimyosin studies.

METHODS

Subjects. We studied 26 male athletes (10 runners, 7 soccer players, 2 waterpolo players, 2 pentathlon athletes, 2 basketball players, 1 swimmer, 1 cyclist and 1 triathlon athlete) with a mean age of 29 ± 11 years and a mean body surface area of 1.74 ± 1.5 m^2. Two athletes were at international competition level (one had participated three times in the Olympic Games and the other once), and the remaining athletes competed at a national level. All athletes showed MRA in rest ECG. Marked repolarization abnormalities were considered when negative T waves ≥2 mm were present in three or more rest ECG leads. All athletes included in the study were examined in the "Residencia Blume," a sports medicine cardiology reference center in Barcelona, Spain. Athletes are referred from eight other local sports medicine centers that monitor a total of 3,500

Abbreviations and Acronyms

ECG = electrocardiogram
In = indium
LV = left ventricle, left ventricular
MRA = marked repolarization abnormalities
Tc = technetium

athletes (from 25 different Olympic events) per year. Clinical and physical examinations, echocardiographic studies, exercise tests and antimyosin studies were carried out in all cases. Rest/exercise myocardial perfusion studies were performed in 17 athletes. The follow-up was between 4 and 20 years (mean 6.7 years). All athletes were informed about study characteristics, including the use of radiotracers, and all gave their written informed consent. The protocol was approved by the Institutional Ethical Committee of the Hospital de Sant Pau of Barcelona.

Echocardiographic study. Echocardiographic studies were performed using a Vingmed Sonotron ultrasonograph CFM 700 with a 3.0-MHz transducer and were evaluated by three independent observers. Echocardiograms were performed in the semirecumbent and left lateral positions in accordance with the American Society of Echocardiography Recommendations (7). Left ventricular diastolic thickness of intraventricular septum and posterior free wall, and diastolic and systolic internal dimensions of right and LV cavities, were evaluated in accordance with standard M-mode echocardiographic criteria (8). In all subjects two-dimensional images were performed to assist in interpretation of data.

The LV mass was calculated using the American Society of Echocardiography's recommended formula (7–9): LV mass (g) = 1.04 ([LV internal diameter + septum thickness + posterior wall thickness]^3—[LV internal diameter^3])—13.6. The LV mass index was calculated from the relation between LV mass and body surface area.

Exercise test. The exercise test was performed using the Bruce protocol on a treadmill (Quinton 500 System). Athletes were encouraged to continue the exercise until exhaustion. Seven athletes stopped the exercise because of leg fatigue. Twelve ECG leads were recorded at rest, during the exercise and 10 min after recovery. Blood pressure was registered at rest and every 3 min during the exercise.

Rest/exercise myocardial perfusion study. The rest/exercise perfusion studies were performed using a two-day protocol. Seven-hundred and forty MBq of ^{99m} technetium (Tc)-tetrofosmin (Myoview, Nycomed Amersham) was intravenously administered twice, once at rest and again at the peak of maximum effort during the exercise test. Athletes were asked to drink a glass of whole milk to accelerate hepatobiliary clearance. Single-photon emission computed tomography studies were performed using a rotating gammacamera (Elscint, Helix HR) with a low-energy, high-resolution collimator. A 10% window was centered over the 140 keV ^{99m}Tc photopeak. Sixty projections of 20 s each were acquired in step-and-shoot mode over a 180° circular orbit, from the 45° right anterior oblique to the 45° left posterior oblique views, with a zoom factor of 1.4 and a 64 × 64 byte matrix. Series of 6.2 mm-thick transverse slices were reconstructed using filtered backprojection with a ramp filter and smoothed with a Butterworth filter (cut-off frequency 0.4 cycles/pixel, power 16 for ^{99m}Tc-tetrofosmin studies). The data were reconstructed in short axis, horizontal long axis and vertical long axis views, and neither scatter nor attenuation correction was applied. The slice set was normalized to the maximum of activity.

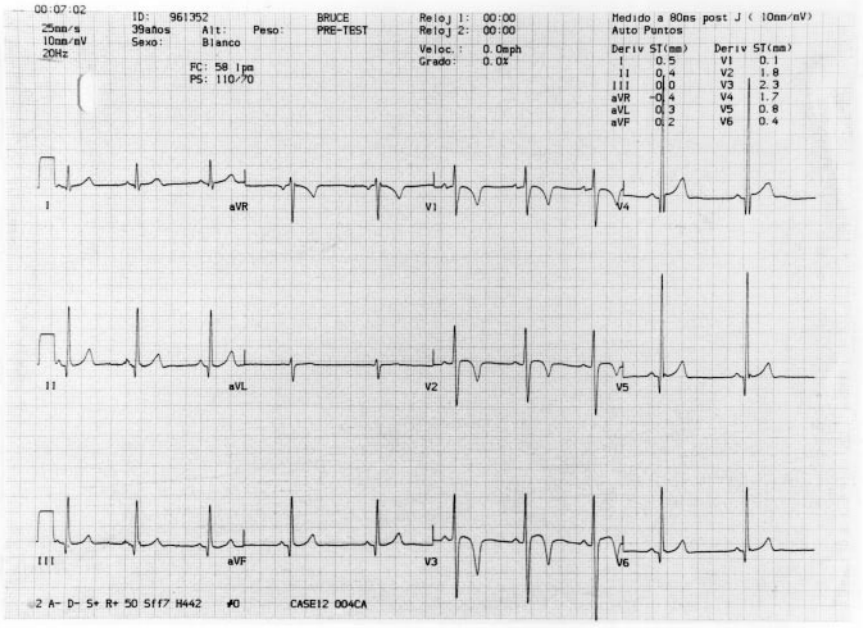

Figure 1. Electrocardiogram of athlete 10 who participated in the Olympic Games in Los Angeles. This electrocardiogram, performed 12 years later when training level was significantly lower, continues to show marked repolarization abnormalities.

Table 1. Results of Echocardiographic and Antimyosin Studies and ECG Pattern (Between Parenthesis ECG Leads) in Athletes With MRA

n (age)	Sport	BSA	MWTs	MWTp	LVD	LVS	MI	HRL	ST level	T wave
1 (25)	B	2.28	13	10	61	40	159	1.57		−5 (V4)
2 (30)	SC	1.71	8	8	47	27	82	1.67	+4 (V3)	−8 (V4)
3 (18)	C	1.59	12	10	57	39	164	1.88	+4 (V2)	
4 (19)	S	1.74	13	11	54	37	184	1.65		−3 (VF)
5 (48)	SC	1.64	10	8	58	36	109	1.52		−7 (V4)
6 (24)	R	1.65	9	9	55	32	140	1.72	+3 (V2)	−5 (V3)
7 (19)	SC	1.83	11	9	49	33	114	1.68	+1 (V3)	−4 (V2)
8 (32)	SC	1.70	11	11	46	24	132	1.42	+2 (V3)	−7 (V4)
9 (18)	WP	1.84	10	8	54	36	214	1.61	+2 (III)	−2 (III)
10 (39)	R	1.68	11	11	50	26	147	1.88	+4 (V3)	−20 (V5)
11 (18)	WP	1.77	10	8	54	32	121	1.38	+3 (V3)	−7 (V4)
12 (39)	R	1.84	8	7	57	31	147	1.51	+2 (V2)	−5 (V1)
13 (36)	R	1.60	11	11	54	38	194	1.87	+3 (V2)	−8 (V1)
14 (58)	T	1.66	11	10	55	34	104	1.56	+2 (V2)	−4 (V1)
15 (38)	R	1.70	12	10	53	35	167	1.47	+3 (V2)	−4 (V1)
16 (39)	R	1.63	9	9	59	40	159	1.62	+3 (V3)	−11 (V3)
17 (34)	SC	1.71	12	9	63	36	156	1.74	+2 (V4)	−18 (V4)
18 (20)	P	1.64	10	10	48	31	101	1.57	+4 (V2)	−5 (V3)
19 (18)	P	1.69	10	8	59	36	121	1.54	+3 (V2)	−7 (V3)
20 (23)	SC	1.92	10	9	50	29	109	1.50	+2 (V2)	−13 (V5)
21 (28)	R	1.85	12	9	52	27	211	1.60	+2 (V2)	−7 (V4)
22 (18)	R	1.70	10	10	59	33	220	1.63		−5 (V4)
Mean ± SD		1.74 ± 0.15	11 ± 1.4	9 ± 1.2	54 ± 4.6	33 ± 4.6	148 ± 39	1.61 ± 0.13	+2.30 ± 1.3	−6.87 ± 4.5

B = basketball player; BSA = body surface area (m^2); C = cyclist; HLR = heart-to-lung ratio (myocardial antimyosin uptake); LVD = left ventricular end-diastolic diameter (mm); LVS = left ventricular end-systolic diameter (mm); MI = mass index (g/m^2); MRA = marked repolarization abnormalities; MWTp = maximal posterior wall thickness (mm); MWTs = maximal septal wall thickness (mm); P = pentathlon athlete; R = runner; S = swimmer; SC = soccer player; SD = standard deviation; T = triathlon athlete; WP = waterpolo player.

Antimyosin study. The antimyosin studies were performed within two weeks of echocardiographic studies. A dose of 0.5 mg of R11-D10-Fab-dietilentriamine-pentaacetic (Centocor Europe, Leiden, the Netherlands) labelled with 74 MBq of ^{111}indium (In) was administered by slow intravenous injection. Planar anterior projection scans of the thorax were acquired 48 h later using a camera with a large view field collimator linked to a computer (Siemens Orbiter, Microdelta) with a medium energy collimator. A 20% window was centered on both energy photopeaks of ^{111}In, and the acquisition time was 10 min. Scans were stored in 128 × 128 frames for subsequent analysis. A semiquantitative method was applied to evaluate the intensity of the myocardial antimyosin uptake, consisting of drawing regions of interest over the heart and lungs on the anterior view of the thorax (10). A heart-to-lung ratio was obtained by dividing the average counts per pixel of the heart by the average counts per pixel of the lungs. A cut-off point >1.55 (normal value + 2 standard deviations) was used to define abnormal studies (10).

Statistical analysis. Results are expressed as mean ± standard deviation of mean. A two-tail Pearson's linear correlation test was used to assess the correlation between variables. Correlation was considered present when $p < 0.05$.

RESULTS

Echocardiography detected signs of hypertrophic cardiomyopathy in four athletes, who were excluded from the study. Clinical and physical examinations were normal in the remaining 22 athletes, none of whom presented adverse clinical events or a decrease in physical performance during the follow-up.

Echocardiographic study. Right and left ventricular dimensions were normal for highly trained athletes. Left ventricular diastolic diameter was 54.2 ± 4.6 mm (range 60.5 to 40.9), and systolic diameter was 33.3 ± 4.6 mm (range 40.1 to 24); thickness of intraventricular septum was 10.5 ± 1.4 mm (range 13.1 to 7.8), and thickness of posterior wall was 9.4 ± 1.2 mm (range 7 to 11.2); LV mass index was 148 ± 39.2 g/m^2 (range 220 to 82) (Table 1). No signs of right ventricular abnormalities were seen. Aortic root and left atria dimensions were within normal limits, and systolic and diastolic functions were normal in all athletes.

Exercise test. Heart rate at exercise was 166 ± 12.4 beats/min (range 141 to 189), and physical fitness, evaluated in metabolic equivalent of the task, was 15.2 ± 2.7 (range 10 to 20). The increase in blood pressure during the test was normal in all cases. Electrocardiogram tracer at rest simulated myocardial ischemia or "pseudoischemia" and tended to normalize during the exercise in all athletes; T wave

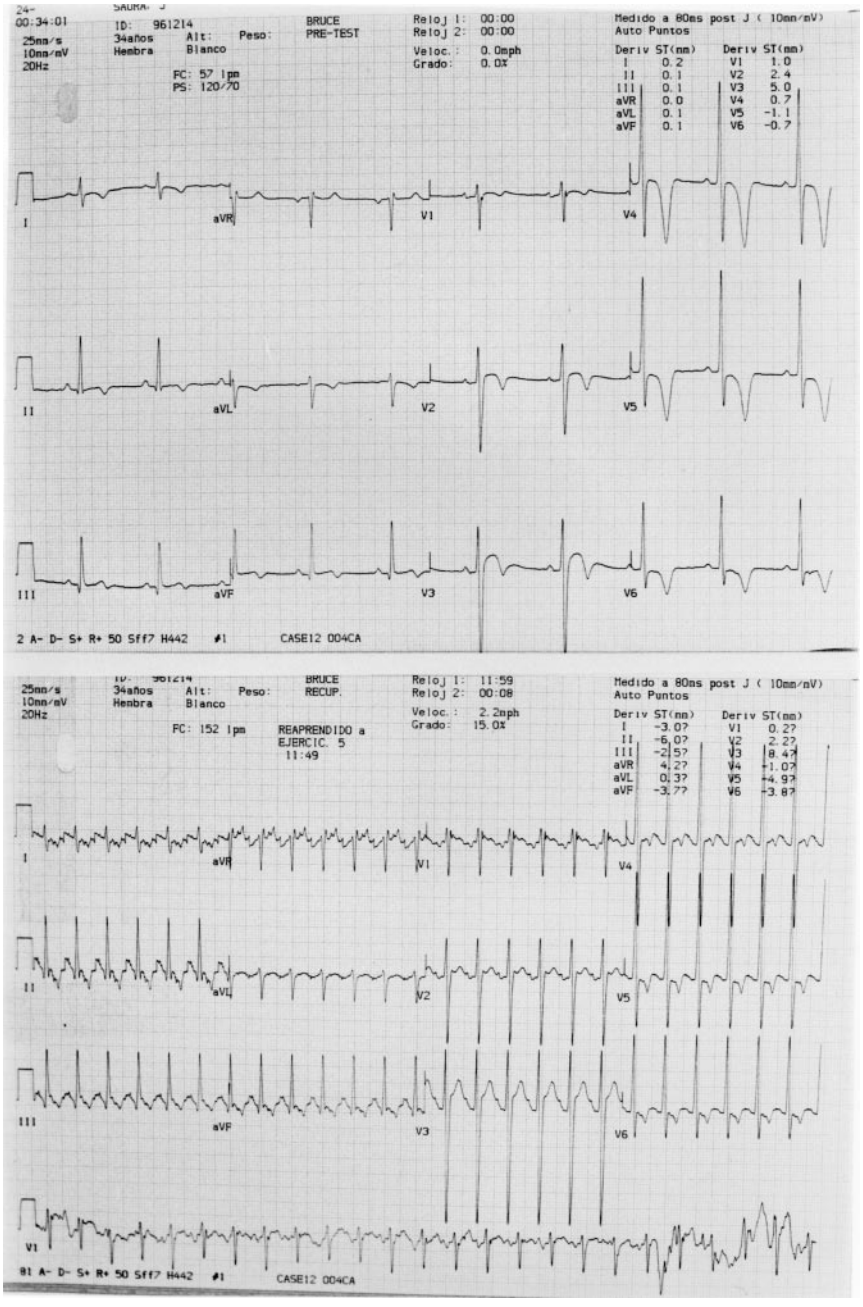

Figure 2. Upper: electrocardiogram with marked repolarization abnormalities at rest. **Lower:** exercise electrocardiogram of the same athlete showing a decrease in the T wave voltage in V4 to V6 and a positive T wave in V2 to V3.

voltage and isoeletric ST segment decreased (Fig. 2). During the recovery period, MRA reappeared in ECG tracer within 8 min. No arrhythmias were recorded.

Rest/exercise myocardial perfusion study. The rest/exercise myocardial distribution of ^{99m}Tc-tetrofosmin was normal, and no images of ischemia were evidenced.

Antimyosin study. Heart-to-lung ratio was 1.61 ± 0.13 (range 1.38 to 1.88) (Table 1). Fifteen athletes (68%) had a heart-to-lung ratio >1.55, showing mild and diffuse myocardial antimyosin uptake. No correlation between the heart-to-lung ratio and the LV mass index or the maximal wall thickness was found.

DISCUSSION

Physical training produces changes in the athlete's cardiovascular system, particularly in heart rate. Sinus bradycardia is the most frequent change, and heart rate at rest can be below 30 beats per minute. Slight changes in ventricular repolarization are also common, especially in early repolarization. These changes are characterized by ST segment elevation ≥0.5 mm in two consecutive leads and by J wave or terminal slurring of R wave, most frequently in precordial leads. In the athlete's heart, these changes are related to modifications of the autonomic nervous system and myocardial structure (8,11–16).

Prevalence and significance of MRA. To our knowledge, there are no data available to date in the scientific literature about the prevalence of MRA in athletes. In Spain, the prevalence of MRA in athletes is unknown, mainly because strict medical controls are not usually required for regular competition. Although MRA is infrequent, it is not a new finding in sports cardiology. Marked repolarization abnormalities in ECG tracer suggest heart disease, but the athletes are free of cardiac symptoms, and they show a normal physical performance in relation to their training level. Moreover, the presence of MRA is not associated with top-ranking training, with prolonged training or with any particular type of sport (16). It has been suggested that MRA could be related to changes in the cardiac autonomic nervous system. Previous studies in athletes with MRA did not show significant differences in plasmatic levels of norepinephrine and dopamine compared with a group of athletes with normal ECG, and, moreover, heart disease was also discarded by echocardiography, stress test and ^{201}T1 perfusion studies (17,18). However, these studies do not enable any definitive conclusions to be drawn about the implication of the autonomic nervous system in MRA.

When MRA in ECG tracer suggest heart disease, it is necessary to determine whether the athlete should continue physical training. In most cases there is no family history of sudden cardiac death or other heart diseases; symptoms at rest and during exercise are absent, and performance level is no different from athletes with normal ECG. An echocardiography is performed in these cases, and, if this is pathologic, it is associated with apical cardiomyopathy (19). For this reason, athletes with hypertrophic cardiomyopathy were excluded from the study in order to avoid their possible influence on the results. It is, therefore, surprising that 4 of 26 athletes (15%) had hypertrophic cardiomyopathy, and this finding suggests the possibility that, although athletes with MRA have no evidence of heart disease, they are not strictly free of some cardiac disorder.

Risk factors and MRA. Risk factors associated with sudden cardiac death are youth, syncope, family history of sudden death and ventricular tachycardia accompanied by clinical and electrophysiologic findings (20). In our study the exercise test was performed until physical exhaustion to exclude ischemic heart disease, especially in older athletes. In all tests the exercise ECG returned to normal, and the MRA reappeared within 8 min of the recovery period; there were no supraventricular or ventricular arrhythmias during the exercise or in the recovery period. Physical performance, evaluated in metabolic equivalents of the task, was at the level of highly trained individuals in all cases. The rest/exercise myocardial perfusion studies were normal, and echocardiographic studies were compatible with highly trained athletes, showing a thickness of interventricular septum and posterior wall within physiological limits (21). Finally, 15 athletes (68%) showed mild and diffuse myocardial antimyosin uptake. Maron et al. (22) reported that sudden cardiac death is more frequent during or after exertion periods, suggesting the importance of hemodynamic collapse as a trigger. Athletes with MRA did not show any risk factor of sudden cardiac death, and the behavior of the systolic blood pressure during exercise test was also normal. There does not, therefore, appear to be any reason to exclude athletes with MRA in ECG at rest from training or competition.

In athletes with MRA and demonstrated heart disease, it is easier to decide on future physical activity. Marked repolarization abnormalities in the context of hypertrophic cardiomyopathy are accompanied by pathological behavior during exercise, coexisting with an abnormal increase in blood pressure (23). The Brugada Syndrome (24), showing ST segment elevation in the right precordial leads, could lead to MRA, but in this study no athletes presented evidence of right bundle branch block or ventricular tachyarrhythmias during the follow-up, thereby excluding this syndrome as the cause of MRA. Right ventricular disease, such as right ventricular dilation in arrhythmogenic right ventricular dysplasia, was excluded by echocardiography, where right ventricular dimensions were normal without pathological findings in all athletes.

Controversial role of myocardial antimyosin study in MRA. More difficult to explain is the mild and diffuse myocardial antimyosin uptake evidenced in 68% of athletes. Myocardial antimyosin uptake is specific for myocyte cell membrane disruption or increased membrane permeability (25,26), including small sarcolemmal breaches seen only with high-resolution electromicroscopy (27). Myocardial antimyosin studies are useful in the noninvasive detection of myocardial cell damage in different clinical situations (26,28–33). Mild and diffuse myocardial antimyosin uptake in athletes with a very good performance suggests active myocyte damage, without clinical or functional consequences. Further studies are needed to understand the meaning of myocardial antimyosin uptake in these subjects. This finding could possibly be related to the high percentage of hypertrophic cardiomyopathy found in this group of athletes.

Follow-up and clinical implications. During the training period, MRA show few changes, and these are always related to modifications in the intensity of training. Therefore, ECG alterations in ventricular repolarization do not disappear completely, and they maintain a similar morphology for many years (Fig. 3 and 4).

In this study differences in heart rate and intensity of training could influence, at least partially, changes in alteration repolarization between the first and later ECG. The persistence of MRA in ECG tracer, despite a decrease in training intensity, supports the lack of relation between the ECG alteration and some specific type of training or sport. Moreover, during the follow-up there was no abnormal loss of fitness, and the progressive decrease in fitness was related to the normal process of aging and subsequent decrease in training intensity.

Athletes were followed from 4 to 20 years, and during

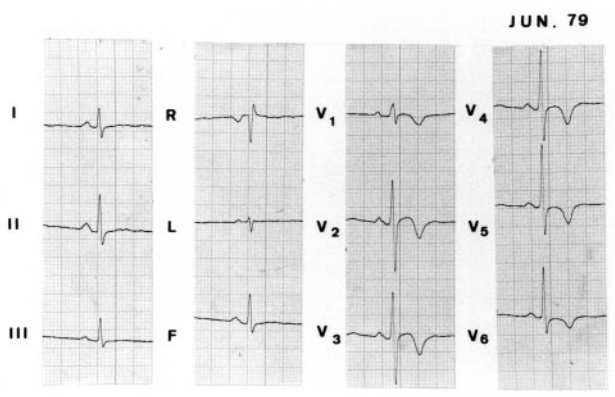

Figure 3. Electrocardiogram at rest of athlete 5 showing marked repolarization abnormalities. This athlete participated in three Olympic Games.

this period there were no symptoms of heart disease in any subject. We should emphasize that two of them (numbers 5 and 10) participated at the Olympic level. These athletes continued in sports competition, and the results of this study demonstrated no reason to limit either the competitive activity or the intensity of physical activity.

In conclusion, despite the significant alterations found in ECG at rest, the performance in the exercise test and the results of echocardiography, myocardial perfusion and antimyosin studies, together with the lack of events during the long-term follow-up, indicate that MRA have no pathological implications and should not, therefore, preclude physical training and competitive availability when a cardiac pathology can be excluded. Thus, the presence of similar ECG alterations must lead to a careful examination of the athlete. The cause of MRA is unknown, and training is likely the trigger. Further research is needed to determine the origin.

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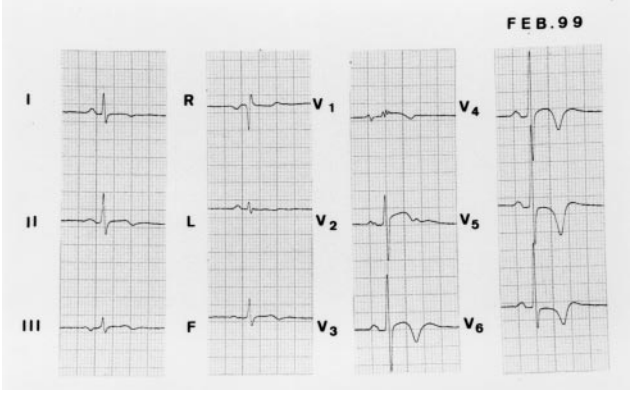

Figure 4. Electrocardiogram at rest of athlete 5 (Fig. 3) 20 years later. The same electrocardiographic repolarization alterations can be seen.

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