

ORIGINAL ARTICLE

Outcomes in Athletes with Marked ECG Repolarization Abnormalities

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ABSTRACT

BACKGROUND

Young, trained athletes may have abnormal 12-lead electrocardiograms (ECGs) without evidence of structural cardiac disease. Whether such ECG patterns represent the initial expression of underlying cardiac disease with potential long-term adverse consequences remains unresolved. We assessed long-term clinical outcomes in athletes with ECGs characterized by marked repolarization abnormalities.

METHODS

From a database of 12,550 trained athletes, we identified 81 with diffusely distributed and deeply inverted T waves (≥ 2 mm in at least three leads) who had no apparent cardiac disease and who had undergone serial clinical, ECG, and echocardiographic studies for a mean (\pm SD) of 9 ± 7 years (range, 1 to 27). Comparisons were made with 229 matched control athletes with normal ECGs from the same database.

RESULTS

Of the 81 athletes with abnormal ECGs, 5 (6%) ultimately proved to have cardiomyopathies, including one who died suddenly at the age of 24 years from clinically undetected arrhythmogenic right ventricular cardiomyopathy. Of the 80 surviving athletes, clinical and phenotypic features of hypertrophic cardiomyopathy developed in 3 after 12 ± 5 years (at the ages of 27, 32, and 50 years), including 1 who had an aborted cardiac arrest. The fifth athlete demonstrated dilated cardiomyopathy after 9 years of follow-up. In contrast, none of the 229 athletes with normal ECGs had a cardiac event or received a diagnosis of cardiomyopathy 9 ± 3 years after initial evaluation ($P=0.001$).

CONCLUSIONS

Markedly abnormal ECGs in young and apparently healthy athletes may represent the initial expression of underlying cardiomyopathies that may not be evident until many years later and that may ultimately be associated with adverse outcomes. Athletes with such ECG patterns merit continued clinical surveillance.

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THE 12-LEAD ELECTROCARDIOGRAM (ECG) shows a spectrum of alterations in young, trained athletes, including, most commonly, repolarization abnormalities and increased R- or S-wave voltage suggestive of left ventricular hypertrophy. Such findings are generally regarded as an innocent consequence of systematic athletic conditioning.¹⁻¹³ However, a small but important subgroup of athletes without evidence of structural heart disease may have particularly abnormal ECG patterns,¹⁴ including diffusely and deeply inverted T waves, suggestive of an underlying cardiac disorder. Such markedly abnormal ECGs in apparently healthy athletes raise a diagnostic question: Do such patterns represent the initial and subtle expression of cardiovascular disease (especially genetic disorders with delayed phenotypic appearance and potentially adverse clinical consequences¹⁵⁻¹⁷) or are they only benign expressions of systematic and intensive athletic conditioning?¹⁴

Despite several observational and cross-sectional surveys performed over the past 30 years exhaustively describing ECG findings in trained athletes,^{1-5,7-12,14} the long-term clinical significance of such abnormal patterns has remained largely unresolved. Therefore, in the present longitudinal study, we evaluated the clinical outcomes associated with markedly abnormal ECGs characterized by distinctive repolarization patterns in young, trained athletes.

METHODS

Since 1982, the Italian government has required by law that all citizens participating in officially sanctioned competitive sports undergo preparticipation screening to rule out the presence of cardiovascular disease that could be associated with increased risk during training and competition.¹⁸ At the Institute of Sports Medicine and Science, young competitive athletes selected for inclusion on national teams undergo a medical evaluation that routinely includes a medical history, a physical examination, 12-lead and exercise ECGs, and a two-dimensional echocardiogram. In addition, athletes are selectively referred to this institution from satellite sports medical centers when ECG abnormalities or abnormal findings from their medical history or physical examination are detected. All the records of clinical data on these athletes are kept in a database maintained by the institute.

At the time each subject is enrolled in the database, a standard 12-lead ECG is obtained with the subject in the supine position during quiet respiration and recorded at 25 mm per second. The ECG tracing is obtained just before the echocardiographic examination and more than 24 hours after the last athletic activity. Incremental exercise testing until exhaustion is performed on a bicycle ergometer (Cardioline SDS 3D or Cardioline ETC system).

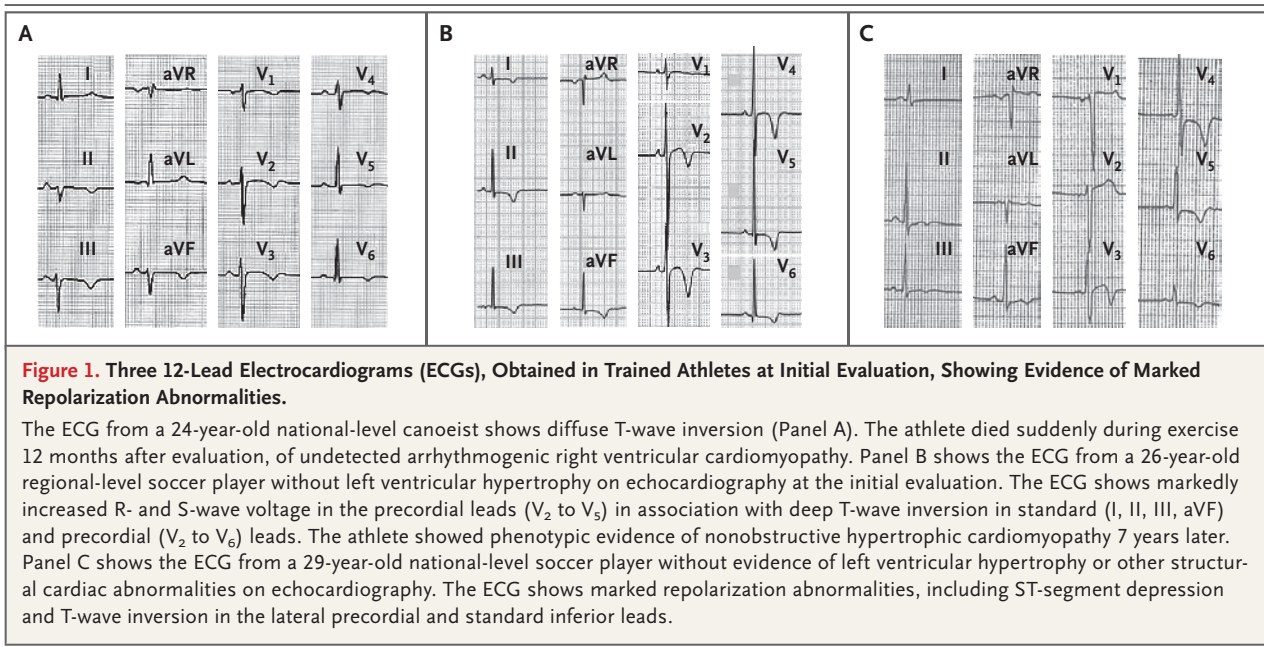
Echocardiographic studies are performed with commercially available instruments (Sonos 5500, Philips). The extent and distribution of left ventricular hypertrophy are assessed from two-dimensional echocardiography, as previously described.¹⁹ Echocardiographic studies routinely include a search for the normal position of the ostia and the proximal course of the epicardial coronary arteries.²⁰

STUDY DESIGN

We conducted a matched case-control study to compare the long-term outcomes in athletes who had marked repolarization abnormalities with the outcomes in a similar group of athletes who had normal ECGs. The study design was approved by the review board of the institute. Written informed consent was waived for the elite athletes examined in our institute within the medical program for the Italian Olympic team (57 of the study group and all 229 of the control group), because these athletes were undergoing a standard clinical evaluation pursuant to Italian law and institute policy. Written informed consent for this investigation was obtained from the remaining 24 athletes, who were referred to the institute for evaluation of specific clinical findings. The analysis was funded by the Italian National Olympic Committee.

We reviewed ECG data from the database for all athletes evaluated at the institute between 1979 and 2001. We identified those subjects in the database with ECGs showing marked repolarization abnormalities, defined as inverted T waves (≥ 2 mm in depth) in at least three leads (exclusive of standard lead III), and predominantly in the anterior and lateral precordial leads V₂ through V₆ (Fig. 1A, 1B, and 1C).

On the basis of clinical and echocardiographic assessment, those subjects with an abnormal ECG who had evidence of structural heart disease at the time of initial evaluation were ex-



cluded from further analysis. The diagnoses of hypertrophic cardiomyopathy and dilated cardiomyopathy were based on currently accepted criteria^{21,22} and were distinguished from physiologic hypertrophy and the dilatation of “athlete’s heart,” as previously described.^{23,24} The criteria for diagnosis of arrhythmogenic right ventricular cardiomyopathy were those of the European Society of Cardiology.²⁵ Because we wanted to evaluate the long-term clinical course of the study subjects, we also excluded those who had not had at least two clinical evaluations recorded at least 1 year apart.

A control group of athletes with normal ECGs and no evidence of structural cardiac disease was assembled from athletes examined at the Institute of Sports Medicine and Science between 1980 and 2000. From this cohort, we initially selected every 20th consecutive athlete (according to the date of enrollment in the database) with a normal ECG pattern. From this group, we selected a subgroup of athletes that was similar to the study group with respect to age, sex, and duration of follow-up (Fig. 2).

STATISTICAL ANALYSIS

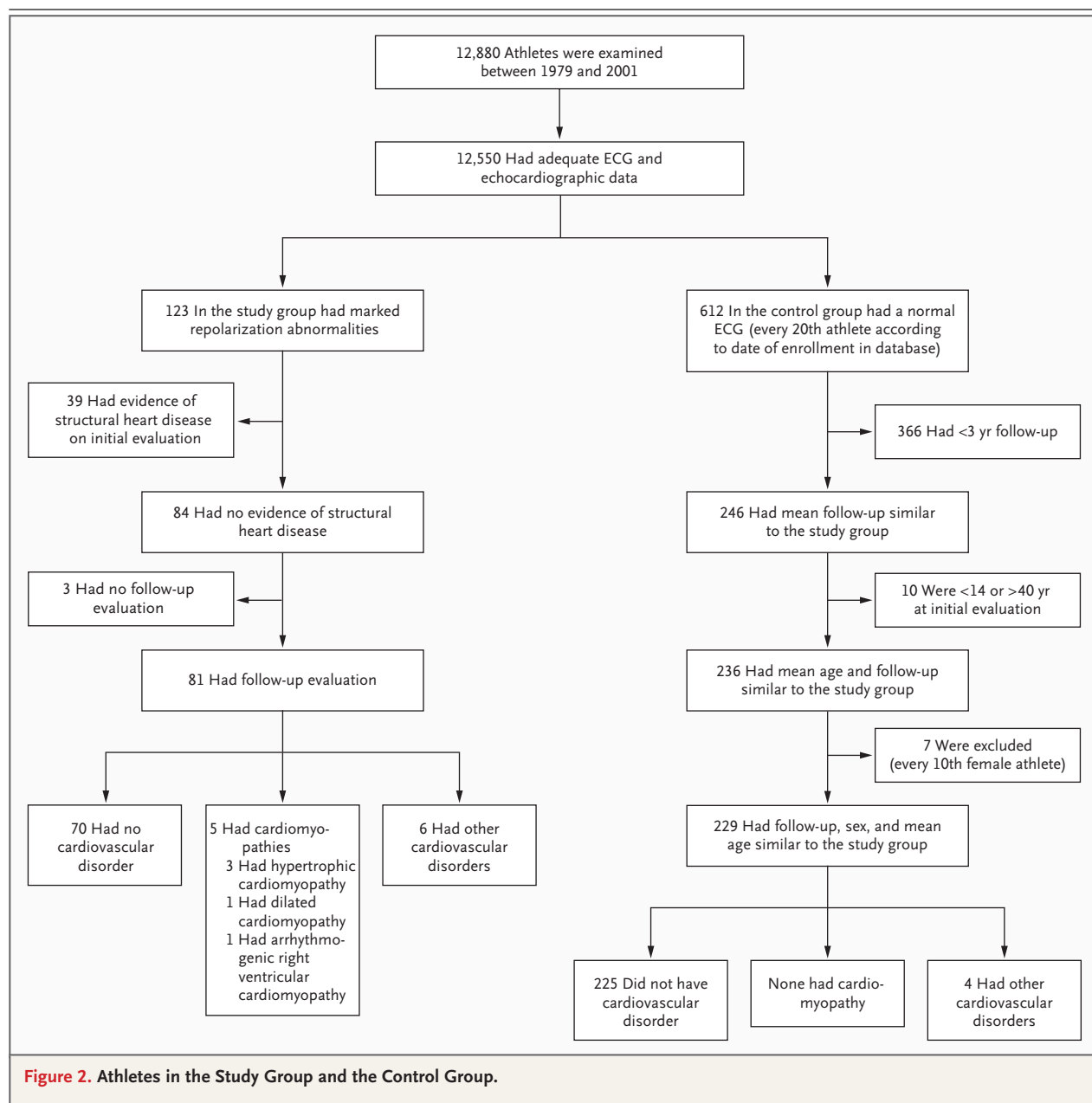
Data are expressed as means \pm SD. Differences between means were assessed by a paired or unpaired Student’s t-test, as appropriate. Differences between proportions were assessed with the chi-square test. The rates of development of cardiac

disease in subjects with repolarization abnormalities and controls were compared with the use of Fisher’s exact test or the chi-square test, as appropriate. A two-tailed P value of less than 0.05 was considered to indicate statistical significance. Logistic-regression analysis was used to analyze the effect of several variables (duration of follow-up, age at the time of change in the ECG, left-ventricular-mass index, and body-surface area) on changes in ECG patterns during the follow-up period. The product-limit method of survival analysis was performed to assess the time to change in the ECG pattern.²⁶

RESULTS

STUDY AND CONTROL COHORTS

Between 1979 and 2001, a total of 12,880 athletes were examined in our institute, of whom 12,550 had ECG and echocardiographic data sufficient for inclusion in this study (Fig. 2). From this database, we identified 123 subjects (1%) who presented with marked repolarization abnormalities. Of these 123 athletes, 39 had echocardiographic and clinical evidence of structural heart disease on initial evaluation, including most commonly hypertrophic cardiomyopathy (17 subjects) but also mitral-valve prolapse (6 subjects), arrhythmogenic right ventricular cardiomyopathy (4), systemic hypertension (4), dilated cardiomyopathy (3), aortic stenosis with bicuspid valve (3), ische-



mic heart disease (1), and myocarditis (1); these 39 athletes were therefore excluded from further analysis.

The remaining 84 athletes showed no evidence of structural cardiovascular disease at initial evaluation according to echocardiographic study or other selected diagnostic tests performed as appropriate (e.g., myocardial scintigraphy, cardiac magnetic resonance imaging, and coronary arteriography). Of these 84 athletes, 81 had at least two clinical evaluations (with 12-lead ECG and

echocardiogram), and therefore they constituted the final study group. The control group included 229 athletes similar in age, sex, and duration of follow-up to the study group (Fig. 2).

In 54 of the 81 athletes (67%), other ECG abnormalities were associated with the deeply inverted T waves, including increased R- or S-wave precordial lead voltages (Sokoloff-Lyon index ≥ 30 mm) in 42, deep and narrow Q waves (≥ 2 mm) in 8, left atrial enlargement in 6, diminished R wave in the anterior precordial leads in 5, and

left-axis deviation (−30 degrees) in 2. The QT intervals were normal in each of these athletes, and none had evidence of the Brugada syndrome.²⁷

DEMOGRAPHIC CHARACTERISTICS

The 81 subjects in the study group included 63 males and 18 females who were 23 ± 6 years of age (range, 15 to 38) at the initial evaluation and 32 ± 10 years (range, 17 to 63) at the most recent assessment (Table 1). The athletes were engaged in a variety of sporting disciplines, most commonly soccer (17 subjects), rowing or canoeing (16), track and field (7), swimming (5), and cycling (4). All had participated in regular training and competition for a substantial number of years (mean, 12; range, 3 to 26), and 57 (70%) had achieved recognition at national or international events, including 14 who had participated in the Olympic Games.

The 229 subjects in the control group included 157 males and 72 females, who were 22 ± 5 years of age (range, 14 to 40) at initial evaluation (Table 1). These athletes also participated in a variety of sporting disciplines, most commonly rowing or canoeing (30 subjects), soccer (18), water polo (16), track and field (14), shooting

(14), and judo (12). Eighty percent had national or international levels of achievement.

CHANGES DURING FOLLOW-UP

Follow-up data were available for a mean of 9 ± 7 years (range, 1 to 27) in the group with marked repolarization abnormalities and for a mean of 9 ± 3 years (range, 3 to 19) in the control group. At the most recent evaluation, 63 of the 81 athletes with an abnormal repolarization pattern (78%) were still engaged in regular training and competition, whereas 17 (21%) had discontinued training and competition and 1 had died.

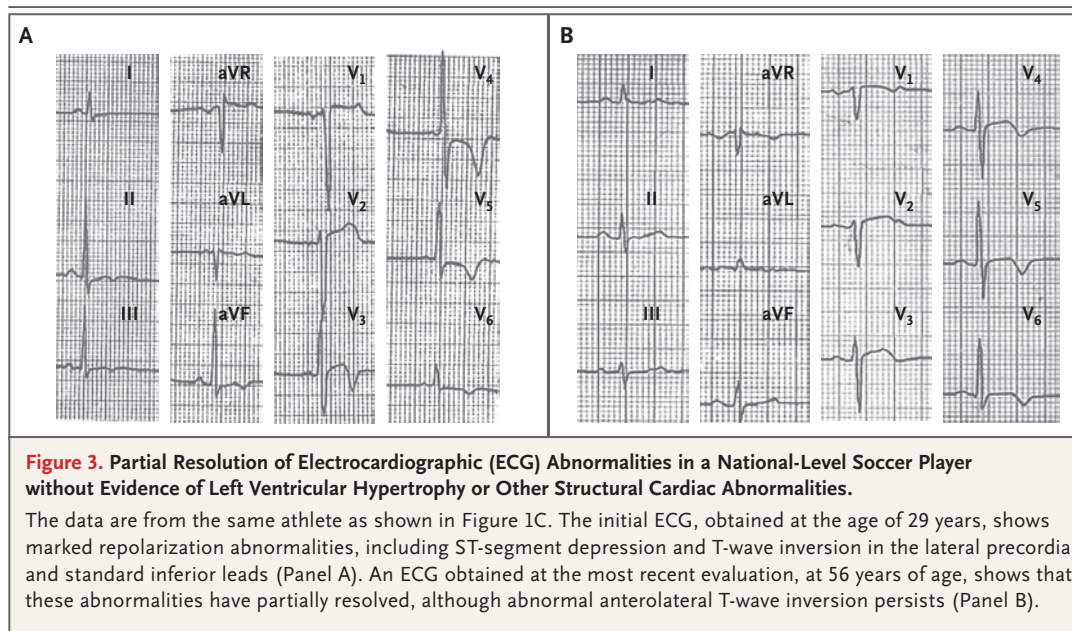
During the follow-up period, repolarization abnormalities on the 12-lead ECG remained essentially unchanged (or showed deeper T-wave inversion) in 54 athletes (67%). In the remaining 27 athletes, ECG patterns either normalized completely (in 12) or became less abnormal (in 15) by showing reduced T-wave inversion (maximum T-wave inversion from 4.5 ± 4 to 2.9 ± 2 mm, $P<0.001$), with fewer leads involved (from 6.1 ± 1 to 4.5 ± 3 mm, $P<0.001$) (Fig. 3A and 3B). The mean period for abnormal ECG patterns to revert (i.e., either normalize or improve) was 11.4 ± 3.5 years (median, 8.5). Logistic-regression analysis showed that nor-

Table 1. Characteristics at Baseline and at Follow-up of 81 Athletes with Distinctly Abnormal 12-Lead ECGs and 229 Control Athletes with Normal ECGs.*

Characteristic	Abnormal ECG (N = 81)	Normal ECG (N = 229)	P Value
Age — yr			0.12
Mean	23 ± 6	22 ± 5	
Range	15–38	14–40	
Male sex — no. (%)	63 (78)	157 (69)	0.16
Body-surface area — m ²	1.88 ± 0.21	1.90 ± 0.22	0.48
Resting heart rate — beats/min	59 ± 12	56 ± 11	0.04
Elite achievement level — no. (%)†	57 (70)	186 (81)	0.09
Follow-up — yr			0.62
Mean	9 ± 7	9 ± 3	
Range	1–26	3–19	
Follow-up ≥ 10 yr — no. (%)	29 (36)	82 (36)	
Cardiovascular conditions during follow-up — no.			
Cardiomyopathy	5	0	0.001
Other cardiovascular conditions	6	4	0.05
Any cardiovascular condition	11	4	0.001

* Plus-minus values are means \pm SD. ECG denotes electrocardiogram.

† Elite achievement level is defined as competition at national or international events.



malization or improvement in ECG repolarization patterns during the observation period was associated with the length of the follow-up ($P < 0.001$).

We also observed partial regression or complete normalization of the abnormal repolarization pattern during exercise testing in 58 (72%) of the 81 athletes with abnormal ECGs. At the most recent evaluation, all these athletes were able to attain a high-intensity workload (peak exercise, 237 ± 60 W) by achieving a maximum heart rate of 166 ± 13 beats per minute. No changes in left ventricular dimensions were observed in the 81 athletes during the follow-up period (mean cavity dimension, 52.7 ± 4.9 to 52.6 ± 4.7 mm; maximum wall thickness, 10.4 ± 1.3 to 10.5 ± 1.4 mm), regardless of change in ECG patterns.

CLINICAL OUTCOME

Of the 81 athletes with abnormal ECGs, evidence of cardiomyopathy developed in 5 (6%) during the period of follow-up and evidence of other cardiovascular disorders developed in 6 (7%), for a total of 11 subjects (14%) (Tables 1 and 2). One participant died suddenly at the age of 24 years (1 year after initial evaluation) from clinically undetected arrhythmogenic right ventricular cardiomyopathy (Fig. 4). Of the 80 surviving athletes, clinical and phenotypic features of hypertrophic cardiomyopathy developed, during an average follow-up period of 12 ± 5 years, in 3 subjects at the ages of 27, 32, and 50 years, including 1 who

had an aborted cardiac arrest (after 16 years of follow-up). These athletes showed relatively mild left ventricular hypertrophy (wall thickness, 13 to 16 mm) in association with a nondilated cavity (end-diastolic dimension, 47 to 50 mm) in the absence of systemic hypertension, as well as mild systolic anterior motion of the mitral valve in one and ventricular fibrillation or ventricular tachycardia in two.²¹ Dilated cardiomyopathy (left ventricular end-diastolic dimension, 62 mm; ejection fraction, 40%) developed in another athlete during a 9-year follow-up.²² Detailed descriptions of the clinical course in these five patients are available in the Supplementary Appendix, available with the full text of this article at www.nejm.org.

Other cardiovascular conditions that developed in the study group included systemic hypertension in three subjects, atherosclerotic coronary artery disease (requiring bypass grafting) in one, myocarditis in one, and supraventricular tachycardia (requiring radiofrequency ablation) in one (Tables 1 and 2). For the remaining 70 athletes with abnormal ECGs (86%), the clinical course remained unremarkable during the average 9-year follow-up period (Fig. 2).

In contrast, none of the 229 athletes with normal ECGs, representing the control group, had evidence of cardiomyopathy at follow-up ($P = 0.001$ for the comparison with the rate of cardiomyopathy in those with abnormal ECGs) (Table 1). Only four (2%) had evidence of other

Table 2. Demographic and Clinical Features of Athletes in Whom Cardiovascular Disorders Developed during Follow-up.*

Athlete	Sport	Level	Age† yr	Duration of Follow-up yr	Cardiovascular Disorder	Initial ECG	Response of ECG to Exercise	Change in ECG during Follow-up	Clinical Outcome
Athlete with abnormal ECG in whom cardiomyopathy developed									
1	Canoeing	National	24	1	Arrhythmic right ventricular cardiomyopathy	Inverted T waves V ₁ –V ₆ , II, III, aVF	No change	None	Sudden death
2	Tennis	Regional	34	16	Hypertrophic cardiomyopathy‡	Inverted T waves V ₄ –V ₆ ; flat aVF	No change	None	Survived cardiac arrest
3	Soccer	Regional	26	7	Hypertrophic cardiomyopathy	Inverted T waves V ₂ –V ₆ , I–III, aVF	No change	T-wave inversion extended to aVL	Asymptomatic
4	Rowing	International	19	13	Hypertrophic cardiomyopathy§	Inverted T waves V ₂ –V ₅ ; flat V ₆ , aVF, I, II	No change	None	Symptomatic (nonsus- tained ventricular tachycardia)
5¶	Basketball	National	38	9	Dilated cardiomyopathy	Inverted T waves V ₃ –V ₆ , II, aVF	No change	None	Asymptomatic
Athlete with abnormal ECG in whom noncardiomyopathic cardiovascular disorders developed									
1	Basketball	Regional	20	4	Myocarditis	Inverted T waves V ₃ –V ₅ ; flat V ₆ , I, aVL	No change	None	Asymptomatic
2	Long-distance running	Regional	23	17	Hypertension	Inverted T waves V ₃ –V ₅ ; flat V ₆ , I, aVL	Improved	Decrease in T-wave inversion	Asymptomatic
3	Swimming	National	25	7	Supraventricular tachycardia	Inverted T waves V ₅ –V ₆ , II, aVF	Improved	None	Radiofrequency abla- tion; asymptomatic
4	Soccer	Regional	26	26	Coronary artery disease	Inverted T waves V ₃ –V ₆ , I, II, aVF	Worsened	Decrease in T-wave inversion	Asymptomatic
5	Cycling	Regional	28	25	Hypertension	Inverted T waves V ₅ –V ₆ , II, aVF	No change	Decrease in T-wave inversion	Asymptomatic
6	Cycling	Regional	38	24	Hypertension	Inverted T waves V ₂ –V ₆ , I, aVL; flat II	Worsened	None	Asymptomatic
Athlete with normal ECG in whom noncardiomyopathic cardiovascular disorders developed									
1	Ice hockey	National	18	14	Supraventricular tachycardia	Normal	No change	None	Radiofrequency abla- tion; asymptomatic
2	Basketball	National	19	12	Myocarditis	Normal	No change	None	Asymptomatic
3	Basketball	National	24	6	Supraventricular tachycardia	Normal	No change	None	Palpitations with effort
4	Karate	National	28	8	Pericarditis	Normal	No change	None	Asymptomatic

* ECG denotes electrocardiogram.

† The age at initial evaluation is given.

‡ Atherosclerotic coronary artery disease was ruled out by angiography.

§ The tunneled (bridged) segment of the left anterior descending coronary artery without atherosclerotic coronary artery disease was identified by coronary angiography.

¶ This athlete was a wheelchair competitor.

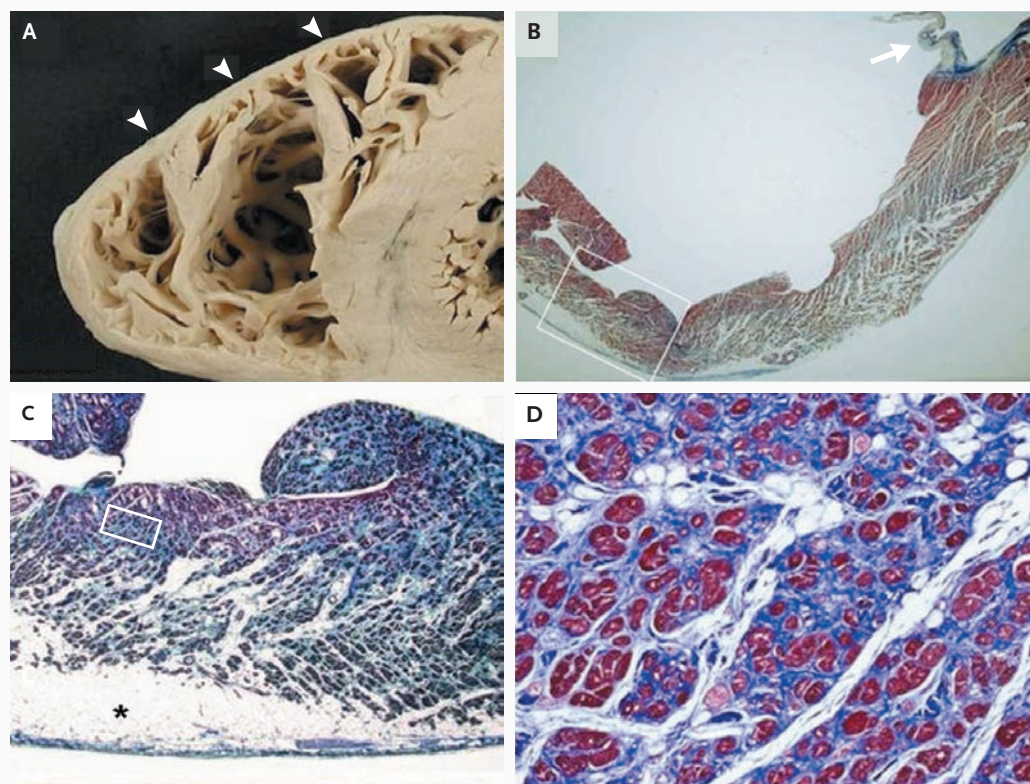


Figure 4. Gross and Histopathological Cardiac Findings in a 24-Year-Old Athlete Who Died Suddenly of Arrhythmogenic Right Ventricular Cardiomyopathy.

The electrocardiogram of this athlete is shown in Figure 1A. Panel A shows a cross section of the heart with a dilated right ventricular chamber, hypertrophied subendocardial trabeculae, and a diffusely thinned (1.5 mm in thickness) anterolateral wall (arrowheads), in the absence of aneurysm formation. Panel B shows a panoramic histologic section of the right ventricular outflow tract, including the pulmonary valve (arrow). Abnormalities are not evident in the myocardium (red staining) at this magnification (Heidenhain's trichrome stain). Panel C represents the boxed area of Panel B at higher magnification, showing areas of fibrofatty replacement of atrophic myocardium. The asterisk indicates epicardial fat, which is regarded as normal. Panel D shows the boxed area of Panel C at higher magnification. Surviving myocytes (red staining) are embedded within fibrous tissue (blue staining) and fat (white staining), an acknowledged feature of arrhythmogenic right ventricular cardiomyopathy.

cardiovascular disorders (Tables 1 and 2). In one of these athletes, myocarditis developed at the age of 19 years, 1 year after the initial evaluation; in another, pericarditis developed at the age of 28 years, 2 years after the initial evaluation. In addition, supraventricular tachycardia was identified in two athletes after 2 and 3 years of follow-up (requiring radiofrequency ablation in one). The overall incidence of cardiovascular abnormalities was therefore 14% (11 of 81 athletes) in the study group, as compared with 2% (4 of 229 athletes) in the control group ($P=0.001$).

In our study population, the negative predictive value of a normal ECG was 100% to exclude

the development of cardiomyopathy and 98% to exclude the development of any cardiac abnormality. The positive predictive value of an abnormal ECG was 6% for cardiomyopathy and 14% for any cardiac condition. Among the study participants in whom cardiomyopathy subsequently developed, none showed improvement or resolution of their marked repolarization abnormalities in the resting ECG over time (Table 2).

DISCUSSION

Highly trained athletes occasionally present with abnormal ECG patterns, many of which are often

regarded as innocent expressions of the cardiac remodeling associated with systematic and intensive exercise conditioning.¹⁻¹³ However, in a small but important subgroup of athletes,¹⁴ ECGs may be markedly abnormal and even bizarre in appearance, suggesting the presence of a pathologic cardiac condition such as hypertrophic cardiomyopathy or arrhythmogenic right ventricular cardiomyopathy.^{21,28,29} Abnormal repolarization patterns have previously been reported to occur in 2 to 4% of large populations of trained athletes who are young adults (aged 18 to 35 years).^{14,30}

Such distinctly abnormal ECGs pose a diagnostic question when they occur in the absence of detectable structural heart disease. These ECG findings may represent the initial, subtle expression of cardiac disease with adverse long-term clinical consequences.¹⁵⁻¹⁷ Alternatively, these ECGs may be innocent expressions of the cardiac remodeling associated with “athlete’s heart.”¹⁴ In an effort to clarify this important issue, we undertook the present long-term study to investigate the clinical outcomes of a unique subgroup of elite competitive athletes who initially presented with marked repolarization abnormalities on the ECG in the apparent absence of cardiac disease.

In the present analysis, we found distinctly abnormal repolarization patterns in 1% of our large population of athletes. A subsequent diagnosis of cardiomyopathy was made in 5 (6%) of the 81 athletes with such abnormalities who had no previous evidence of cardiac disease. Furthermore, two of these five athletes had major adverse cardiac events (a rate of 0.3% per year). One survived a cardiac arrest due to hypertrophic cardiomyopathy and one died suddenly of arrhythmogenic right ventricular cardiomyopathy; both were without previous cardiac symptoms.

In contrast, neither cardiomyopathy nor a major adverse cardiac event subsequently developed in any of the patients in the control group. Other cardiovascular disorders occurred in the study group (systemic hypertension, coronary artery disease, myocarditis, and supraventricular tachycardia) and the control group (myocarditis, pericarditis, and supraventricular tachycardia), although it is not likely that these conditions were related to the original abnormal ECGs.

Our experience, therefore, provides a useful perspective on isolated, markedly abnormal ECGs

in young, asymptomatic athletes. Contrary to previous reports describing such ECG patterns as innocent manifestations of “athlete’s heart” without adverse clinical consequences,^{14,31} the present study shows that these abnormal ECGs may represent the initial expression of genetic cardiac disease, preceding by many years phenotypic expression and adverse clinical outcomes.³²

Another insight derived from our investigation is the potential difficulty in clinical recognition of both arrhythmogenic right ventricular cardiomyopathy and hypertrophic cardiomyopathy, particularly in young, physically active (and asymptomatic) people. Arrhythmogenic right ventricular cardiomyopathy was not identified during the lifetime of our athlete who died suddenly, despite the heightened awareness of that disease within the Italian national preparticipation screening program.¹⁸ In retrospect, the clinical evaluation did not create a strong suspicion of this diagnosis in this athlete because the repolarization abnormalities were not those most typically identified in this disease (T-wave inversion was diffuse rather than confined to the anterior precordial leads). Furthermore, echocardiography did not show marked enlargement of the right ventricular chamber or segmental wall-motion abnormalities, and electrophysiological study with programmed ventricular stimulation did not induce ventricular tachyarrhythmia (see the Supplementary Appendix).

On the basis of our data, it seems reasonable that, in the setting of large-scale preparticipation screening, ECGs showing marked repolarization abnormalities may be useful for identifying athletes at risk for the subsequent development of structural heart disease. These observations underscore the importance of greater diagnostic scrutiny and continued clinical surveillance of trained athletes who present with such distinctly abnormal ECGs. On the basis of our observations, it seems likely that serial ECG alone is not sufficient for such surveillance, but echocardiography and selective additional testing are necessary to clarify the cardiac diagnosis. Conversely, the finding of a normal ECG during preparticipation screening can be regarded as reasonably reliable evidence to exclude the presence of potentially lethal cardiac disease and can serve as a source of reassurance to young athletes.³³

In summary, we investigated the clinical

course of trained athletes with marked repolarization abnormalities on the ECG. Such abnormalities were uncommon but were associated with a disproportionately increased risk of the

subsequent development of structural cardiac disease.

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REFERENCES

1. Maron BJ, Pelliccia A. The heart of trained athletes: cardiac remodeling and the risks of sports, including sudden death. *Circulation* 2006;114:1633-44.
2. Huston TP, Puffer JC, Rodney WM. The athletic heart syndrome. *N Engl J Med* 1985;313:24-32.
3. Venerando A, Rulli V. Frequency, morphology and meaning of the electrocardiographic anomalies found in Olympic marathon runners and walkers. *J Sports Med Phys Fitness* 1964;50:135-41.
4. Hanne-Paparo N, Wendkos MH, Brunner DT. T wave abnormalities in the electrocardiograms of top-ranking athletes without demonstrable organic heart disease. *Am Heart J* 1971;81:743-7.
5. Lichtman J, O'Rourke RA, Klein A, Karliner JS. Electrocardiogram of the athlete: alterations simulating those of organic heart disease. *Arch Intern Med* 1973;132:763-70.
6. Roeske WR, O'Rourke RA, Klein A, Leopold G, Karliner JS. Noninvasive evaluation of ventricular hypertrophy in professional athletes. *Circulation* 1976;53:286-91.
7. Zeppilli P, Pirrami MM, Sassara M, Fenici R. T wave abnormalities in top ranking athletes: effects of isoproterenol, atropine, and physical exercise. *Am Heart J* 1980;100:213-22.
8. Nishimura T, Kambara H, Chen CH, Yamada Y, Kawai C. Noninvasive assessment of T-wave abnormalities on precordial electrocardiograms in middle-aged professional bicyclists. *J Electrocardiol* 1981;14:357-64.
9. Oakley DG, Oakley CM. Significance of abnormal electrocardiograms in highly trained athletes. *Am J Cardiol* 1982;50:985-9.
10. Balady GJ, Cadigan JB, Ryan TJ. Electrocardiogram of the athlete: an analysis of 289 professional football players. *Am J Cardiol* 1984;53:1339-43.
11. Douglas PS, O'Toole ML, Hiller WDB, Hackney K, Reichel N. Electrocardiographic diagnosis of exercise-induced left ventricular hypertrophy. *Am Heart J* 1988;116:784-90.
12. Zehender M, Meinertz T, Keul J, Just H. ECG variants and cardiac arrhythmias in athletes: clinical relevance and prognostic importance. *Am Heart J* 1990;119:1378-91.
13. Björnstad H, Smith G, Storstein L, Meen HD, Hals O. Electrocardiographic and echocardiographic findings in top athletes, athletic students and sedentary controls. *Cardiology* 1993;82:66-74.
14. Pelliccia A, Maron BJ, Culasso F, et al. Clinical significance of abnormal electrocardiographic patterns in trained athletes. *Circulation* 2000;102:278-84.
15. Niimura H, Bachinski LL, Sangwatanaroj S, et al. Mutations in the gene for human cardiac myosin-binding protein C and late-onset familial hypertrophic cardiomyopathy. *N Engl J Med* 1998;338:1248-57.
16. Maron BJ, Niimura H, Casey SA, et al. Development of left ventricular hypertrophy in adults with hypertrophic cardiomyopathy caused by cardiac myosin-binding protein C gene mutations. *J Am Coll Cardiol* 2001;38:315-21.
17. Maron BJ, Seidman JG, Seidman CE. Proposal for contemporary screening strategies in families with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2004;44:2125-32.
18. Pelliccia A, Maron BJ. Preparticipation cardiovascular evaluation of the competitive athlete: perspectives from the 30-year Italian experience. *Am J Cardiol* 1995;75:827-9.
19. Pelliccia A, Maron BJ, Spataro A, Proshan M, Spirito P. The upper limit of physiologic cardiac hypertrophy in highly trained elite athletes. *N Engl J Med* 1991;324:295-301.
20. Pelliccia A, Spataro A, Maron BJ. Prospective echocardiographic screening for coronary artery anomalies in 1,360 elite competitive athletes. *Am J Cardiol* 1993;72:978-9.
21. Maron BJ, McKenna WJ, Danielson GK, et al. American College of Cardiology/ European Society of Cardiology clinical expert consensus document on hypertrophic cardiomyopathy: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents and the European Society of Cardiology Committee for Practice Guidelines. *J Am Coll Cardiol* 2003;42:1687-713.
22. Gavazzi A, De Maria R, Renosto G, et al. The spectrum of left ventricular size in dilated cardiomyopathy: clinical correlates and prognostic implications. *Am Heart J* 1993;125:410-22.
23. Maron BJ, Pelliccia A, Spirito P. Cardiac disease in young trained athletes: insights into methods for distinguishing athlete's heart from structural heart disease, with particular emphasis on hypertrophic cardiomyopathy. *Circulation* 1995;91:1596-601.
24. Pelliccia A, Culasso F, Di Paolo FM, Maron BJ. Physiologic left ventricular cavity dilatation in elite athletes. *Ann Intern Med* 1999;130:23-31.
25. McKenna WJ, Thiene G, Nava A, et al. Diagnosis of arrhythmogenic right ventricular dysplasia/cardiomyopathy. *Br Heart J* 1994;71:215-8.
26. Armitage P, Berry G. Statistical methods in medical research. 3rd ed. Oxford, England: Blackwell Scientific, 1994:277.
27. Antzelevitch C, Brugada P, Brugada J, Brugada R, Towbin JA, Nademanee K. Brugada syndrome: 1992-2002: a historical perspective. *J Am Coll Cardiol* 2003;41:1665-71.
28. Maron BJ, Wolfson JK, Ciró E, Spirito P. Relation of electrocardiographic abnormalities and patterns of left ventricular hypertrophy identified by 2-dimensional echocardiography in patients with hypertrophic cardiomyopathy. *Am J Cardiol* 1983;51:189-94.
29. Thiene G, Nava A, Corrado D, Rossi L, Pennelli N. Right ventricular cardiomyopathy and sudden death in young people. *N Engl J Med* 1988;318:129-33.
30. Sharma S, Whyte G, Elliot P, et al. Electrocardiographic changes in 1000 highly trained junior elite athletes. *Br J Sports Med* 1999;33:319-24.
31. Serra-Grima R, Estorch M, Carrió I, Subirana M, Bernà L, Prat T. Marked ventricular repolarization abnormalities in highly trained athletes' electrocardiograms: clinical and prognostic implications. *J Am Coll Cardiol* 2000;36:1310-6.
32. Corrado D, Basso C, Rizzoli G, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? *J Am Coll Cardiol* 2003;42:1959-63.
33. Pelliccia A, Di Paolo FM, Corrado D, et al. Evidence for efficacy of the Italian national pre-participation screening programme for identification of hypertrophic cardiomyopathy in competitive athletes. *Eur Heart J* 2006;27:2196-200.

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