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Long-Term Clinical Significance of Frequent and Complex Ventricular Tachyarrhythmias in Trained Athletes

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OBJECTIVES The aim of this study was to clarify the clinical relevance of ventricular tachyarrhythmias assessed by 24-h ambulatory electrocardiograms (ECG) in a large, unique, and prospectively evaluated athletic population.

BACKGROUND For athletes with ventricular tachyarrhythmias, the risk of sudden cardiac death associated with participation in competitive sports is unresolved.

METHODS We assessed 355 competitive athletes with ventricular arrhythmias (VAs) on a 24-h ambulatory (Holter) ECG that was obtained because of either palpitations, the presence of ≥3 premature ventricular depolarizations (PVDs) on resting 12-lead ECG, or both.

RESULTS Athletes were segregated into three groups: Group A with ≥2,000 PVDs/24 h (n = 71); Group B with ≥100 <2,000 PVDs/24 h (n = 153); and Group C with only <100 PVDs/24 h (n = 131). Cardiac abnormalities were detected in 26 of the 355 study subjects (7%) and were significantly more common in Group A (21/71, 30%) than in Group B (5/153, 3%) or Group C athletes (0/131, 0% $p < 0.001$). Only the 71 athletes in Group A were excluded from competition. During follow-up (mean, 8 years), 70 of 71 athletes in Group A and each of the 284 athletes in Groups B and C have survived without cardiovascular events. The remaining Group A athlete died suddenly of arrhythmogenic right ventricular cardiomyopathy while participating in a field hockey game against medical advice.

CONCLUSIONS Frequent and complex ventricular tachyarrhythmias are common in trained athletes and are usually unassociated with underlying cardiovascular abnormalities. Such VAs (when unassociated with cardiovascular abnormalities) do not convey adverse clinical significance, appear to be an expression of "athlete's heart syndrome," and probably do not per se justify a disqualification from competitive sports. (J Am Coll Cardiol 2002;40:446–52) © 2002 by the American College of Cardiology Foundation

Sudden cardiac deaths occurring on the athletic field in young and healthy-appearing sports participants, presumably largely related to ventricular tachyarrhythmias, are highly visible events that continue to generate great concern within the lay and medical communities (1–5). However, the risk associated with competitive sports in athletes with ventricular tachyarrhythmias identifiable by Holter recording is presently unresolved. Furthermore, although there are

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little data available regarding the long-term clinical significance of ventricular arrhythmias (VAs) in healthy-appearing athletes (6), premature ventricular depolarizations (PVDs) are a frequent finding in such individuals (7–9).

At present, it is unresolved whether such ventricular tachyarrhythmias should be regarded as benign or potentially life-threatening electrical disorders during intense physical activity, in the presence or absence of structural heart disease. Therefore, the aim of the present study is to clarify the clinical relevance of ventricular tachyarrhythmias identified by 24-h ambulatory (Holter) electrocardiogram (ECG) in a large, unique, and prospectively evaluated athletic population.

METHODS

Patient selection. The case records of the Institute of Sports Science were reviewed from January 1984 to March 1999, and 355 athletes had been assessed with 24-h ambulatory (Holter) ECG (from a total population of 15,889 athletes), if they met the following criteria: 1) ≥3 PVDs on resting 12-lead ECG (n = 337); and/or 2) history of palpitations (n = 18).

Each of the 355 athletes underwent a cardiovascular evaluation (in addition to 24-h Holter ECG monitoring), including medical history and physical examination, 12-lead ECG, two-dimensional echocardiography, symptom-limited exercise ECG, and chest X-ray. Holter ECGs were recorded during periods of active training and included an

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Abbreviations and Acronyms

ARVC = arrhythmogenic right ventricular cardiomyopathy
ECG = electrocardiogram
EP = electrophysiologic
LBBB = left bundle branch block
MRI = magnetic resonance imaging
NSVT = nonsustained ventricular tachycardia
PVD = premature ventricular depolarization
VA = ventricular arrhythmia
VT = ventricular tachycardia

average of 1 h in a training session similar to that performed by the athlete, with the remaining time occupied by usual daily activities. Athletes with particularly frequent and complex PVDs on ambulatory (Holter) ECG monitoring were selected on a clinical basis to undergo additional testing for the purpose of detecting or defining underlying cardiovascular disease, including magnetic resonance imaging (MRI) (n = 42), nuclear scintigraphy (n = 16), endomyocardial biopsy (n = 10), and electrophysiologic (EP) study with programmed ventricular stimulation (n = 24). Of the 355 athletes included in the study population, 230 had been routinely examined at our institution as part of the Italian national preparticipation screening program for competitive athletes (10,11), and the other 125 athletes were referred to us for cardiac evaluation because of a suspicion of cardiovascular disease. Athletes were engaged in 18 different sporting disciplines, most commonly soccer (25%), basketball (14%), and volleyball (10%), and had participated in vigorous training programs for one to 13 years (median four years); 110 (30%) had achieved international recognition in World Championship and Olympic Games; and 245 (70%) competed at the national level. Mean age of the athletes at the time of Holter recording was 24.8 ± 12.4 years (range 14 to 35 years). All 355 athletes had periodic evaluations every 6 to 12 months over a follow-up period of 2 to 15 years (mean 8.4 ± 6.3 years).

The criteria used for the diagnosis of arrhythmogenic right ventricular cardiomyopathy (ARVC) were those previously recommended (12). Diagnosis of myocarditis was based on the histologic appearance of biopsy specimens in accord with the Dallas criteria (13). Dilated cardiomyopathy was diagnosed based on recognition of a dilated left ventricular cavity (end-diastolic dimension ≥60 mm) associated with systolic left ventricular dysfunction (ejection fraction ≤45% and/or segmental wall motion abnormalities) (14). A bicuspid aortic valve without hemodynamic evidence of stenosis or significant valvular regurgitation was regarded only as an echocardiographic finding rather than a true abnormality. At the time of Holter monitoring, no athlete was taking antiarrhythmic or other cardioactive medications.

EP studies. Twenty-four athletes with the most frequent and complex arrhythmias on Holter ECG were selected on clinical indications for EP study: 10 with ≥10,000 PVDs/24 h, nine with ≥10,000 PVDs and ≥1 nonsustained ventricular tachycardia (NSVT), and five with ≥2,000 PVDs and ≥1 episode of NSVT. Eight of these 24 athletes also had palpitations. Ventricular stimulation was performed using a programmable stimulator (Medtronic 5328, Minneapolis, Minnesota), delivering rectangular pulses of 2 ms duration at twice the diastolic threshold. Up to three extra stimuli were introduced after eight ventricular paced beats at three drive cycle lengths (600, 500, and 400 ms) and in two right ventricular sites (apex and outflow tract). In 18 athletes who were not inducible under basal conditions, programmed stimulation was also carried out with isoproterenol infusion.

Statistics. Age is expressed as the mean ± SD (standard deviation). For all other variables, frequency distributions are reported. Differences between subgroups and multiple tests analysis were assessed using Kruskal-Wallis analysis. A two-tailed p value <0.05 was considered evidence of statistical significance. Statistical analyses were performed using BMPD Statistical Software (University of California, Los Angeles, California) with 3S program (1995).

RESULTS

Frequency of PVDs. Based on the 24-h Holter ECG data, the 355 athletes were segregated into three groups. Group A was comprised of 71 athletes with both frequent and complex PVDs (≥2,000 PVDs and ≥1 burst of NSVT/24 h). Group B consisted of 153 athletes with less frequent arrhythmias (100 to 2,000 PVDs without NSVT/24 h). Group C consisted of 131 athletes with <100 PVDs and without NSVT/24 h (Table 1).

GROUP A. In the 71 Group A athletes, frequency of PVDs/24 h ranged from 2,000 to 43,000 (mean 10,850 ± 7,500), including 24 (34%) who had ≥10,000 PVDs/24 h. Each of the 71 athletes had ≥1 couplet (mean 70 ± 22, range 7 to 280). Thirty-eight of these 71 athletes (54%) also had 1 to 179 bursts of NSVT (mean 4), consisting of 3 to 28 consecutive beats, at heart rates of 130 to 270 beats/min. In addition, nine of 24 athletes with ≥10,000 PVDs had ≥1 run of NSVT (Fig. 1). Only 8 of the 71 Group A athletes (11%) reported palpitations, and none had episodes of impaired consciousness or other cardiac symptoms.

GROUP B. In the 153 athletes of Group B, PVDs ranged from 100 to 1,890 (mean 1,211 ± 850); eight athletes had one couplet, but none had NSVT. Ten of the 153 Group B athletes (6%) reported palpitations, and none had impaired consciousness or other cardiac symptoms.

GROUP C. In the 131 athletes of Group C, PVDs ranged from 3 to 98 (mean 55 ± 22). No athlete in Group C had couplets or NSVT or reported palpitations.

Cardiovascular abnormalities. OVERALL ATHLETE GROUP. Of the 355 athletes, 329 (93%) showed no evidence of relevant cardiovascular abnormalities based on clinical

Table 1. Demographic and Clinical Data in 355 Competitive Athletes With Ventricular Tachyarrhythmias

	Group A (≥2,000 PVDs and ≥1 NSVT)	Group B* (≥100 to <2,000 PVDs)	Group C* (<100 PVDs)	p Value
No. athletes	71	153	131	
Age	24 ± 10	24 ± 10	25 ± 11	NS
Male:Female	51:20	120:33	102:29	NS
Palpitations†	8 (11%)	10 (6%)	0	0.0013‖
12-lead ECG abnormalities‡	15 (21%)	5 (3%)	2 (1.5%)	< 0.001¶
Echo abnormalities§	21 (30%)	8 (5%)	0	< 0.001¶

*NSVT was absent in these subgroups. †Defined as a frequent sensation of irregular heart beat (also during exercise), unassociated with dizziness. ‡Increased R and/or S wave ≥30 min, inverted T waves (≥2 leads), deep Q waves (≥2 mm), LBBB or RBBB, left axis deviation. §Mitral valve leaflet redundancy and prolapse (n = 11); dilated cardiomyopathy (end-diastolic dimension ≥60 mm) associated with systolic left ventricular dysfunction (ejection fraction ≤45% and/or segmental wall motion abnormalities) (n = 4); segmental wall motion abnormalities consistent with either ARVC and myocarditis (n = 11); and bicuspid aortic valve without aortic regurgitation (n = 3); ‖Group A versus Group C and Group B versus Group C ($p < 0.05$); ¶Group A versus Group B and Group A versus Group C ($p < 0.05$).

ECG = electrocardiogram; Echo = two-dimensional echocardiography; NSVT = nonsustained ventricular tachycardia; PVDs = premature ventricular depolarizations.

examination and noninvasive testing. The other 26 athletes (7%) had cardiovascular abnormalities, all known to be associated with VAs (15–17), including mitral valve prolapse with mild-to-moderate regurgitation in 11, ARVC in seven, myocarditis in four, and dilated cardiomyopathy in four.

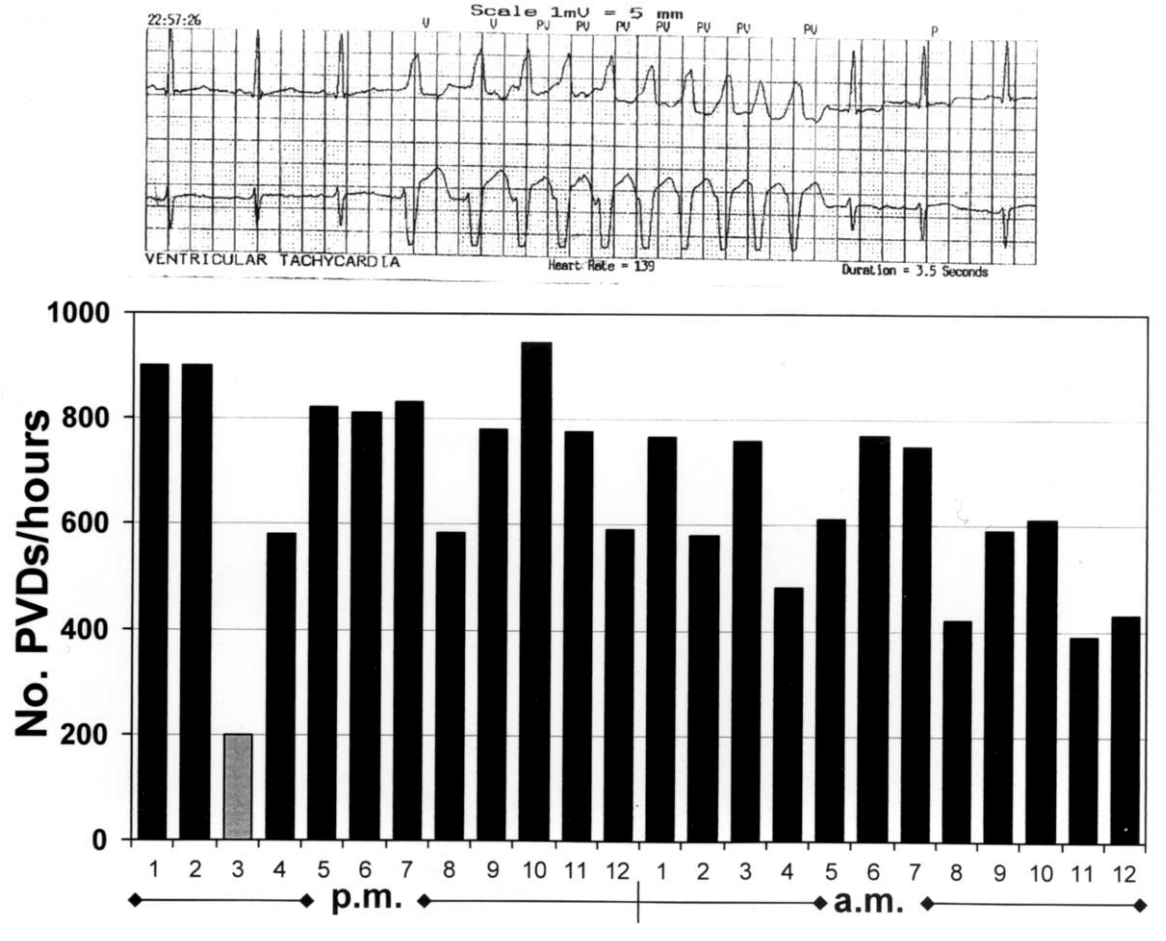

Figure 1. Segment of 24-h Holter electrocardiogram recording from a 24-year-old male basketball player with history of frequent palpitations. **(Top)** Asymptomatic 10-beat burst of nonsustained ventricular tachycardia (shortest R-R interval, 300 ms). Intervals between the initial beat and subsequent ectopic beats gradually shorten as the rate of discharge of the ectopic focus increases. The electrophysiologic study with programmed ventricular stimulation was normal. **(Bottom)** Hourly profile of premature ventricular depolarizations (PVDs) over 24 h. There is a total of 12,186 PVDs during a 24 h period largely without significant differences between the morning and evening. Only during a training session (at 3 PM) was there a distinctly reduced number of PVDs (200/h).

Table 2. Prevalence of Structural Cardiovascular Abnormalities in 355 Competitive Athletes With Ventricular Tachyarrhythmias

	Group A (≥2,000 PVDs and ≥1 NSVT)	Group B* (≥100 to <2,000 PVDs)	Group C* (<100 PVDs)	p Value
No. of athletes	71	153	131	
ARVC	7 (10%)	0	0	< 0.001†
MVP	6 (9%)	5 (3%)	0	0.0042‡
Myocarditis	4 (5.5%)	0	0	0.0003†
DCM	4 (5.5%)	0	0	0.0003†
Totals	21 (30%)	5 (3%)	0	< 0.001†

*NSVT was absent in these subgroups; †Group A versus Group B and Group A versus Group C ($p < 0.05$); and ‡Group A versus Group C ($p < 0.05$).

ARVC = arrhythmogenic right ventricular cardiomyopathy; DCM = dilated cardiomyopathy; MVP = mitral valve prolapse; Other abbreviations as in Table 1.

RELATIONSHIP OF CARDIOVASCULAR ABNORMALITIES TO ARRHYTHMIA SUBGROUPS. Cardiovascular abnormalities were significantly more common in Group A (21/71, 30%) than in Group B (5/153, 3%) and Group C (0/131, 0%; $p < 0.001$) (Table 2). Group A athletes with or without cardiovascular abnormalities did not differ with respect to PVDs, couplets, and NSVT: those athletes with cardiovascular abnormalities showed 8,411 ± 11,000 PVDs, 60 ± 108 couplets, and 6.2 ± 6.1 NSVT bursts in 24 h of Holter ECG recording; and those without abnormalities had 11,217 ± 9,000 PVDs, 80 ± 184 couplets, and 11 ± 35 NSVT ($p > 0.05$).

Morphology of PVDs and relationship to cardiovascular abnormalities. Premature ventricular depolarizations with left bundle branch block (LBBB) (frequently associated with vertical axis) (Fig. 2) occurred with similar prevalence in Groups A (46/71, 65%), B (120/153, 78%), and C (88/131, 67%; NS). The occurrence of right bundle branch block PVDs also did not differ significantly between Groups A (19/71, 27%), B (36/153, 24%), and C (32/131; 24%;

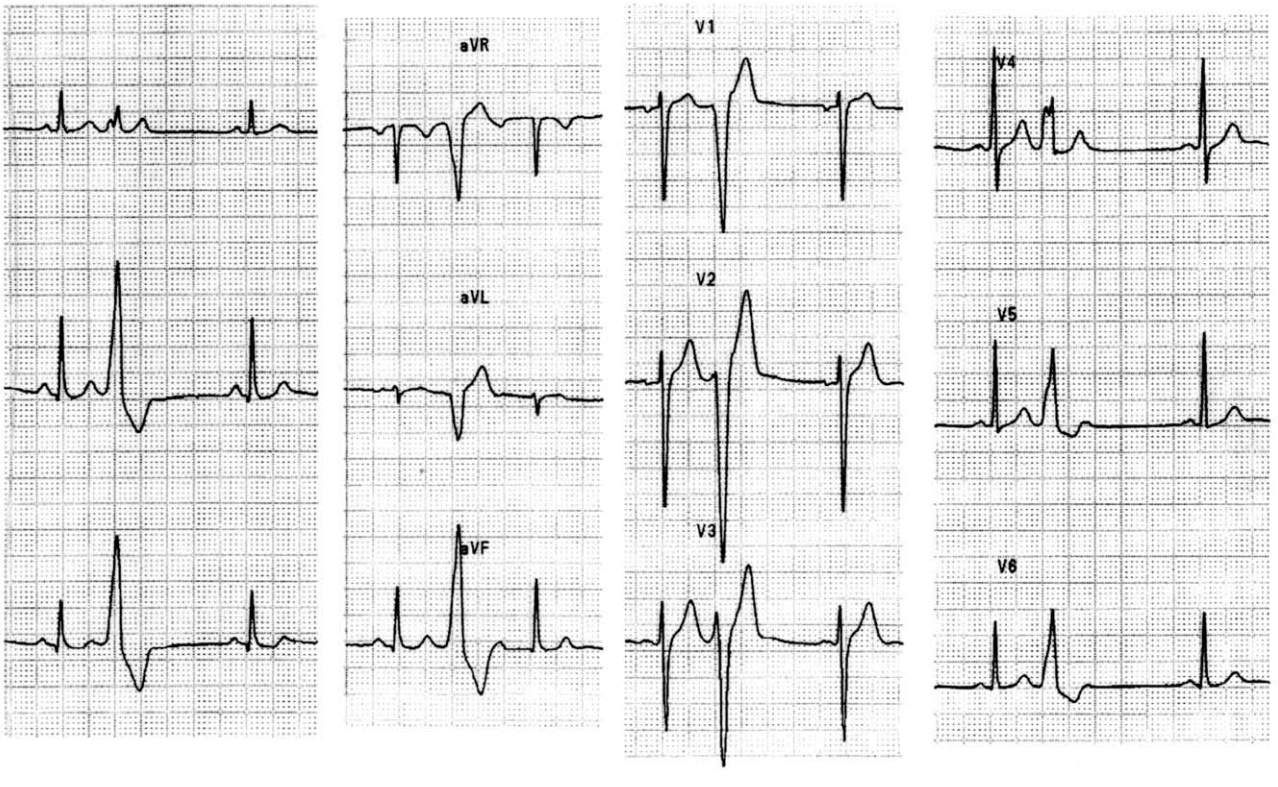

Figure 2. Resting 12-lead electrocardiogram (ECG) showing left bundle branch block premature ventricular depolarization pattern and inferiorly oriented QRS axis from an asymptomatic 27-year-old soccer player. Otherwise, ECG pattern is normal. Noninvasive testing excluded underlying cardiovascular abnormalities.

NS). Of the 71 athletes in Group A, LBBB PVDs were found more frequently in the absence (35/46; 76%) than in the presence of structural cardiac disease (11/46; 24%; $p < 0.001$). No athletes in Groups B and C with LBBB PVDs showed cardiovascular abnormalities.

Utility of invasive and noninvasive testing in the identification of cardiovascular abnormalities. The 12-lead ECG failed to show evidence of Brugada and long QT syndromes in any athlete, although T-wave inversion in precordial leads V_1–V_3 raised a consideration for ARVC in four athletes, ultimately diagnosed by MRI or myocardial biopsy. Echocardiography identified mitral valve prolapse in 11 athletes and dilated cardiomyopathy in four. Of the 42 athletes who underwent MRI, cardiovascular abnormalities were detected in 12, including six with ARVC. Ten athletes had myocardial biopsy, and a diagnosis of cardiovascular disease was made in 8 (myocarditis in 4 and ARVC in 4).

Most athletes showed no PVDs or NSVT during and immediately after exercise testing, including 45 athletes in Group A (65%), 110 in Group B (72%), and 122 in Group C (93%). No athlete experienced cardiac symptoms (or impaired consciousness) during exercise testing.

EP studies. In only one of the 24 athletes with EP studies (a 32-year-old cyclist with ARVC and 12,000 PVDs and 5 NSVT bursts on Holter ECG) was sustained VT provoked by programmed ventricular stimulation. In the other 23 athletes (13 without and 10 with cardiovascular abnormalities), either no arrhythmia or only NSVT was induced. The athlete who died with ARVC had refused to undergo EP study.

Follow-up. Each of these 71 athletes with frequent and complex VAs (Group A) was disqualified from competitive sports for a minimum of three months, based on the Italian guidelines for determining eligibility in competitive athletes with cardiovascular abnormalities (18), which closely resemble the recommendations of the 26th Bethesda Conference (19).

Over the follow-up, one of these athletes, a 24-year-old man with ARVC, died suddenly while participating in a competitive field hockey game (against medical advice), six months after official disqualification. This athlete had 2,100 PVDs and two bursts of NSVT (4 and 6 beats at 180/min) on Holter recording and also had occasional palpitations. The other 70 Group A athletes, as well as all Group B and Group C athletes with less frequent arrhythmias, who were allowed to resume competition and training, survived to the end of the follow-up period without incurring cardiac symptoms or events.

Pharmacologic treatment. Of the 71 athletes in Group A, only eight (all with underlying cardiovascular diseases) received drug treatment with beta-blockers ($n = 5$), propafenon ($n = 2$), or enalapril ($n = 1$). This treatment was associated with reduction in the total number of PVDs and/or of complex arrhythmias in five patients (mitral valve prolapse in 2 and ARVC in 3). Specifically, three of these athletes with ≥10,000 PVDs and NSVT showed the disappearance of NSVT and reduction of PVDs to <500/24 h with beta-blocker or propafenon treatment. The two other athletes associated showed disappearance of NSVT but persistence of PVDs (7,534 ± 1,450 before vs. 6,880 ± 1,607 after drug treatment). In the remaining three patients, drugs did not reduce ectopy (6,583 ± 886 PVDs and 6 ± 1 episodes of NSVT before vs. 6,286 PVDs and mean 5 ± 1 episodes of NSVT after treatment). No athlete in Group B or C received drugs.

DISCUSSION

Several ambulatory (Holter) ECG studies have shown VAs, primarily PVDs, in a high proportion of apparently healthy athletes and some normal untrained subjects (8,20–27). The clinical assessment of these arrhythmias is of particular significance because of the recognition that young, otherwise healthy athletes can harbor unsuspected and potentially lethal cardiovascular diseases, which can result in sudden arrhythmic death (1–4). For these reasons, we thought it is timely and important to analyze a large athletic population with respect to ventricular tachyarrhythmias and the presence or absence of associated cardiovascular abnormalities. Indeed, these observations potentially impact on clinical decision making with respect to the eligibility (or disqualification) of athletes with frequent and complex VAs participating in intense sports training and competition (18,19).

To this purpose, we have examined the clinical significance of ventricular tachyarrhythmias identified by ambulatory (Holter) ECG in a large population of 355 highly trained athletes. Overall, only 7% of our athletes harbored structural cardiovascular abnormalities that were the likely cause of these arrhythmias, and prevalence of these structural abnormalities was 15 times higher in athletes with frequent and complex ventricular tachyarrhythmias than in those with less frequent arrhythmias. Nevertheless, over the eight-year follow-up period, risk of sudden death proved to be exceedingly low whether or not cardiovascular abnormalities were present and despite the presence of complex VAs that otherwise might reasonably imply a high risk of sudden cardiac death. Indeed, just one athlete of the 355 died suddenly during athletic competition (0.3%; annual mortality = 0.17%), a 24-year-old field hockey player with ARVC, which was associated with 2,100 PVDs and two brief runs of NSVT, who continued competition against medical advice.

Of note, the low-risk status of our athletes may be in part attributable to the fact that we identified few examples of those cardiac diseases known to be the most commonly associated with sudden death in populations of trained athletes, such as hypertrophic cardiomyopathy or the coronary anomalies of wrong sinus origin (1–3). In the present study, the most common anomaly associated with VAs was mitral valve prolapse, and none of these athletes died suddenly. Nevertheless, we wish to sound a note of caution that certain cardiac diseases associated both with ventricular

tachyarrhythmias and with sudden death in athletes (such as myocarditis) (1,19) may be challenging to identify clinically and require a high index of suspicion (28,29). Furthermore, studies with MRI showed the presence of small areas of fatty replacement in patients with apparently idiopathic right outflow tract tachyarrhythmias (30,31), and we therefore we cannot exclude the possibility that some of our athletes who did not undergo MRI and/or invasive testing might have (mild) morphologic right ventricular abnormalities responsible for VAs. However, considering the large number of athletes with VAs reported in this study and their favorable clinical outcome, we believe that it is exceedingly unlikely such a rare disease could be responsible for the arrhythmias identified in many of our athletes.

Furthermore, recent advances in laboratory DNA analysis have demonstrated a genetic basis for some arrhythmogenic syndromes unassociated with left ventricular hypertrophy (long QT syndrome, Brugada syndrome, and polymorphic VT) (32,33). Because molecular studies and mutational analysis were not part of our study design, we cannot definitively exclude the possibility that such uncommon genetic disorders were present in a very small minority of our athletes with VAs.

VAs in the absence of structural heart disease. Perhaps the most difficult subgroup with regard to clinical practice guidelines are those athletes with frequent and complex VAs in the absence of structural heart disease. Such individuals present a clinical dilemma regarding their eligibility for sports (18,19). Our longitudinal follow-up data are persuasive in supporting the view that frequent and complex ventricular tachyarrhythmias, very commonly detected with ambulatory ECG (Holter) monitoring in trained athletes without cardiovascular abnormalities, appear benign and probably do not require alteration in athletic lifestyle (23–27). In addition, our inability to induce sustained ventricular tachyarrhythmias during EP study in the vast majority of these athletes supports this recommendation. Furthermore, we have assembled preliminary data showing that athletic deconditioning has the effect of abolishing frequent and complex VAs in most athletes (34). Consequently, it would appear that such arrhythmias on Holter monitoring, even in athletes subjected to the unique environmental conditions and stress of intense sports training and competition (potentially with alterations in blood volume and electrolytes), do not convey an ominous prognosis in the absence of underlying structural heart disease. On the other hand, it is possible that disqualification from intensive training and competition could have favorably influenced the outcome and decreased the likelihood of sudden death in athletes with particularly frequent and complex VAs in the absence of cardiovascular abnormalities.

Utility of preparticipation cardiovascular evaluations. Our findings also suggest that preparticipation cardiovascular evaluations are effective not only in identifying and disqualifying athletes with VAs and ARVC but also in possibly preventing sudden cardiac death (2). Supportive of this view is our observation that the six athletes in this study identified with ARVC and frequent and complex VAs, who were disqualified from sports, have all survived to the present (over an average five-year follow-up period). However, the other athlete with ARVC and frequent and complex VAs died suddenly during competitive sports activities; although this athlete showed frequent PVDs and NSVT on Holter recording and was officially disqualified from competition in accord with the Italian consensus panel guidelines (18), he nevertheless continued to participate in national level field hockey against medical advice. We can only speculate that if this athlete had discontinued competitive sports, his risk of having a sudden cardiac death would have greatly diminished (1,19). Similar recommendations for disqualification from intense competitive sports apply to other heart diseases such as myocarditis, dilated cardiomyopathy, and mitral valve prolapse, particularly when they are associated with frequent and complex VAs (19).

No sudden cardiac deaths occurred in athletes in whom there were frequent and complex VAs without cardiovascular abnormalities, suggesting that these athletes do not require restriction from competitive athletics.

Conclusions. In a highly trained athletic population presenting with frequent and complex ventricular tachyarrhythmias on ambulatory Holter ECG, only about one-third harbored structural cardiovascular abnormalities likely to be responsible for the irregularities (Group A). Therefore, such arrhythmias were particularly common in the absence of underlying disease and compatible with survival without symptoms or cardiovascular events to the end of an eight-year follow-up period. These findings underscore the view that ventricular tachyarrhythmias in athletes subjected to intense physical exertion during training and competition do not usually develop unfavorable consequences and that, in athletes without cardiovascular abnormalities, they would appear to represent another previously unappreciated expression of the "athlete's heart syndrome," probably insufficient per se to definitively dictate withdrawal from competitive sports.

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