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Cardiac specialized conduction system in competitive athletes

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Abstract. Competitive athletes are widely regarded as a special group of healthy individuals with a unique lifestyle who are seemingly invulnerable and often capable of extraordinary physical achievement.
Athlete's heart is generally regarded as a benign increase in cardiac mass, with specific circulatory and cardiac morphological alterations, that represents a physiological adaptation to systematic training. However, the clinical profile of athlete's heart has expanded considerably over the last several years as a result of greater accessibility to large populations of trained athletes studied systematically with, ECG, ambulatory Holter ECG monitoring, stress test, echocardiography and cardiac magnetic resonance. As a consequence, there is increasing recognition of the impact that prolonged conditioning has on cardiac remodeling, which may eventually mimic certain pathological conditions, such as Brugada syndrome, with the potential for sudden death or disease progression.
These findings indicate that atrioventricular conduction system abnormalities may play a fatal arrhythmogenic role and raise questions regarding the prevention of electrical instability in young people engaged in active sports. At last many drugs have been associated with adverse events in Brugada syndrome patients and have been indicated to provoke the characteristic Brugada syndrome-linked ECG abnormalities and/or (fatal) ventricular tachyarrhythmias.
Keywords: *atrioventricular conduction, sudden death, exercise, athletes*.

Introduction

The cardiovascular benefits of regular physical exercise have been well-documented, with overwhelming evidence from epidemiological and intervention studies, suggesting that cardiovascular disease is largely a disease associated with physical inactivity (1,2). Exercise plays a beneficial role in the prevention and treatment of cardiovascular disease, with an inverse and robust relationship between physical activity and mortality risk. With such overwhelming evidence to support the promotion of physical activity within the community, the competitive retirement or even death of an athletic individual due to a cardiac pathological mechanism is a tragic and highly publicised event (3,4).
Competitive athletes are widely regarded as a special subgroup of healthy individuals with a unique lifestyle who are seemingly invulnerable and often capable of extraordinary physical achievement.
The heart of trained athletes can have a variety of changes known as athlete's heart. Athlete's heart is generally regarded as a benign increase in cardiac mass, with specific circulatory and cardiac morphological alterations, and electrical changes that show up on an ECG, that represents a physiological adaptation to systematic training (5).
Syncope, defined as a transient loss of consciousness accompanied by loss of postural tone, is common in trained athletes. In a large cohort of Italian athletes, roughly 6% reported syncope in the prior 5 years (6,7).
The approach to the athletic patient with syncope begins with a detailed history, physical examination, and 12-lead ECG (8). The resting 12-lead ECG should be inspected for abnormalities of conduction - QT prolongation, pre-excitation, right bundle-branch block with early precordial ST elevation suggestive of Brugada syndrome (BrS) and structural heart disease - left bundle-branch block, LV hypertrophy with repolarization abnormalities, diffuse T-wave inversions (5).
Notable is the evidence that, many drugs have been reported to induce the type-1 BrS-ECG and/or (fatal) arrhythmias in BrS-patients.

Therefore, patients with BrS should be advised not to use these drugs or to use them only under controlled conditions (9).

Cardiac morfo-functional aspects in athlete's heart

The heart has an electrical conduction system makes of two nodes (special conduction cells) and a series of conduction pathways. The heart begins beating with an electrical impulse from the sinoatrial (SA) node. The SA node is the pacemaker of the heart, responsible for setting rate and rhythm and is located in the wall of the right atrium. The impulse spreads through the walls of the atria, causing them to contract. Then, the impulse moves through the atrioventricular (AV) node (a relay station) located at the junction between the atria and ventricles. As the impulse travels down the bundles, the ventricles contract and the cycles repeats itself, this cycle of atrial and ventricular contractions pumps blood of the heart to the rest of the body (6).

Resting and exercise heart rate are controlled by the sympathetic and parasympathetic nervous system. The sympathetic division of the autonomic nervous system prepares the body for physical activity by increasing heart rate, blood pressure and respiration. The sympathetic division also stimulates the release of glucose from the liver for energy. Once exercise begins, the sympathetic nervous system is activated and the heart rate rises quickly. Heart rate also rises by simply thinking about exercise, which is referred to as anticipatory heart rate response (10). The parasympathetic division helps to slow down heart rate and respiration. At rest, the heart is controlled by the parasympathetic division, which is why the average resting heart rate is 60 beats per minute or less. One of the explanations of why endurance athletes have such a low resting heart rate following training is due to increased parasympathetic response. During exercise, the release of epinephrine and norepinephrine stimulate receptors in the heart which causes heart rate to increase (5). Therefore, exercise acts as a trigger for lethal ventricular tachyarrhythmia, given the susceptibility imposed by underlying (and usually unsuspected) cardiac disease (8).

Recent data has documented an increased prevalence of supraventricular, complex ventricular and profound bradyarrhythmias in endurance-trained athletes, predominantly occurring in veteran athletes (11). Several forms of idiopathic ventricular arrhythmia have been identified in athletes which, by definition, originate in hearts without structural abnormalities. The clinical significance of these arrhythmias remains to be fully elucidated. Yet, in support of the potential pathological changes in the cardiac electrical activity, several studies have reported an incomplete reversal of left ventricular hypertrophy in retired elite athletes suggesting, in part, a pathological remodelling process (12,13).

Because of the heightened vagal tone that accompanies physical conditioning, trained athletes are known to commonly incur innocent arrhythmias and conduction alterations, such as sinus bradyarrhythmia, junctional rhythm, and first-degree or Wenckebach AV block (Mobitz type I). However, the application of ambulatory (Holter) ECG monitoring to trained athletes unexpectedly documented substantial ectopy with frequent premature beats and complex ventricular tachyarrhythmia (including couplets and bursts of nonsustained ventricular tachycardia) in many such individuals. These findings suggest that a variety of arrhythmias are part of the athlete's heart spectrum. Indeed, such rhythm disturbances have not been associated with adverse clinical events and are usually abolished or substantially reduced after relatively brief periods of deconditioning (as well as during physical training sessions and exercise testing). Even in athletes with heart disease, resolution of ventricular tachyarrhythmia with deconditioning is common and may represent a potential mechanism by which sudden death risk is reduced by withdrawal of these individuals from training and competition, in accord with consensus panel recommendations (14).

A few observational studies have reported mild-to-moderate postrace elevations in biochemical cardiac-specific markers (plasma cardiac troponin T and I) suggestive of transient myocardial injury in some participants after prolonged and strenuous endurance athletic events, such as triathlons and marathons (15,2). At present, there is no evidence that these subclinical findings are associated with permanent clinical consequences. Some studies have also identified transient and reversible systolic and diastolic dysfunction after extreme athletic events.

Although data defining the physiological and morphological adaptations of systematic training are considerable, it nevertheless remains

unresolved whether the current profile of athlete's heart can be extrapolated to all subgroups within this physically active and diverse population: those of different ages, sports disciplines, and racial or ethnic origin. Indeed, there are limited data defining the adaptations of athlete's heart in females, in modestly trained individuals in youth sports programs, and in blacks and other minorities (2).

In competitive athletes, the differential diagnosis between nonpathological cardiac changes associated with training (commonly referred to as "athlete's heart") and certain cardiac diseases with the potential for sudden death is an important and not uncommon clinical problem. Such crucial diagnostic distinctions most frequently involve Brugada syndrome, which is the most common cause of sudden death in young competitive athletes (3,4). Our awareness of this issue, as well as the parallel consideration of preparticipation athletic screening, has been heightened by several recent high-visibility catastrophies involving elite soccer, volleyball and basketball players who died suddenly and unexpectedly from cardiovascular disease (14).

The distinction between athlete's heart and cardiac disease has particularly important implications, because identification of cardiovascular disease in an athlete may be the basis for disqualification from competition in an effort to minimize risk. By the same token, the improper diagnosis of cardiac disease in an athlete may lead to unnecessary withdrawal from athletics, thereby depriving that individual of the varied benefits of sport (3, 2).

Nonetheless, he devastating impact of even relatively infrequent sudden deaths in young athletes offers justification for restriction from competition to reduce the risk related to silent and unsuspected cardiac disease. For athletes in whom cardiovascular disease has been identified (either by preparticipation screening or under other circumstances), important considerations arise with respect to the appropriate formulation of eligibility and disqualification decisions for competitive sports.

Recently, strict diagnostic criteria and risk stratification for the identification of high-risk patients with Brugada syndrome patients have been suggested. Thus, the diagnosis of Brugada syndrome can only be made on the basis of a typical ECG pattern and only a coved type ECG (Brugada type 1) is diagnostic of the disease and, if spontaneously occurring, apparently has a poorer prognosis (16,17). Although for European countries only scanty data exist as to the prevalence of the disease in the general population, the situation is even worse among endurance-trained athletes.

Recurrent exercise-related syncope in endurance-trained athletes is believed not to be associated with an adverse outcome, if structural abnormalities of the heart are absent. This, however, does not hold for syncope in individuals with Brugada syndrome, which is a potentially life threatening primary electrical disease. Individuals with a Brugada ECG and a history of syncope have a high risk for sudden cardiac arrest which amounts to 27% if they are inducible. In rare cases, syncope in Brugada syndrome may be due to a vasovagal mechanism (8).

Brugada syndrome

Brugada syndrome was first described in 1992 in a series of patients with sudden death who had similar, peculiar electrocardiogram abnormalities. It was later found that many of these patients had abnormal function of their sodium ion channels (3,4) .

Brugada syndrome is characterized by coved type ST- elevation in the right precordial leads (V1–V3) and increased risk of sudden death in the absence of structural heart disease.

ECG abnormalities constitute the hallmark of Brugada syndrome. They include repolarization and depolarization abnormalities in the absence of identifiable structural cardiac abnormalities or other conditions or agents known to lead to ST-segment elevation in the right precordial leads (10).

Three types of repolarization patterns are recognized (Fig. 1).

Type 1 is characterized by a prominent coved ST-segment elevation displaying J-wave amplitude or ST-segment elevation ≥2 mm or 0.2 mV at its peak followed by a negative T-wave, with little or no isoelectric separation (4,10).

Type 2 also has a high take-off ST-segment elevation, but in this case, J-wave amplitude (≥2 mm) gives rise to a gradually descending ST-segment elevation (remaining ≥1 mm above the baseline), followed by a positive or biphasic T-wave that results in a saddle back configuration (3,10).

Type 3 is a right precordial ST-segment elevation of <1 mm of saddle back type, coved type, or both, it presents also J-wave amplitude <2 mm.

It should be stressed that delineation of the *J* wave is sometimes tricky and that these descriptions are based on the correct placement of the precordial leads, although characteristic ECG features obtained with alternative placement of the right precordial leads in a superior intercostal space in individuals with high clinical suspicion may also disclose the presence of the arrhythmic substrate.

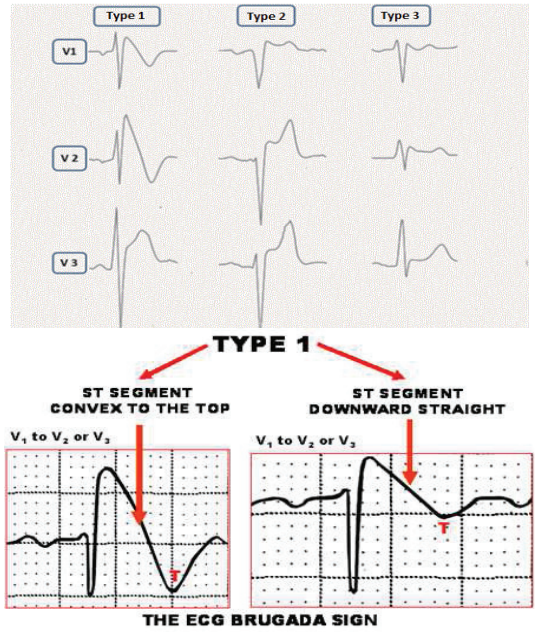

Figure 1. ECG pattern in Brugada syndrome

Brugada syndrome should be considered in the following cases:

- *Appearance of type 1*: ST-segment elevation (coved type) in more than one right precordial lead (V_1 to V_3), in the presence or absence of a sodium channel blocker, and one of the following likely indicates Brugada syndrome: documented ventricular fibrillation; self terminating polymorphic ventricular tachycardia; a family history of SCD (<45 years); coved type ECGs in family members; electrophysiological inducibility; syncope; or nocturnal agonal respiration. There should be no other factor(s) that can account for the ECG abnormality. The appearance of the ECG features without these clinical symptoms is referred to as an idiopathic Brugada ECG pattern (not Brugada syndrome) (13,18).
- *Appearance of type 2*: ST-segment elevation ("saddle-back type") in more than 1 right precordial lead under baseline conditions with conversion to type 1 after challenge with a sodium channel blocker is considered equivalent to case 1 above. A drug-induced ST-segment elevation to a value >2 mm should raise the possibility of Brugada syndrome when 1 or more clinical criteria are present. On the basis of our limited knowledge at present, a patient with a negative drug test (ie, no change in the ST-segment in response to a sodium channel blocker) is unlikely to have the Brugada syndrome; drug-induced ST elevation to <2 mm is considered inconclusive (19).
- *Appearance of type 3*: ST segment elevation in more than 1 lead under baseline conditions with conversion to type 1 after challenge with a sodium channel blocker is considered equivalent to case 1 above and should be screened accordingly. Drug-induced conversion of type 3 to type 2 ST-segment elevation is considered inconclusive (20).

Patients who do not fully fulfil the proposed criteria (eg, type 1 ECG with a J-wave amplitude of only 1mm), but who have one or more of the clinical criteria defined above, should be considered seriously. Most often, a drug challenge will disclose the diagnosis Brugada syndrome (3,6).

Particular problems exist in the pediatric population because of the lack of control data, the different chest morphology, and the age-dependent predominance of right ventricular forces. Typical ECG patterns, however, have been observed in small infants, where eventual lethal arrhythmias might actually resemble Sudden Infant Death syndrome. Hence, suspect symptoms with typical electrocardiographic features and/or a family history for sudden cardiac death, even at young age, should alert pediatricians to the possibility of Brugada syndrome (3,4).

Drugs and Bruganda syndrome patients

The presence of type-1 ECG has been linked to an increased risk for ventricular tachyarrhythmias, cardiac arrest and sudden death in Brugada syndrome patients (9). Importantly, many drugs have been reported to induce the type-1 ECG and/or (sometimes fatal) arrhythmias in Brugada syndrome patients. Therefore, it is necessary to advice patients with Brugada syndrome not to use these drugs, or to do so only in controlled conditions so that its potential pro-arrhythmic effect or the lack thereof can be documented and treated if necessary.