Life saving pre-participation athletic screening

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Abstract
Sudden cardiac death (SCD) of a young athlete is the most tragic event in sports. Competitive sports activity is associated with an increase in the risk of arrhythmic SCD in susceptible subjects with clinically silent cardiovascular disorders. Screening including 12-lead electrocardiogram (ECG) has been demonstrated to allow identification of athletes affected by malignant cardiomyopathies at a pre-symptomatic stage and leads to substantial reduction of SCD during sports. We report a case of a life-saving pre-participation cardiovascular evaluation in a young athlete.

Keywords: arrhythmogenic right ventricular cardiomyopathy; electrocardiogram; pre-participation screening; implantable cardioverter defibrillator; sports cardiology.

Case report
A 23-year-old male competitive soccer player was referred for routine pre-participation cardiovascular screening, based on family and personal history, physical examination and 12-lead electrocardiogram (ECG) as first-line evaluation. The athlete was completely asymptomatic and he had unremarkable family history and physical examination findings. Standard ECG showed depolarization/repolarization abnormalities and ventricular arrhythmias that were highly suggestive of arrhythmogenic right ventricular cardiomyopathy (ARVC) (Fig. 1A). There were typical negative T-waves in inferior and anterolateral precordial leads as well as isolated premature ventricular beats with a left bundle branch block (LBBB) and superior axis morphology. Moreover, there was a non-specific right intraventricular conduction defect in the form of localized slowing of the terminal part of QRS complex in V1 and V2 leads. Because of the abnormal ECG features, the patient underwent further diagnostic work-up to achieve a definitive diagnosis of ARVC. Laboratory exams were normal. During 24-hour (12 lead-ECG) Holter monitoring, the patient had frequent premature ventricular beats (~12,000/24 hours) with two morphologies (LBBB/superior axis [prevalent] and LBBB/inferior axis) and, most important, he experienced exercise-dependent non-sustained ventricular tachycardia (Fig. 1B). Transthoracic echocardiogram revealed moderate right ventricular (RV) dilatation with akinesia of the anterolateral wall and hypokinesia of the posterobasal wall; right ventricular outflow tract (RVOT) dilatation (RVOT/aortic diameter ratio 1.38); mild dilatation of the left ventricle with no wall motion abnormalities;
and normal flow across all cardiac valves. Contrast-enhanced cardiac magnetic resonance (CMR) demonstrated the presence of RV aneurysms and large fibrofatty scar of the anterolateral wall (Fig. 2). The patient then underwent invasive 3-dimensional endocardial voltage mapping using CARTO system (Biosense Webster, Diamond Bar, California) that showed a large RV electroanatomical scar in the anterolateral region, which was concordant with CMR findings. RV endomyocardial biopsy displayed extensive fibrofatty myocardial replacement with islands of degenerating residual myocytes.

In the light of the clinical data (major ECG, arrhythmic, and morpho-functional abnormalities) and according to International Task Force diagnostic criteria [4], the patient was diagnosed with “definite ARVC.” Accordingly, he was disqualified from competitive sport activity and was advised to refrain from any physical exercise. In addition, he was prescribed beta-blocker therapy (atenolol 50 mg per day), which was proven to be successful in preventing effort-induced ventricular arrhythmia by a control stress testing.

Unfortunately, beta-blockers therapy was not tolerated because of symptomatic sinus bradycardia (30–35 bpm) and was withdrawn. The athlete was then scheduled for prophylactic implantation of defibrillator (ICD). One month after the ICD implant, the patient reported falling off his mountain bike without loss of consciousness. On interrogation of the device at the time of the event, it was demonstrated that the athlete had experienced an episode of ventricular flutter that was appropriately detected by the device and successfully interrupted by shock therapy (Fig. 3).

Discussion
The present article reports on a representative case of “life-saving” pre-participation screening. The diagnosis of ARVC in the young athlete resulted in the prevention of SCD not only because of disqualification from competitive sports but also thanks to the subsequent close follow-up and clinical management. The former athlete became a patient who entered a clinical program of risk stratification and prophylactic ICD implantation for prevention of SCD.

Pre-participation screening
A nationwide program for screening young competitive athletes has been implemented in Italy since 1982 [1–3]. The flow chart of the Italian protocol of cardiovascular pre-participation screening is reported in Fig. 4 [2]. The long-term Italian experience demonstrated that pre-participation ECG identifies athletes affected by potentially lethal cardiomyopathies such as hypertrophic cardiomyopathy (HCM) and ARVC.
Twenty-four years after screening implementation, the annual incidence of SCD in screened athletes decreased by 89%, while the incidence of SCD in unscreened population remained unchanged. Most of the reduction was attributable to fewer deaths from HCM and ARVC [2]. The importance of identification by ECG screening of asymptomatic athletes with cardiovascular diseases relies on the concrete possibility of SCD prevention by lifestyle modification, including restriction of competitive sports activity and concomitant prophylactic treatment by anti-arrhythmic drugs, beta-blockers and ICD therapy [4]. We previously reported that athletes who did not obtain eligibility for competition because of cardiovascular reasons have a good long-term clinical course thanks to the subsequent medical management [1].
ARVC
ARVC is an inheritable heart muscle disease characterized pathologically by fibrofatty replacement of the RV myocardium [5]. Molecular genetic studies showed that ARVC is a desmosomal disease resulting from genetically defective cell-adhesion proteins such as plakoglobin, desmoplakin, plakophilin-2, desmoglein-2, and desmocollin-2 [5–7]. Clinical manifestations are related to electrical instability, including either ventricular tachycardia (VT) of RV origin or ventricular fibrillation (VF), which may lead to SCD, mostly in young people or athletes [5,8]. Ventricular arrhythmia worsens during or immediately after exercise and participation in competitive athletics is associated with an increased risk for SCD [5,8–10]. The disease affects men more frequently than women and becomes clinically overt most often in the second or third decade of life. Clinical diagnosis of ARVC is often difficult because of the nonspecific nature of the disease and the broad spectrum of phenotypic manifestation, ranging from severe to concealed forms. In 1994 an International Task Force proposed criteria for the clinical diagnosis of ARVC based on the presence of major and minor criteria encompassing electrocardiographic, arrhythmic, morpho-functional, histopathologic, and genetic factors [11]. These Task Force diagnostic criteria have been revised in 2010 [12]. The most important therapeutic objective in ARVC is to prevent arrhythmic sudden death. The ICD is the most effective tool against arrhythmic SCD, although antiarrhythmic drugs and catheter ablation may play a role for treatment of non life-threatening arrhythmia [5,13].

SCD during sports
Athletes have a 5.4 times greater risk to die suddenly from ARVC than sedentary population [9]. The arrhythmogenic effect of exercise was reproduced by animal model study of genetically altered mice subjected to endurance training [14].

The most frequent clinical manifestations of ARVC consist of ECG depolarization/repolarization changes mostly localized to right precordial leads, arrhythmias of RV origin and global and/or regional morphologic and functional alterations of the right ventricle [5,8,11,12]. The disease course is often silent and SCD can be the first clinical manifestation. Thus, the challenge is the early identification of still asymptomatic individuals on the basis of ECG abnormalities [15,16]. Final diagnosis relies on visualization of morphofunctional RV abnormalities by current imaging techniques (such as echocardiography, angiography, or cardiac magnetic resonance) and, in selected cases, by histopathologic demonstration of fibrofatty substitution at endomyocardial biopsy [5,8,17].

It is noteworthy that more than 80% of athletes who die from ARVC have ECG changes or ventricular arrhythmias [1,2,10]. Most common ECG abnormalities include right precordial inverted T-waves (beyond lead V1) in 88%, right precordial QRS duration >110 msec in 75%, and ventricular arrhythmias with a left bundle branch block pattern, mostly in the form of isolated/coupled premature ventricular beats or non-sustained ventricular tachycardia, in 75%. These ECG abnormalities could raise the suspicion of an underlying heart muscle disease at pre-participation evaluation and lead to further testing for a definitive diagnosis. Right precordial T-wave inversion (beyond V1) appears to be the most sensitive clinical marker for the presence of a potentially fatal ARVC in apparently healthy young competitive athletes [5,10].

According to recommendations for sports eligibility [18], athletes with clinical diagnosis of ARVC are excluded from all competitive sports. This recommendation is independent of age, gender, and phenotypic appearance and does not differ for those athletes without symptoms, or treatment with drugs, or interventions with surgery, catheter ablation, or implantable defibrillator.

ICD therapy in ARVC
Therapeutic options in ARVC patients include beta-blockers, antiarrhythmic drugs, catheter ablation, and ICD [13]. Although ICD confers optimal protection against SCD in ARVC patients, the significant rate of inappropriate interventions and complications, as well as the psychological repercussions mostly in the younger age group, argue strongly against indiscriminate device implantation [7]. The best candidates for ICD therapy are patients with prior cardiac arrest and those with VT with hemodynamically instable VT (i.e., associated with syncope or shock); syncope which remains unexplained after exclusion of non-cardiac causes and vaso-vagal mechanisms is also considered a valuable predictor of sudden death and represents “per se” an indication for ICD implantation [5,19,20]. In this high-risk group of patients, the rate of appropriate ICD intervention against life-threatening ventricular tachyarrhythmias (that in all likelihood
would have been fatal in the absence of shock therapy) is approximately 8–10% per year and the estimated mortality reduction at 36 months of follow-up ranges from 24–35% [5,19]. On the contrary, ICD implantation for primary prevention in the general ARVC population seems to be unjustified. As indicated by a recent multicenter study on prophylactic device implantation in ARVC patients with no sustained VT or VF, asymptomatic probands and relatives do not benefit from ICD therapy, regardless of familial sudden death or inducibility at programmed ventricular stimulation [20]. This patient cohort carries a low arrhythmic risk over a long-term follow-up (ICD intervention rate < 1 per year), in addition to a significant rate of device-related complications and inappropriate discharges. Patients with well-tolerated sustained VT or non-sustained VT on Holter or exercise testing have an intermediate arrhythmic risk (ICD intervention rate ~1–2% per year). In this patient subgroup, the decision for ICD implantation needs to be individualized. Our young athlete with ARVC received an ICD because of demonstration of non-sustained VT which, most important, occurred during effort. This is a recognized sign of malignant arrhythmic outcome [5,8–10].

Conclusions
The present case highlights the importance of ECG screening in identifying asymptomatic athletes with genetic cardiomyopathy or channelopathies because of the concrete possibility of SCD prevention by lifestyle modification, including restriction of competitive sports activity and concomitant prophylactic treatment by beta-blockers and/or implantable cardioverter-defibrillator therapy.

References