Arrhythmogenic right ventricular cardiomyopathy and sports activity

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This editorial refers to ‘Association of competitive and recreational sport participation with cardiac events in patients with arrhythmogenic right ventricular cardiomyopathy: results from the North American multidisciplinary study of arrhythmogenic right ventricular cardiomyopathy’1, by A.C. Ruwald et al., on page 1735.

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited heart muscle disease characterized by ventricular electrical instability which may lead to arrhythmic cardiac arrest, mostly in young people and athletes.1 Molecular genetics studies have provided significant insights towards our understanding of the pathogenesis of ARVC, showing that it is a genetic disorder resulting from defective desmosomal proteins.2 The pathological hallmark of the disease is the progressive loss of myocardium with subsequent myocyte death and fibrofatty scar which predisposes to life-threatening ventricular arrhythmias.3 Competitive sports activity increases the risk of sudden cardiac death (SCD) by five-fold in adolescent and young adults with ARVC.4 Sports has also been implicated as a factor promoting disease progression and worsening of the arrhythmic substrate (Figure 1). Genetically determined impairment of cell to cell adhesion may lead to myocyte death, especially during mechanical stress that occurs during competitive sports activity.1 Kirchhof et al.5 demonstrated that in heterozygous plakoglobin-deficient mice, endurance training accelerated the development of right ventricular (RV) abnormalities and ventricular arrhythmias. James et al.6 confirmed in humans that endurance sports and frequent exercise increase age-related penetrance, risk of ventricular tachyarrhythmias, and occurrence of heart failure in ARVC desmosomal gene carriers.

Prevention of sudden cardiac death in competitive athletes

Early identification of affected patients by preparticipation screening and disqualification from competitive sports activity may prevent SCD. A time-trend analysis of the incidence of SCD in young competitive athletes aged 12–35 years in the Veneto region of Italy demonstrated a 90% decrease of SCD in athletes after the introduction of the nationwide ECG screening programme.7 This mortality reduction was a reflection of a lower incidence of SCD from cardiomyopathies (ARVC and hypertrophic cardiomyopathy), as a result of increasing identification over time of affected athletes at preparticipation screening. Accordingly, there is general consensus that restriction of participation in competitive sports activity can be regarded as a treatment modality of patients with ARVC to reduce the risk of SCD.

Participation in recreational sports

Expert recommendations for sports eligibility of patients with heart disease focused on those athletes who are engaged in competitive sports.8 However, many young patients with ARVC wish to participate in recreational and leisure time exercise activity, given the recognized beneficial effects of a physically active lifestyle. In this issue of the journal, Ruwald et al.9 provided new and important data on disease presentation and outcomes according to sports participation in 108 ARVC probands with a diagnosis of either definite or borderline ARVC. The authors reported that ARVC patients who were engaged in competitive sports had earlier clinical presentation of the disease, more pronounced RV dilatation/dysfunction, and a greater risk of ventricular tachyarrhythmias/death compared with patients who participated in recreational activities or were inactive. The study demonstrated that the absolute risk of ventricular tachyarrhythmias/death at 40 years after birth was high in patients practising recreational sports (33%) but did not differ significantly from that of physically inactive ARVC patients (22%). Besides adding weight to the previous studies,6,10 the strength of the present study is that it presents new information for recommendations on lifestyle and sports eligibility in patients with ARVC, by providing potentially important reassurance that not all exercise is the same and that patients with ARVC may be able to derive the benefits of leisure time exercise without excess risk. However, the weakness of the study is that its methodology does not provide enough scientific support for recommendations on the level of sports allowed to...
ARVC patients. A study definition of competitive vs. recreational sports activity was lacking and it was up to the individual patients to assess on the enrolment questionnaire whether they believed that they participate in sports on a competitive or a recreational level or if they defined themselves as inactive. Most importantly, the intensity of the physical exercise was not quantified. Although they do not

Figure 1 Schematic representation of the course of arrhythmogenic right ventricular cardiomyopathy from desmosomal gene mutation to phenotypic expression and cardiac arrest due to ventricular fibrillation. Sports activity may promote development of phenotypic expression, accelerate disease progression, and trigger life-threatening ventricular arrhythmias (see text for more details).
take part in competition, recreational sportsmen, particularly those engaged in long-distance running or cycling, often exercise more than competitive athletes such as soccer players. 11 Better differentiation between competitive and recreational subjects would have been possible by quantification of the weekly volume of training. Although there were no statistically significant differences between recreational subjects and the small cohort of inactive subjects, the conclusion that ‘affected or borderline ARVC probands may be able to participate in recreational sports with the same risk of ventricular tachyarrhythmias/death as ARVC patients who are inactive’ is not supported by adequate statistical power because of the small subgroup size.

Healthy gene carriers

While according to the Bethesda conference healthy gene carriers are not precluded from participation in competitive sports, the guidelines of the European Society of Cardiology are more prudently restrictive and allow only leisure time sporting activities. 2 This latter recommendation is based on the assumption that regular exercise training and competitive sports can play a role in triggering cellular mechanisms leading to the development and progression of the disease phenotype in the presence of a predisposing gene abnormality. The penetrance of ARVC is age related and accounts for a latent-phenotypic expression (i.e. during the second to fourth decade of life). 3 This implies that a normal pre-participation evaluation of adolescents and young adults carrying a pathogenetic desmosomal gene mutation does not exclude the possibility that clinical manifestations of the disease including malignant arrhythmic events and unexpected SCD may occur later.

Implantable cardioverter defibrillator

The US and European recommendations consistently recommended restriction from competitive sport activities in ARVC patients with an implantable cardioverter defibrillator (ICD), with the possible exception of some low-intensity sports without associated risk of trauma to the device. 4,5 Reasons for non-eligibility include the increased risk of adrenergic-dependent arrhythmias, greater rate of inappropriate interventions, possible injury to the patient, and damage to the ICD system. The international ICD Sports Safety Registry 6 showed that patients with ARVC were more likely to receive appropriate shocks during competition/sports practice than those affected by other cardiomyopathies. The implant of an ICD should not be considered a justification for participation in competitive sports of patients with ARVC, for one more reason, i.e. participation in competitive sports plays a major role in disease progression, substrate worsening, and adverse outcome.

Conclusions

A link between competitive sports activity and the risk of SCD in patients with ARVC has been definitively established. Ruwald et al. 7 provided new and clearly relevant information in support of less restrictive recommendations for participation of ARVC patients in recreational exercise programmes. However, interpretation of the study results and translation into daily medical practice needs great caution in the light of the methodological limitations and because the absolute risk of non-competitive sports remains high. Further studies on larger ARVC patient populations over longer follow-up periods are required before drawing the definitive conclusion that ARVC patients can safely participate in recreational sports.

Conflict of interest: None declared.

References