COMMENTARY

Sport and Arrhythmogenic Right Ventricular Cardiomyopathy

A viewpoint on ARVC in sport by Z.B. Vezi, M. Tshifularo, B. Mayosi and A. Okreglicki

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ABSTRACT **Sudden deaths have been reported in sportspersons and have been related to physical activity. It is possible that exercise may be a trigger of potentially lethal arrhythmias in susceptible individuals or may be the factor that converts a defect of genotype to an abnormal and arrhythmogenic phenotype. Patients with Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) may be at higher risk of sports-related arrhythmias and sudden death. In the South African ARVC registry, 56% of patients were involved in regular sport participation. Various potential mechanisms linking sport and exercise to arrhythmias in patients with ARVC may exist.**
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Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) is a degenerative disease of cardiomyocytes resulting in fibro-fatty replacement and atrophy.[1] Although it affects mainly the right ventricle, the left ventricle may be involved. It may lead to arrhythmias, sudden cardiac death or heart failure. Affected individuals may be asymptomatic. The prevalence is unclear, but in the region of 1/1000, and it is familial in up to 50%.[2]

ARVC is primarily a desmosomal condition. Although there is no reason to believe that this desmosomal defect is regional and is known to affect both ventricles, it appears that the right ventricle takes the brunt pathophysiologically. The exact mechanism is still conjecture, but shear forces and stretch may play an important part.

Physical activity has many health-related, medical and cosmetic advantages. However, there is concern that its effects may not only be positive. Numerous reports of athletes dying suddenly, often of arrhythmias, gain much media coverage. It is possible that exercise may not only trigger potentially lethal arrhythmias in patients with an arrhythmia substrate but actually unveil subclinical cardiac conditions. Sport, possibly, is the factor that converts a defect of genotype to that of a specific abnormal potentially arrhythmogenic phenotype.

The South African ARVC registry has been set up to study this condition. Data collected may help begin to answer questions regarding presentation and ventricular involvement. In the registry, baseline data have been collected, including physical and sporting activity.

When the registry had recruited 75 patients with ARVC, with 61 of these being probands, it was analyzed for sport participation and exercise activity (Table 1). Of the 75 affected individuals, 42 (56%) were involved in regular sport participation, mostly aerobic exercise. The most common activity was road running, in 14 patients, followed by 6 involved with swimming and 6 with surfing. Nine patients were involved in a combination of sport activities, mostly running and swimming (Table 2).

TABLE 1: Demographic details of patients in the CASSA ARVC Registry (June 2008)

Number (n)	75
Gender	♂ = 51; ♀ = 24
Age (yrs)	Average age: ♂ - 41; ♀ - 44
	Range: 11 - 82 years
Sports Participation (% known)	42 (56%)
Symptoms	Palpitations (+++++)
	Near syncope (++++)
	Syncope (+++)
	Effort Intolerance (++)
	Chest Pain (+)
Medication	Atenolol>Sotalol=Amiodarone

TABLE 2: Type of sport and number of participants in the CASSA ARVC registry

Road Running	Swimming	Surfing	Soccer	Rugby	Squash	Rowing	Combination
14	6	6	3	2	2	1	9

It remains an interesting observation that amongst the ARVC patients, exercise participation is so common and at a level that appears to be higher than in the general population.

The link between endurance sport and ARVC may be more than coincidental, as shown in animal studies, in which endurance training accelerates the development of right ventricular dysfunction and arrhythmia in heterozygous plakoglobin-deficient mice, a defect of which is also known to occur in some ARVC patients.[3] It is our speculation that the right ventricle stretches from the increased venous return during exercise. Indeed, it has been suggested that the right ventricle might have a greater propensity to disease than the left ventricle because of its thinner wall and dilatory response to exercise.[4] In a person with a genetic predisposition to desmosomal failure, such stretch may result in disruption of the cardiac myocytes, resulting in their death and the macroscopic, ante or post mortem, observations seen in ARVC with structural fibro-fatty changes and severely dilated, thinned-out right ventricles.

The continued hemodynamic stress may further contribute to or exacerbate cardiac arrhythmias. There are data describing the association of exercise and right ventricular dysfunction. Post exercise RV, not LV, regional wall motion abnormalities and evidence of injury have been described in the past.[5,6] These may have been precipitated by high pulmonary artery (PAP) pressures: it has been noted that prolonged exercise at high altitudes may cause PAP to reach 65mmHg.[6] In some patients who develop pulmonary edema commonly seen at high altitude, high pulmonary artery pressures have been observed to occur during exercise at low altitude and to cause right ventricular and atrial dilatation.[7,8] It is possible that the patients with ARVC who are prone to arrhythmias may also develop high pulmonary pressures during exercise, resulting in ventricular stretch with its electropathophysiological consequences and right ventricular tachycardia. Another mechanism accounting for exercise-related arrhythmia may be due to the degenerative changes of ARVC, which may result in denervation of the myocardium and subsequent autonomic nerve terminal supersensitivity with abnormal response to catecholamines, resulting in pro-arrhythmic delayed afterdepolarizations during exercise.[9]

Heidbuchel et al. recently looked at a cohort of 46 high endurance athletes and observed a high number of arrhythmic symptoms, sudden cardiac deaths, inducible ventricular tachycardia and structural cardiovascular abnormalities.[10] He also noted that most arrhythmic events occurred with mild or moderate activity and none during competitive participation. This is similar to our observation that most of the South African registry patients who experienced symptoms during exercise, were participating in non-competitive sporting activity. Most of Heidbuchel's patients met criteria for ARVC, so they termed this an "acquired right ventricular dysplasia".[10]

Patients with ARVC often receive ß-blockers for control. Most of the patients in the South African registry are on atenolol. In sport "addicted" ARVC patients, it is not uncommon to find that they refuse to cease partaking in physical exercise activity. This together with the additional non-compliance of ß-blocker therapy, due to the unacceptable chronotropic side effects in sport, may double their risk of developing arrhythmias.

At present the link between sport and ventricular involvement in a condition such as ARVC, although now shown in the experimental animal model, remains speculative in humans. International registries may help confirm the association and genetic, hemodynamic and additional animal studies may establish the pathological link. The South African ARVC registry hopes to provide some of these answers.

REFERENCES:

1. McKenna WJ, Thiene G, Nava, et al. Diagnosis of arrhythmogenic right ventricular dysplasia/cardiomyopathy. Task Force of the Working Group Myocardial and Pericardial Disease of the European Society of Cardiology and of the Scientific Council on Cardiomyopathies of the International Society and Federation of Cardiology. Br Heart J 1994;71:215-8.
2. Hamid SM, Norman M, Quirashi A, et al. Prospective evaluation of relatives for familial arrhythmogenic right ventricular cardiomyopathy/dysplasia reveals a need to broaden diagnostic criteria. J Am Coll Cardiol 2002;40:1445-50.
3. Kirchhof P, Fabritz L, Zwiener M, et al. Age- and training dependent development of arrhythmogenic right ventricular cardiomyopathy in heterozygous plakoglobin-deficient mice. Circulation 2006;114:1799-806.
4. Awad MM, Calkins H, Judge DP. Mechanisms of disease; molecular genetics of arrhythmogenic right ventricular dysplasia/cardiomyopathy. Nat Clin Pract Cardiovasc Med 2008;5:258-267.
5. Douglas PS, O'Tolle ML, Woolard J. Regional wall motion abnormalities after prolonged exercise in the normal left ventricle. Circulation 1990;82:2108-14.
6. Davila-Roman VG, Guest TM, Tuteur PG, et al. Transient right but not left ventricular dysfunction after strenuous exercise at high altitude. J Am Coll Cardiol 1997; 30:468-73.
7. Kiencke S, Bernheim A, Maggiorini M, et al. Exercise-Induced Pulmonary Artery Hypertension. A rare finding. J Am Coll Cardiol 2008;51:513-514.
8. Bossone E, Rubenfire M, Bach D, et al. Range of Triscuping regurgitation velocity at rest and during exercise in normal adult men: Implications for the diagnosis of pulmonary hypertension. J Am Coll Cardiol 1999;33:1662-1666.
9. Wichter T, Hindricks G, Lerch H, et al. Regional myocardial sympathetic dysinnervation in arrhythmogenic right ventricular cardiomyopathy. Circ 1994;89:667-683.
10. Heidbuchel H, Hoogsteen J, Fagard R, et al. High prevalence of right ventricular involvement in endurance athletes with ventricular arrhythmias. Role of an electrophysiologic study in risk stratification. Eur Heart J 2003;24:1473-80.