EDITORIAL COMMENTARY

Exercise-induced arrhythmogenic right ventricular cardiomyopathy: A clinical syndrome in motion

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Exercise-induced arrhythmogenic right ventricular cardiomyopathy (ARVC), a theoretical disease entity, has an unusual history. Lacking a diagnostic gold standard, it is a diagnosis of exclusion built upon a foundation of research compiled for ARVC.

In 2003, the first suspicion that exercise per se could cause a syndrome fulfilling 1994 ARVC criteria was described by Heidbüchel and colleagues in Belgium and the Netherlands.[1,2] In a case series of "46 high-level endurance athletes, predominantly cyclists, with complex ventricular arrhythmias," 27 (59%) met definite ARVC criteria while another 14 (30%) met some lesser criteria.[1] Genetic testing was not performed and only 1 subject had a family history of ventricular arrhythmias. The importance of risk stratification was highlighted by 9 patients who died suddenly, none of whom had an implantable cardioverter-defibrillator (ICD), over a median follow-up of 2 years. Of these, 8 (89%) died during light or moderate physical activity.

In 2021, Lie and colleagues from the "Oslo group" in Norway described 43 subjects with a history of competitive athletics for >6 consecutive years and who fulfilled 2010 ARVC criteria.[3,4] Exercise-induced arrhythmogenic cardiomyopathy was considered, given absence of family history and absence of relevant genetic mutations. In multivariable logistic regression analysis, only left ventricular (LV) mechanical dispersion was a statistically significant predictor for life-threatening arrhythmic events. In light of this finding, La Gerche suggested, "perhaps it is time that the term exercise-induced ARVC is updated to exercise-induced arrhythmogenic cardiomyopathy to better reflect its various clinical expressions."[5]

KEYWORDS Arrhythmogenic right ventricular cardiomyopathy; Electroanatomic mapping; Exercise; Magnetic resonance imaging

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In this issue of *Heart Rhythm Case Reports*, Darden and colleagues[6] report a 25-year-old man with a history of endurance exercise participation and frequent premature ventricular complexes (PVCs) who met definite diagnosis for ARVC by satisfying 1 major and 2 minor 2010 modified Task Force criteria. His primary exercise exposure was training for and participation in marathons and ultramarathons over a decade. As he was negative for significant family history and genetic screening, he was diagnosed with exercise-induced ARVC in a fashion similar to the Oslo group.[3]

This case report has several notable features. First, it illustrates the dynamic nature of exercise-induced ARVC. Second, it suggests the role of electroanatomic voltage mapping should be revisited in the high-density mapping era. Third, it suggests that a waiting period with detraining may be useful prior to primary-prophylaxis ICD consideration. Fourth, LV involvement supports moving away from the term "exercise-induced ARVC."

On baseline evaluation, features satisfying the major criterion were regional right ventricular (RV) dyskinesis of the basal to mid free wall and a ratio of RV end-diastolic volume to body surface area of 134.8 mL/m^2 on cardiac magnetic resonance imaging (MRI). Two minor criteria included a terminal activation duration of the QRS complex measured at 60 milliseconds in electrocardiogram lead V_1 in the absence of complete right bundle branch block and 807 PVCs per hour on 14-day ambulatory monitoring.

After a 6-month detraining period, the cardiac MRI abnormalities and the PVC burden improved such that they no longer met thresholds for ARVC criteria. This was accomplished by transitioning from endurance running, with an estimated metabolic equivalents (METs) of 9.8, to golf and yoga, with estimated METs of 4.8 and 2.5, respectively.[7] Thus, the patient could be considered to have "resolved exercise-induced ARVC." A compelling question becomes, "How many patients with suspected exercise-induced ARVC can achieve disease resolution with detraining?" In addition, whether disease manifestations can identify when resolution or regression is no longer possible is of interest.

Programmed electrical stimulation and voltage mapping via electrophysiology study for sudden death risk

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Table 1 2019 Heart Rhythm Society arrhythmogenic cardiomyopathy consensus statement[7] criteria for primary-prophylaxis implantable cardioverter-defibrillator consideration at baseline and after a 6-month detraining period in the patient reported by Darden and colleagues[6]

Criteria	Baseline	After detraining
Major		
Nonsustained ventricular tachycardia	No	No
Inducibility to ventricular tachycardia at electrophysiology study	No	Not assessed
Left ventricular ejection fraction ≤49%	Yes	No
Minor		
Male sex	Yes	Yes
>1000 premature ventricular contractions/24 h	No	No
Right ventricular dysfunction	Yes	No
Proband status	N/A	N/A
≥2 desmosomal variants	N/A	N/A

N/A = not applicable.

stratification were given class IIa and IIb recommendations, respectively, in the 2015 International Task Force consensus statement.[8] Voltage mapping was not recommended as a "routine diagnostic tool," as it was recognized to be "an invasive, expensive, and highly operator-dependent technique."[8] The only study cited used an older system with point-by-point acquisition such that RV voltage maps were created with a mean average ± standard deviation of 195 ± 22 points.[9] Abnormal bipolar voltage maps, but not abnormal unipolar voltage maps, were associated with major arrhythmic events on multivariable analysis.

In the 2019 Heart Rhythm Society arrhythmogenic cardiomyopathy consensus statement, VT inducibility, but not an abnormal voltage map, was listed under primary-prophylaxis ICD recommendation criteria.[7] The role of voltage mapping in the current, high-density era should be studied, as it may be faster, more affordable, and more reproducible than earlier techniques.

In the case report by Darden and colleagues, VT inducibility would have raised the recommendation for a primary-prophylaxis ICD from class IIb to IIa.[7] However, the dynamic nature of exercise-induced ARVC should also be considered, as the patient no longer met ICD recommendation after detraining (Table 1). In addition, if the diagnosis of exercise-induced ARVC excludes those with genetic causes, as the Oslo group supports, then proband status and desmosomal variants criteria would not apply.[3,7] Thus, extrapolation of these criteria to the exercise-induced ARVC population deserves scrutiny. Even those with a number of risk factors for sudden death may benefit from reevaluation after a waiting period of detraining, rather than proceeding immediately with ICD placement. A wearable cardioverter-defibrillator could offer temporary protection.

The real-life impact of detraining and ICD placement should not be underestimated. Individuals devoted to endurance athletics, many of whom are young, are likely committed for more than general health purposes. These pursuits may be intricate facets of their personal identities and social circles. The addition of an ICD on top of exercise restrictions may be psychologically challenging.[10]

The disconnect between the patient presented by Darden and colleagues and using terminology derived from the ARVC population is also highlighted by LV involvement. The only major criterion for ICD consideration in the patient was the LV ejection fraction of 49% (Table 1) on cardiac MRI, which improved to 61% after detraining.[6,7] Moreover, our review of the cine MRI videos suggests a subtle regional hypokinesis in the mid to apical lateral walls. If this were to be corroborated by review of short-axis imaging (not provided in the case report), the possibility of biventricular involvement would be raised. We agree that the current definition appears to be RV-"centric" and that the more general term of "arrhythmogenic cardiomyopathy" may be a more accurate description of the clinical phenomenon.[5]

In conclusion, using comprehensive evaluation and reporting of a single patient, Darden and colleagues compel the cardiology community to rethink the existing paradigm of exercise-induced ARVC. The time appears ripe for moving toward a set of recommendations specific to this dynamic clinical syndrome, perhaps under the name of exercise-induced arrhythmogenic cardiomyopathy.[5]

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