# Clinical overlap between healthy athletes and athletes with arrhythmogenic right ventricular cardiomyopathy

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**Introduction:** The extensive physiological cardiac remodelling that results from the haemodynamic stress of endurance exercise shares many features with the pathological manifestations of arrhythmogenic right ventricular cardiomyopathy (ARVC), giving rise to a significant diagnostic challenge for clinicians. Contemporary discriminators of disease have been derived from comparisons between healthy athletes and non-athletic ARVC patients. Differentiation between healthy and diseased athletes may be more difficult.

**Purpose:** To assess published clinical differentiators of physiological remodelling from ARVC in a cohort of endurance athletes.

**Methods:** This project utilises data from the Pro@heart consortium comprising elite endurance athletes that have received comprehensive cardiac phenotyping using cardiac magnetic resonance imaging, echocardiography, resting and ambulatory electrocardiography and cardiopulmonary exercise testing. Measures of cardiac structure and function with potential to differentiate health and disease were assessed in healthy endurance athletes without symptoms or suspicion of ARVC, endurance athletes diagnosed with ARVC (meeting ARVC task force criteria) and athletes with suspected sub-clinical ARVC (complex ventricular arrhythmias and ≥1 task force criteria). One way ANOVA assessed differences in continuous variables, while Chi Square with pair wise Z test and Bonferroni p value correction were used to test for differences in nominal data.

**Results:** Athletes with ARVC and athletes with suspected ARVC displayed more clinical indicators of ARVC compared to healthy athletes (table 1). While a greater proportion of athletes with ARVC and suspected ARVC met ≥1 and ≥3 indicators of pathology compared to healthy athletes, it was relatively common for healthy athletes to meet ≥1 criteria (53%) and ≥3 criteria (14%) (table 2). Comparison of mean values showed right ventricular ejection fraction (RVEF) and right ventricular fractional area change (RV FAC) were lower in athletes with or suspected to have ARVC compared to healthy athletes, however no significant differences in burden of ventricular premature beats (VPB) were noted (table 1). A high burden of VPBs, evidence of ventricular arrhythmia, evidence of late gadolinium enhancement (LGE), a low RVEF, and a reduced RV FAC were more prevalent in athletes with ARVC compared to healthy athletes (table 2). However, there was clinically relevant overlap in all measures between healthy and diseased athletes (table 2). Right ventricular to left ventricular volume ratio was a particularly poor discriminator of pathology (table 1 & 2).

**Conclusion:** Electrophysiological, structural and functional abnormalities are not uncommon in healthy athletes resulting in significant overlap with athletic ARVC patients. Future research is required to identify better clinical discriminators of disease, and to assess the clinical significance of abnormal measures in ostensibly healthy athletes

**Table 1: Comparison of descriptive and cardiac characteristics between healthy athletes, athletes with arrhythmogenic right ventricular cardiomyopathy and athletes with suspected arrhythmogenic right ventricular cardiomyopathy**

| | Healthy N=367 | ARVC N=7 | Suspected ARVC N=8 | *P* Value |
|---|---|---|---|---|
| **Age, years** | 42±19 | 41±12 | 44±7 | 0.69 |
| **Sex, M** | 273 (74) | 6 (86) | 6 (75) | 0.79 |
| **BMI, kg/m$^2$** | 24±3 | 23±2 | 22±3 | 0.39 |
| **Percent pred $VO_2$max[1], %** | 127±21 | 102±23 | 121±13 | <0.00* |
| **VPB/24hrs** | 3 [0, 26] | 978 [175, 4599] | 575 [42, 3433] | 0.08 |
| **RVEF, %** | 50±6 | 39±7 | 45±3 | <0.00* |
| **RV FAC, %** | 39±9 | 29±9 | 30±13 | <0.00*† |
| **RV/LV EDV ratio** | 1.14±0.12 | 1.32±0.28 | 1.21±0.10 | 0.23 |
| **Number of clinical indicators displayed** | 1±1 | 4±4 | 4±2 | 0.01*† |

[1]Friend Registry (Myers et al 2017). *Statistically significant between healthy athletes and athletes with ARVC, †Statistically significant between healthy athletes and athletes with suspected ARVC

**Table 2: Prevalence of clinical indicators of arrhythmogenic right ventricular cardiomyopathy in healthy athletes, athletes with arrhythmogenic cardiomyopathy and athletes with suspected arrhythmogenic right ventricular cardiomyopathy**

| | Healthy n=367 | ARVC n=7 | Suspected ARVC n=8 | *P* Value |
|---|---|---|---|---|
| **Electrocardiography** | | | | |
| ≥500 VPB/24h | 25 (7) n=359 | 4 (57) | 4 (50) | <0.01*† |
| ≥1000 VPB/24h | 14 (4) n=359 | 3 (43) | 2 (25) | <0.01*† |
| ≥1 VPB on resting ECG | 11 (3) n=357 | 3 (43) | 0 (0) | <0.01* |
| Ventricular arrhythmia | 28 (8) n=359 | 6 (86) | 8 (100) | <0.01*† |
| **Cardiac Imaging** | | | | |
| LGE | 98 (30) n=330 | 4 (100) n=4 | 5 (83) n=6 | <0.01*† |
| RVEF ≤45% | 68 (21) n=331 | 3 (75) n=4 | 2 (33) n=6 | 0.02* |
| RVEF ≤40% | 20 (6) n=331 | 2 (50) n=4 | 0 (0) n=6 | <0.0* |
| RV FAC ≤30% | 56 (15) n=365 | 3 (43) | 4 (50) | 0.01† |
| RV/LV EDV ratio >1.2 | 79 (24) n=329 | 2 (50) n=4 | 3 (50) n=6 | 0.17 |
| **Combined clinical indicators** | | | | |
| Athletes meeting ≥1 clinical indicator | 194 (53) | 7 (100) | 8 (100) | <0.01*† |
| Athletes meeting ≥3 clinical indicators | 53 (14) | 3 (43) | 5 (63) | <0.01*†^ |

*Statistically significant between healthy athletes and athletes with ARVC, †Statistically significant between healthy athletes and athletes with suspected ARVC, ^Statistically significant between athletes with ARVC and athletes with suspected ARVC