Serial hormones	Median (IQR); nmol/l	Variation coefficient (%), median (IQR)	p-value
Total testosterone	14.0 (8.8-21.0)	10.7 (6.3-43.9)	0.24
Estradiol	100.0 (76.8-122.3)	12.9 (4.1-56.8)	0.56
Progesterone	1.4 (1.0-2.3)	18.6 (0.1-33.2)	0.33
SHBG	38.2 (30.7-62.5)	6.5 (0.7-12.3)	0.42
DHEA-S	4.1 (2.1-7.1)	17.5 (4.9-53.0)	0.09

Table S1. Serial hormone measurements in 11 patients

P- values determined by paired Student´s t-test.

	Multivariable Model 1		Multivariable Model 2		Multivariable Model 3	
Variables	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Total testosterone, per 1nmol/l increase	1.5 (1.2-2.2)	**0.002**	1.8 (1.2-2.8)	**0.004**	1.7 (1.1-2.4)	**0.007**
Age, per 1 year increase	1.0 (0.9-1.1)	0.82				
BMI, per 1 kg/m2 increase	1.1 (0.8-1.4)	0.64				
LVEF per 1% increase			0.9 (0.7-1.1)	0.29		
RV FAC per 1 % increase			0.8 (0.7-0.9)	**0.038**		
Task Force score per 1 point increase					2.2 (1.1-4.4)	**0.038**

Table S2. Increasing serum testosterone is an independent predictor of MACE in male ARVC/D patients.

Multivariable regression models to determine odds ratios for increasing testosterone levels associated with adverse arrhythmic outcomes for the male ARVC/D population (n=39). OR=odds ratio, CI= confidence interval. P values < 0.05 were considered significant.

		Outcome		
Variables	All Patients n=15	Favourable n=8	Adverse n= 7	p-value
Age (years)	52 (45-59)	49 (42-61)	52 (48-59)	0.4
Systolic blood pressure (mmHg)	115 (106-125)	118 (108-129)	1110 (102-120)	0.28
Diastolic blood pressure (mmHg)	75 (70-78)	77 (70-80)	73 (70-75)	0.19
BMI (kg/m^2)	24 (22-26)	24 (22-28)	24 (22-26)	1.00
ARVC/D Task force score	5 (3-6)	4 (3-5)	6 (6-8)	**0.03**
LVEF, (%)	57 (37-63)	61 (52-66)	45 (35-59)	0.15
RV FAC, (%)	25 (21-41)	32 (18-43)	25 (21-28)	0.69
Physical activity				
Sedentary, n (%)	7 (47)	6 (75)	1(14)	**0.03**
Recreational sports, n (%)	8 (53)	2 (25)	6 (86)	**0.04**
hs-c TnT, (ng/l)	5 (5-10)	5 (4-5)	8 (7-10)	**0.02**
pro-BNP, (ng/l)	353 (123-1134)	205 (71-448)	986 (179-3400)	0.72
Glucose, (mmol/l)	5.0 (4.6-5.4)	4.7 (4.1-5.0)	5.1 (4.9-6.0)	0.54
Insulin, (mIU/l)	5 (4.7-14.5)	4.8 (3.8-11.2)	12.6 (4.8-31.0)	0.16
Diabetes, n (%)	4(26)	2 (25)	2 (29)	1.00
Total cholesterol, (mmol/l)	5.0 (4.4-6.1)	5.1 (4.1-6.0)	4.7 (4.4-6.1)	0.95
HDL cholesterol, (mmol(l)	1.5 (1.2-1.8)	1.5 (1.1-1.8)	1.6 (1.2-1.8)	0.54
Triglycerides, (mmol/l)	1.0 (0.8-2.1)	1.2 (1.0-2.3)	1.0 (1.0-2.5)	0.86

Table S3. Baseline clinical characteristics of female patients (n=15) and association with adverse arrhythmic outcomes

Data are presented as median (IQR); Mann-Whitney U test was used for comparison of continuous variables, and Fisher's exact test for categorical variables. P values < 0.05 were considered significant.

Supplementary methods

DNA was extracted from peripheral macrophages. First, ARVC/D associated genes were analysed. When available, a targeted clinical exome panel sequencing was performed by Next Generation sequencing with the TruSight One sequencing panel (Illumina, San Diego, CA). All variants were confirmed using Sanger sequencing. Variant prediction was done using the tools PolyPhen-2 (Harvard University, Cambridge, Massachusetts, USA), SIFT (J. Craig Venter Institute Maryland, USA), and MutationTaster (Charite Universitätsmedizin, Berlin, Germany). The following databases were used to analyze the sequences in detail: Human Gene Mutation Database (Biobase, Wolfenbuettel, Germany), 1000 Genomes Project (Cambridge, Massachusetts, USA), and Exome Aggregation Consortium browser (ExAC) (Cambridge, Massachusetts, USA). Mutations/variants were considered as pathogenic or likely pathogenic if they had a minor allele frequency below 2% and where predicted as disease associated using Polyphen-2, SIFT and Mutation Taster. We also considered pathogenic novel radical mutations and all mutations reported previously as disease causing in the HGMD Professional or/and the ARVC-Database (*26*) and/or ClinVar reports. For the titin (TTN)-gene, where several variants are of unknown significance, only radical were considered as potentially pathogenic.