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Clinical significance of electrocardiographic right ventricular hypertrophy in athletes: comparison with arrhythmogenic right ventricular cardiomyopathy and pulmonary hypertension

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Aims Pre-participation cardiovascular screening of young athletes may prevent sports-related sudden cardiac deaths. Recognition of physiological electrocardiography (ECG) changes in healthy athletes has improved the specificity of screening while maintaining sensitivity for disease. The study objective was to determine the clinical significance of electrocardiographic right ventricular hypertrophy (RVH) in athletes.

Methods and results Between 2010 and 2012, 868 subjects aged 14–35 years (68.8% male) were assessed using ECG and echocardiography (athletes; $n = 627$, sedentary controls; $n = 241$). Results were compared against patients with established right ventricular (RV) pathology (arrhythmogenic right ventricular cardiomyopathy, $n = 68$; pulmonary hypertension, $n = 30$). Sokolow-Lyon RVH (R[V1]+S[V5orV6] $>$ 1.05 mV) was more prevalent in athletes than controls (11.8 vs. 6.2%, $P = 0.017$), although RV wall thickness (RVWT) was similar (4.0 $\pm$ 1.0 vs. 3.9 $\pm$ 0.9 mm, $P = 0.18$). Athletes exhibiting electrocardiographic RVH were predominantly male (95.9%), and demonstrated similar RV dimensions and function to athletes with normal electrocardiograms (RVWT; 4.0 $\pm$ 1.1 vs. 4.0 $\pm$ 0.9 mm, $P = 0.95$, RV basal dimension; 42.7 $\pm$ 5.2 vs. 42.1 $\pm$ 5.9 mm, $P = 0.43$, RV fractional area change; 40.6 $\pm$ 7.6 vs. 42.2 $\pm$ 8.1%, $P = 0.14$). Sensitivity and specificity of Sokolow-Lyon RVH for echocardiographic RVH ($>$5 mm) were 14.3 and 88.2%, respectively. Further evaluation including cardiac magnetic resonance imaging did not diagnose right ventricular pathology in any athlete. None of the cardiomyopathic or pulmonary hypertensive patients exhibited voltage RVH without additional ECG abnormalities.

Conclusion Electrocardiographic voltage criteria for RVH are frequently fulfilled in healthy athletes without underlying RV pathology, and should not prompt further evaluation if observed in isolation. Recognition of this phenomenon should reduce the burden of investigations after pre-participation ECG screening without compromising sensitivity for disease.

Keywords Echocardiography • Electrocardiography • Exercise

Introduction

It is well established that intense physical exercise may act as a trigger for life-threatening ventricular arrhythmias in individuals harbouring electrical or structural disorders of the myocardium.[1] Observational data indicate that pre-participation screening incorporating health questionnaire, physical examination, and 12-lead electrocardiography (ECG) may reduce the incidence of sports-related sudden cardiac death.[2] The issue of screening is complicated by the fact that electrocardiographic alterations can be observed in individuals

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engaging in regular sporting activity, and may occasionally overlap with phenotypically mild cardiomyopathy.[3–5] Recognition of several training-related ECG patterns has increased the specificity of screening, without compromising sensitivity for disease.[6]

Athletic adaptation of the left side of the heart has been extensively studied, and clinical algorithms to differentiate between physiological left ventricular (LV) remodelling and hypertrophic cardiomyopathy are established in both adult and adolescent athletes.[4,5,7,8] A growing body of data indicates that the athlete's right ventricle undergoes structural and functional adaptation in synergy with the left ventricle,[9,10] and may exhibit physiological alterations that mimic those observed in conditions such as arrhythmogenic right ventricular cardiomyopathy (ARVC).[11,12] Although ECG evidence for right ventricular hypertrophy (RVH) is reported in as many as 12% of young athletes,[13] current recommendations for its interpretation differ between authorities. While European guidance advocates further investigation to exclude 'pathological right ventricular (RV) dilatation/hypertrophy',[14] recent international consensus recommendations consider the evidence for such a strategy to be lacking 'until careful studies are made of the voltage measurements in the involved leads. . .of normals and athletes'.[15] The aim of the present study was to assess the clinical significance of electrocardiographic RVH in athletes, with the aim of further refining the specificity of existing screening criteria.

Methods

Subjects

Athletes

In the UK, the charitable organization Cardiac Risk in the Young subsidizes cardiovascular evaluations for several elite sporting organizations that mandate pre-participation screening of all member athletes.[16] Between 2010 and 2012, 627 athletes competing at international (77.0%), national (9.1%), or regional level (13.9%) were recruited to the present study, and underwent assessment by health questionnaire, physical examination, ECG, and two-dimensional echocardiography. The cohort was aged between 14 and 35 years, and 438/627 (69.9%) were male. All participants provided written consent for screening and study enrolment, and ethical approval was obtained from the local Research Ethics Committee in accordance with the Declaration of Helsinki. Athletes with any previous history of cardiac or pulmonary disease, systemic hypertension, diabetes mellitus, family history of cardiomyopathy, or family history of pre-mature ($\leq$40 years) sudden cardiac death were excluded from the study. Athletes with electrocardiographic evidence of ventricular pre-excitation or complete bundle branch block were also excluded.

Non-athletic controls

Cardiac risk in the young also offers cardiovascular evaluation to any young individual (aged 14–35 years), irrespective of the athletic status, wishing to be tested for conditions pre-disposing to sudden cardiac death. The protocol comprises of a health questionnaire, physical examination, and 12-lead ECG. Non-athletic control cases were recruited for additional echocardiography if they led a sedentary lifestyle ($\leq$3 h of organized physical activity per week). Control subjects and athletes were matched for age, gender, and ethnicity. Exclusion criteria were identical to those applied in athletes. The final control cohort composed of 241 sedentary individuals, of whom 159/241 (66.0%) were male.

Pathological cohorts

Two disease groups with established RV pathology, an ARVC cohort ($n = 68$) and a pulmonary hypertensive cohort ($n = 30$), were evaluated on the basis of their propensity to cause pathological RV dilatation and/or hypertrophy as well as sports-related sudden cardiac death.[14,17] Both groups consisted of adult patients under follow-up in a UK tertiary cardiac referral centre. To simulate cases that might be detected during the screening of athletes, the pulmonary hypertensive cohort was restricted to asymptomatic, mild cases (invasively measured mean pulmonary artery pressure between 26 and 40 mmHg) that had been detected through surveillance echocardiography (congenital, thromboembolic, and connective tissue disease-related aetiologies)[18] The 2010 Modified Task Force criteria were used to define ARVC.[19] Approximately two-fifths of the ARVC cohort (39.7%) consisted of asymptomatic individuals detected through family screening. To prevent comparison with compound pathologies, exclusion criteria for the pathological cohorts included ischaemic heart disease, LV dysfunction or hypertrophy, arterial hypertension, and chronic primary lung diseases.

Twelve-lead electrocardiography

A standard 12-lead ECG was performed in the supine position using either a MAC 5000 or MAC 5500 digital resting recorder (GE Medical Systems, Milwaukee, WI, USA) as described elsewhere.[20] Measurements were made on anonymized recordings using callipers. Current international guidelines and consensus statements were used to define abnormal electrocardiograms.[14,15,17] Left ventricular hypertrophy (LVH) was defined according to the Sokolow-Lyon voltage criterion (SV1 + RV5/6 $>$ 3.5 mV). The normal frontal cardiac axis was considered to be $>-30^\circ$ but $<120^\circ$. T-wave inversion (TWI) ≥ -0.1 mV in $\geq$2 contiguous leads was considered significant. Leads V1-V4 were subclassified as anterior precordial leads. Partial right bundle branch block was defined as QRS duration $>$100 ms but $<$120 ms, with rSR′ morphology in lead V1 and qRS in V6. Right ventricular hypertrophy was defined according to several established diagnostic criteria, including the R:S ratio (V1) $>$ 1, R:S ratio (V5) $<$ 1, R:S ratio (V6) $<$ 1, R′ $>$ 1.0 mV if rSR′ in V1, and R(V1) $>$ 0.7 mV.[21] The Sokolow-Lyon voltage criterion for RVH (R-wave in lead V1 + S-wave in lead V5 or V6 $>$ 1.05 mV) was studied in detail, since it is referred to specifically in guidelines for ECG interpretation in athletes.[14,15] In addition, the Sokolow-Lyon RVH criterion in combination with right-axis deviation ($>120^\circ$) was studied, since it is cited as a potential marker of RV pathology in the most recent international consensus document relating to abnormal ECG findings in athletes (the 'Seattle Criteria').[17] The term 'isolated' is used to describe electrocardiographic anomalies observed in the absence of other ECG features considered 'uncommon and training-unrelated' in athletes.[14]

Transthoracic echocardiography

Echocardiographic examinations were performed with the subject at rest, in the left lateral decubitus position using the following commercially available ultrasound systems; Vivid-I (GE Healthcare, Milwaukee, WI, USA), CX50, or iE33 (Philips Medical, Bothel, WA, USA). A complete echocardiographic study of the left and right sides of the heart was performed according to current guidelines from the European Society of Cardiology and the American Society of Echocardiography.[22,23] Echocardiographic studies were saved to compact discs as numeric files to generate anonymity, and cardiac measurements were repeated independently by an experienced cardiologist (A.Z.) blinded to the identity of the subject. Right ventricular end-diastolic wall thickness (RVWT) was measured in the focused subcostal view at the level of the tip of the anterior tricuspid leaflet, taking care to exclude the pericardium and trabeculations from the measurement. Echocardiographic RVH was defined as

RVWT > 5 mm.[22] Right ventricular regional wall motion abnormalities were defined as akinetic, dyskinetic, or aneurysmal, in accordance with diagnostic criteria for ARVC.[19]

Further evaluation

Athletes with suspected cardiac pathology on the basis of history, physical examination, 12-lead ECG, and echocardiography were subjected to more comprehensive assessment (exercise ECG, ambulatory monitoring, signal-averaged ECG, and cardiac magnetic resonance imaging), as has been described elsewhere.[12] Specific triggers for additional evaluation included RV regional wall motion abnormalities, and TWI in ≥2 contiguous leads.[19] Athletes exhibiting substantial LV hypertrophy (males with maximal LV wall thickness >12 mm; females >11 mm) were assessed further to exclude hypertrophic cardiomyopathy.[5,24] Echocardiographic RVH (RVWT > 5 mm) was investigated further if accompanied by cardiovascular symptoms, electrocardiographic TWI, or abnormal indices of RV systolic or diastolic function (fractional area change <35%, tricuspid annular plane systolic excursion <16 cm, or early myocardial relaxation velocity [E′] <8 cm/s).[23] In the absence of prolonged longitudinal data relating to ethnic differences in athletic cardiac remodelling, identical referral criteria were applied to athletes of all ethnicities.

Statistical analysis

Values are expressed as means ± standard deviation or percentages, as appropriate. The Kolmogorov–Smirnov test was used to assess normality of distributions. Group differences were tested using the unpaired Student's *T*-test or Mann–Whitney *U* test. The χ^2 test or Fisher's exact test were used to test proportional differences between groups. Multivariable linear regression models were constructed to identify independent determinants of RVWT. Inter-observer and intra-observer reproducibility of RVWT measurements were assessed using intraclass correlation coefficient analysis and reported as: coefficient (95% confidence interval). Our findings in athletes and ARVC patients were used to generate a hypothetical athletic screening population, to test the utility of various ECG markers for the detection of ARVC. Although estimates for the prevalence of ARVC are variable, we used the commonly quoted value of 1 in 2000 of the general population.[17] Statistical analysis was performed using the SPSS software, version 20 (Chicago, IL, USA). Two-tailed *P*-values < 0.05 were considered to indicate significance throughout.

Results

Athletes and control subjects

None of the participating athletes or control subjects reported symptoms suggestive of underlying cardiovascular pathology. All subjects exhibited a blood pressure ≤140/90 mmHg. Baseline demographics, ECG, and echocardiographic data of athletes and controls are demonstrated in *Table 1*. Athletes and controls were of similar age, gender, and ethnic composition. The majority of athletes and controls (66.2%) was Caucasian; the remainder were of African or Afro-Caribbean origin. Partial right bundle branch block, T-wave inversion, and Sokolow-Lyon LVH were more common in athletes, who also revealed a more positive axis than controls. Sokolow-Lyon was the only criterion for RVH that differed significantly between athletes and controls (11.8 vs. 6.2%, $P = 0.017$). Biventricular cavity dimensions and LV mass index were greater in athletes than controls, although mean RVWT did not differ between the two groups (4.0 ± 1.0, range 2–7 mm vs. 3.9 ± 0.9, range 2–6 mm; $P = 0.18$). Athletes more often demonstrated absolute RVWT values >5 mm compared with controls (6.1 vs. 1.5%, $P = 0.026$).

Table 1 Comparison of baseline demographics, ECG, and echocardiographic data between athletes and controls

	Athletes ($n = 627$)	Controls ($n = 241$)	*P*-value
Age, years	21.5 ± 5.0	21.2 ± 6.1	0.56
Male, %	69.9	66.0	0.29
Caucasian, %	67.3	63.5	0.30
Training, h/week	19.8 ± 7.5	1.9 ± 0.7	<0.001
Heart rate, b.p.m.	60 ± 12	70 ± 13	<0.001
PR interval, ms	162 ± 27	149 ± 20	<0.001
Axis,°	60 ± 33	52 ± 32	<0.001
pRBBB, %	4.8	1.7	0.032
TWI, %	10.5	5.8	0.036
LVH (Sokolow), %	33.0	25.3	0.033
RVH (Sokolow), %	11.8	6.2	0.017
R:S(V1) >1, %	3.2	1.1	0.19
R:S(V5) < 1, %	0.8	1.1	0.36
R:S(V6) <1, %	0.5	1.7	0.12
R(V1) ≥ 0.7 mV, %	9.7	13.8	0.10
rSR′(V1) >1.0 mV, %	0.3	0	1.00
LVEDD, mm	52 ± 5	48 ± 4	<0.001
LVMI, g/m^2	113 ± 26	90 ± 21	<0.001
RVOT1, mm	32 ± 6	29 ± 5	<0.001
RVD1, mm	42 ± 6	36 ± 5	<0.001
RVFAC, %	42 ± 8	43 ± 8	0.06
RVWT, mm	4.0 ± 1.0	3.9 ± 0.9	0.18

Data are expressed as means ± SD or percentages as appropriate.
B.p.m., beats per minute; LVEDD, LV end-diastolic dimension; LVH, left ventricular hypertrophy; LVMI, LV mass index; pRBBB, partial right bundle branch block; R:S, ratio of R wave amplitude to S wave amplitude; RVD1, RV basal dimension; RVFAC, RV fractional area change; RVH, right ventricular hypertrophy; RVOT1, proximal RV outflow tract dimension in parasternal short-axis view, RVWT, RV free wall thickness; TWI, T-wave inversion.

Athletes with Sokolow-Lyon right ventricular hypertrophy vs. athletes without Sokolow-Lyon right ventricular hypertrophy

Athletes exhibiting Sokolow-Lyon RVH were almost exclusively male (95.9%). Compared with athletes that did not fulfil the criterion, those with voltage RVH were younger, demonstrated a longer mean QRS-interval, and had a greater prevalence of right-axis deviation >120° (8.1 vs. 0.2%, $P < 0.001$). There were no other significant differences between these two groups with respect to baseline demographics, ECG patterns, or any biventricular structural or functional parameters (*Table 2*). Additionally, athletes with the combination of Sokolow-Lyon RVH *and* right-axis deviation ($n = 6$) were compared with all other athletes ($n = 621$). No significant differences were observed between these two groups, although sample size is likely to have been a limiting factor (Supplementary material online, *Table S5*).

Table 2 Comparison of baseline demographics, ECG, and echocardiographic data between athletes positive vs. athletes negative for Sokolow-Lyon right ventricular hypertrophy

	Athletes: ECG + ve for RVH ($n = 74$)	Athletes: ECG –ve for RVH ($n = 553$)	*P*-value
Age, years	19.9 ± 4.4	21.7 ± 5.0	0.003
Male, %	95.9	66.4	<0.001
BSA, m^2	2.0 ± 0.2	1.9 ± 0.2	0.08
Caucasian, %	64.9	67.6	0.69
Endurance, %	66.2	66.4	1.00
Heart rate, b.p.m.	61 ± 12	60 ± 12	0.42
QRS-interval, ms	95.3 ± 10.5	92.3 ± 10.7	0.020
Axis,°	75.9 ± 46.9	57.7 ± 29.8	<0.001
RAD (>120°), %	8.1	0.2	<0.001
pRBBB, %	9.5	4.2	0.07
LVH (Sokolow), %	33.8	32.9	0.90
TWI, %	12.2	10.3	0.69
LVEDD, mm	52.1 ± 5.1	51.7 ± 4.9	0.42
LVMI, g/m^2	117 ± 28	112 ± 25	0.19
RAA, cm^2	18.7 ± 4.5	18.3 ± 4.6	0.54
RVOT1, mm	32.0 ± 5.3	31.9 ± 5.8	0.85
RVD1, mm	42.7 ± 5.2	42.1 ± 5.9	0.43
RVWT, mm	4.0 ± 1.1	4.0 ± 0.9	0.95
RVFAC, %	40.6 ± 7.6	42.2 ± 8.1	0.14
RV E′, cm/s	15.3 ± 4.3	15.1 ± 4.7	0.78
PASP, mmHg	20.1 ± 5.4	22.1 ± 5.2	0.05

Data are expressed as means ± SD or percentages as appropriate.
B.p.m., beats per minute; E′, early myocardial relaxation velocity; LVEDD, LV end-diastolic dimension; LVH, left ventricular hypertrophy; LVMI, LV mass index; PASP, pulmonary artery systolic pressure; pRBBB, partial right bundle branch block; RAA, right atrial area; RAD, right-axis deviation; RVD1, RV basal dimension; RVFAC, RV fractional area change; RVH, right ventricular hypertrophy; RVOT1, proximal RV outflow tract dimension in parasternal short-axis view, RVWT, RV free wall thickness; TWI, T-wave inversion.

Electrocardiography findings in athletes with echocardiographic right ventricular hypertrophy

The prevalence of Sokolow-Lyon RVH, either in isolation or in combination with Sokolow-Lyon LVH, was similar in athletes with echocardiographic RVH (>5 mm) and those with normal RVWT (*Table 3*). Compared with athletes with normal RVWT, athletes with echocardiographic RVH more frequently displayed isolated inferior TWI (10.7 vs. 0.2%, $P < 0.001$) and isolated anterior TWI (10.7 vs. 2.3%, $P = 0.039$).

Utility of electrocardiographic criteria for detecting echocardiographic right ventricular hypertrophy in athletes and controls

All of the electrocardiographic criteria for RVH demonstrated poor sensitivity (ranging from 0 to 17.9%) and poor positive predictive value (PPV, 0 to 10.9%) for the detection of echocardiographic RVH in athletes. Specificity and negative predictive values (NPV) of the same criteria were generally high (88.2 to 99.1%), reflecting the low prevalence of echocardiographic RVH among healthy athletes. The criterion exhibiting the greatest utility was R(V1) ≥ 0.7 mV (sensitivity 17.9%, specificity 90.5%, PPV 10.9%, and NPV 94.4%). The Sokolow-Lyon criterion was also a poor predictor of echocardiographic RVH in sedentary control subjects (sensitivity 0%; specificity 93.7%; PPV 0%; NPV 99.1%).

Table 3 Electrocardiographic findings in athletes exhibiting echocardiographic right ventricular hypertrophy

	Athletes with RVWT >5 mm	Athletes with RVWT ≤5 mm	*P*-value
Normal ECG, %	39.3	49.9	0.24
Isolated Sokolow RVH, %	10.7	4.2	0.13
Isolated Sokolow LVH, %	10.7	23.2	0.16
Isolated inferior TWI, %	10.7	0.2	<0.001
Isolated anterior TWI, %	10.7	2.3	0.039
Isolated pRBBB, %	3.6	0.9	0.27
pRBBB + LAD, %	3.6	0.5	0.17
Sokolow LVH + inferior TWI, %	3.6	0.7	0.22
Sokolow LVH + anterior TWI, %	3.6	1.6	0.40
Sokolow RVH + LVH, %	3.6	3.5	1.00

LAD, left-axis deviation; LVH, left ventricular hypertrophy; pRBBB, partial right bundle branch block; LAD, left-axis deviation; RVH, right ventricular hypertrophy; TWI, T-wave inversion.

Subsequent investigations

A total of eight athletes (1.3%) revealed minor congenital abnormalities requiring surveillance echocardiography [bicuspid aortic valve, $n = 3$ (0.5%); mitral valve prolapse, $n = 3$ (0.5%); mild pulmonary stenosis, $n = 2$ (0.3%)]. In each of these cases, the electrocardiogram was normal. A further 92 athletes (14.7%) revealed features at initial evaluation that warranted further investigation to exclude a cardiomyopathy (TWI, $n = 51$; apparent RV wall motion abnormality, $n = 8$; echocardiographic LVH, $n = 20$; TWI and echocardiographic LVH, $n = 5$, TWI and echocardiographic RVH, $n = 8$). Among these, 74/92 (80.4%) were male and 49/92 (53.3%) were black. Fourteen athletes (15.2%) declined investigation or attended other cardiac institutions for assessment. The remaining 78/92 (84.8%) were investigated comprehensively, which did not result in any athlete being diagnosed with cardiac pathology. None of the athletes exhibiting TWI in conjunction with RVWT >5 mm revealed any pathological features on further assessment. All of the athletes with apparent RV wall motion abnormalities at initial assessment demonstrated normal wall motion upon cardiac magnetic resonance imaging.

Table 4 Utility of electrocardiographic markers for the detection of arrhythmogenic right ventricular cardiomyopathy assessed by simulated screening of a hypothetical athletic population

	Prevalence (Athletes) %	Prevalence (ARVC) %	Sensitivity for ARVC %	Specificity for ARVC %	PPV for ARVC %	NPV for ARVC %
Sokolow-Lyon RVH	11.8	1.5	1.5	88.2	0.0	99.9
Any TWI	10.5	69.1	69.1	89.5	0.3	99.9
Anterior TWI	7.3	58.8	58.8	92.7	0.4	99.9
Inferior TWI	3.5	26.5	26.5	96.5	0.4	99.9
Lateral TWI	0.6	17.6	17.7	99.4	1.4	99.9
Right-axis deviation	1.1	5.9	5.9	98.9	0.3	99.9
Left-axis deviation	2.6	4.4	4.4	97.4	0.1	99.9
Right atrial enlargement	1.1	1.5	1.5	98.9	0.1	99.9
Left atrial enlargement	2.8	7.4	7.7	97.2	0.1	99.9
Q-waves	0.0	10.3	10.3	99.9	99.9	99.9
ST depression	0.1	2.9	2.9	99.9	2.1	99.9
Epsilon waves	0.0	1.5	1.5	99.9	99.9	99.9

The data are based on an estimated ARVC prevalence of 1 in 2000 of the general population.
ARVC, arrhythmogenic right ventricular cardiomyopathy; NPV, negative predictive value; PPV, positive predictive value; RVH, right ventricular hypertrophy; TWI, T-wave inversion.

Determinants of right ventricular wall thickness in athletes

Univariate predictors of increased RVWT were body surface area, male gender, LV end-diastolic dimension, LV wall thickness, and RV basal dimension. Stepwise multiple linear regression revealed LV end-diastolic dimension to be the only independent predictor of RVWT ($\beta = 0.232$, CI = 0.184–0.280, $P < 0.001$).

Reproducibility of echocardiographic right ventricular measurements

Right ventricular basal dimension measurements were highly reproducible; inter-observer coefficient = 0.87 (0.68–0.95), intra-observer coefficient = 0.93 (0.81–0.97). Right ventricular wall thickness measurements were moderately reproducible; inter-observer coefficient = 0.69 (0.23–0.88), intra-observer coefficient = 0.61 (0.24–0.83).

Electrocardiography and echo findings in arrhythmogenic right ventricular cardiomyopathy and pulmonary hypertension patients

Arrhythmogenic right ventricular cardiomyopathy cohort

Sixty-eight ARVC patients were assessed (age 39.8 ± 14.9 years, range 14–74 years, 51.5% ≤ 35 years old, 66.2% male). Among these, 39.7% were asymptomatic. A minority (16.2%) revealed abnormal physical signs (irregular pulse, 5/68 cases, murmur, 6/68 cases). The mean RVWT was 3.2 ± 1.5 mm. Sokolow-Lyon LVH was seen in 4/68 cases (5.9%). Only 1/68 cases (1.5%) exhibited Sokolow-Lyon RVH, with associated superior-axis deviation (238°) and a family history of ARVC. A further five cases (7.4%) demonstrated either R(V1) ≥ 0.7 mV, R:S(V1) > 1, or R:S(V5/V6) < 1, which were always associated with other anomalies (TWI, 4/5 cases; pathological Q-waves, 1/5 cases; atrial enlargement by voltage criteria, 1/5 cases; left-axis deviation, 1/5 cases). The simulated screening of a hypothetical athletic population, based on the prevalence of ECG anomalies in our athlete and ARVC cohorts, further demonstrates the poor utility of Sokolow-Lyon RVH for the detection of ARVC when compared with traditional markers such as T-wave inversion (*Table 4*).

Pulmonary hypertension cohort

Thirty patients with mild, asymptomatic pulmonary hypertension were assessed (age 58.1 ± 17.4 years, range 27–80 years, 20.0% ≤35 years old, 46.7% male). Abnormal physical findings were detected in 73.3% of cases (loud or abnormally split heart sounds, 18/30 cases; murmur, 8/30 cases). The mean RVWT was 6.5 ± 2.1 mm, and the mean pulmonary artery pressure was 32.7 ± 6.6 mmHg. None demonstrated Sokolow-Lyon LVH. Sokolow-Lyon RVH was observed in 10/30 cases (33.3%), and was always associated with other anomalies (TWI, 6/10 cases; superior-axis deviation, 1/10 cases; ST-depression, 3/10 cases; atrial enlargement, 2/10 cases). In total, 14/30 (46.7%) of the pulmonary hypertension cohort exhibited one or more of the RVH criteria assessed in this study, and in all cases, additional pathological ECG anomalies were present.

Discussion

Clinical significance of electrocardiographic right ventricular hypertrophy in athletes

We recently published data demonstrating frequent electrical and structural right ventricular remodelling in elite athletes, resulting in significant diagnostic overlap with ARVC.[12] The present study further exemplifies the electrical manifestations of RV adaptation that are commonly observed in such individuals. Sokolow-Lyon RVH was present in around one in eight athletes, a figure similar to that previously reported in the literature,[13,25] and twice as frequent as in sedentary controls. Electrocardiographic RVH was identified

almost exclusively in male athletes, who are known to develop more profound physiological cardiac adaptations than their female counterparts.[3] Similar to the relationship between voltage LVH and LV dimensions, all voltage-based criteria for RVH correlated poorly with RV dimensions. Of all the criteria for RVH, only Sokolow-Lyon, which is particularly dependant on QRS amplitudes, was more common in athletes than in controls. These findings are likely to reflect the influence of factors such as chest wall morphology and body habitus on the magnitude of QRS voltages.[21] Importantly, electrocardiographic RVH in isolation was not associated with cardiac pathology in asymptomatic athletes. On the basis of these considerations, it would seem reasonable to conclude that isolated voltage RVH is representative of the normal spectrum of physiological cardiac adaptations resulting from regular exercise training.

Utility of right ventricular hypertrophy voltage criteria in arrhythmogenic right ventricular cardiomyopathy and pulmonary hypertension

The ECG and echocardiographic findings in the ARVC and pulmonary hypertension cohorts provide insight into the combinations of anomalies that are truly indicative of underlying RV pathology. Voltage RVH was rarely observed in the ARVC cohort, while it was a common finding in pulmonary hypertension. However, in all patients with RV disease, voltage RVH was associated with other pathological ECG changes or physical findings that would have warranted echocardiographic assessment in their own right. Consequently, none of the ARVC or pulmonary hypertension cases would have escaped detection on the basis of a decision not to subject individuals exhibiting isolated voltage RVH to echocardiography. It is also noteworthy that the magnitude of echocardiographic RVH in athletes participating in this study was mild; only 0.9% revealed an RVWT in excess of 6 mm, while none exceeded 7 mm. In contrast, traditional electrocardiographic criteria for RVH have been derived from studies of patients with advanced cardiac disease. By way of example, most of the criteria assessed in this study, including the Sokolow-Lyon criterion, R(V1) $\geq$ 0.7 mV, R:S(V1) $>$ 1, and R:S(V5/6) $<$ 1, were derived from a study of 60 patients, of whom 73% suffered from congenital heart disease, with RVWT often confirmed during surgical or autopsy examination.[26] In addition, 40% of subjects in the aforementioned study were $\leq$5 years old, and the majority demonstrated associated axis deviation and/or T-wave inversions. The results of the present study therefore

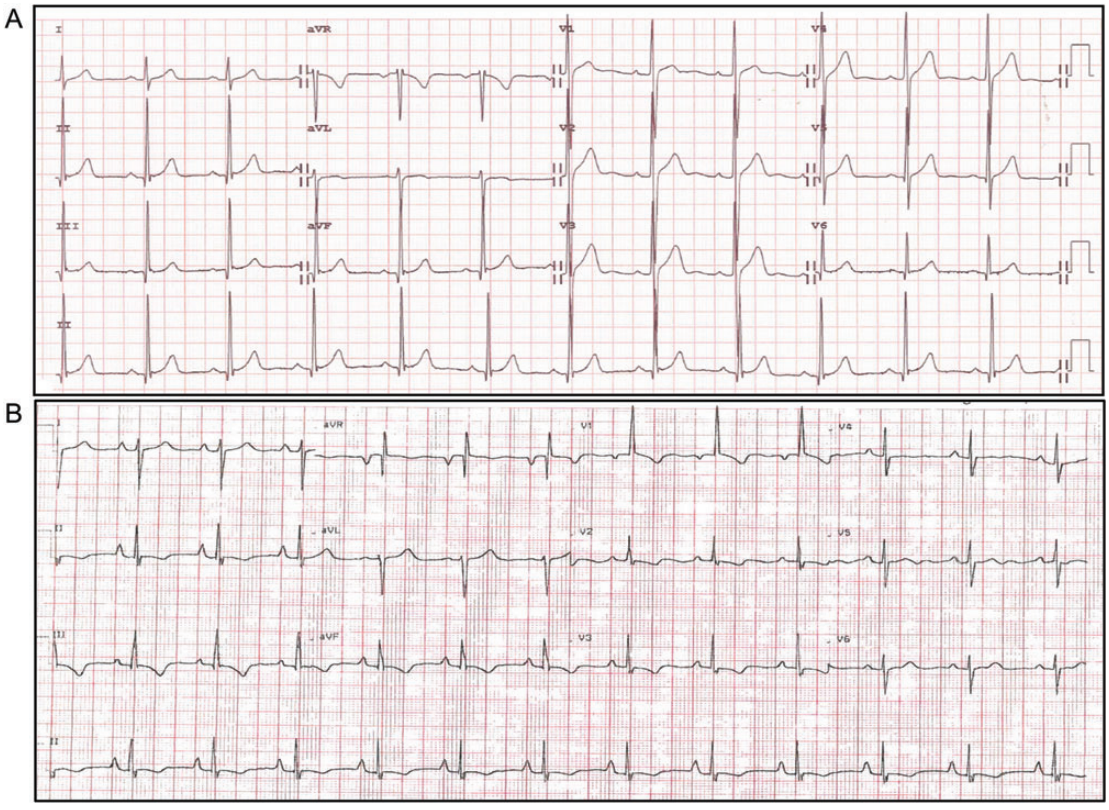

Figure 1 Electrocardiographic right ventricular hypertrophy. (*A*) 12-lead electrocardiogram of a 16-year-old male soccer player, demonstrating right ventricular hypertrophy by the Sokolow-Lyon voltage criterion (RV1+SV5/6 $>$ 1.05 mV) There is associated Sokolow-Lyon left ventricular hypertrophy (SV1+RV5/6 $>$ 3.5 mV). (*B*) 12-lead electrocardiogram of a 16-year-old female with pulmonary hypertension secondary to a ventricular septal defect. Right ventricular hypertrophy is evident by multiple criteria (Sokolow-Lyon, R[V1] $>$ 0.7 mV, R:S[V1] $>$ 1). There is associated right-axis deviation $>$120°, right atrial enlargement, and widespread ST-segment/T-wave abnormalities.

underscore the limitations of extrapolating clinically derived data to asymptomatic, low-risk groups such as young athletes.

Clinical implications

Benign vs. pathological electrocardiographic patterns

In asymptomatic young athletes, RVH by voltage criteria appears to be a benign phenomenon that is almost exclusively observed in males, and which fails to discriminate between physiology and disease. In contrast, the co-existence of pathological Q-waves, T-wave inversion, axis deviation, ST-segment depression, or atrial enlargement by voltage criteria demonstrate much greater accuracy for the detection of cardiac pathology (*Figure 1*). Voltage LVH, which is commonly identified in athletes, was extremely rare in the pathological cohorts assessed in this study, and may therefore serve as an additional discriminator between physiological cardiac remodelling and right heart disease. It is also of interest that athletes with an RVWT >5 mm were more likely to exhibit TWI in the anterior or inferior precordial leads compared with athletes with normal RVWT. Since none of the athletes was found to have an underlying pathological substrate on further assessment, it is tempting to speculate that the observed TWI may be an electrical manifestation of a mildly thickened RV wall. However, since increased RVWT was associated with confounding factors such as increased LV end-diastolic dimension and LV wall thickness, the data are insufficient to support a definitive explanation for this observation based on our findings alone.

Implications for pre-participation screening recommendations

Current European Society of Cardiology guidelines recommend that Sokolow-Lyon RVH should prompt further assessment for 'pathological RV dilatation/hypertrophy' in young athletes.[14] The results of the present study indicate that such a strategy would be associated with an unacceptably high rate of false positive screening outcomes. In contrast, our data provide support for international consensus guidelines which state that 'voltage-only criteria for RVH are. . .not applicable to young athletes. . .additional findings such as right atrial abnormalities, T-wave inversion, and/or right-axis deviation are necessary to elicit further evaluation . . . .'[15] The most recently published recommendations for ECG interpretation in young athletes, from an expert consensus panel convened in Seattle, suggest that Sokolow-Lyon RVH should be accompanied by right-axis deviation (>120°) before further investigation is initiated.[17] It is noteworthy that in the present study, athletes with Sokolow-Lyon RVH were some 40-fold more likely to exhibit concomitant right-axis deviation (8.1 vs. 0.2%) compared with athletes without Sokolow-Lyon RVH. The combination of these ECG findings may therefore also represent a benign manifestation of factors such as a slender body habitus. In the view of these considerations, we would suggest that athletes demonstrating this particular combination should not be subjected to further assessment in the absence of adverse symptoms, physical findings, or family history.

Study limitations

We acknowledge the limitations of reproducibly quantifying the thin, heterogeneous RV wall using a single acquisition in one echocardiographic imaging plane. The study objective was to provide practical guidance for physicians involved in the screening of athletes, during which this imaging modality is the immediately accessible tool. However, even in athletes who underwent detailed additional evaluation, voltage RVH was not found to indicate any generalized pathology. The relative rarity of ARVC and pulmonary hypertension in youth limited the recruitment of age-matched pathological cohorts. Nevertheless, isolated voltage RVH was not observed in any patient, including those ≤35 years of age. The incomplete investigation of a minority of athletes reflects difficulties in coordinating a nationwide screening service; young athletes are often reluctant to undergo the evaluation of minor anomalies which might result in exclusion from future sports participation. The self-referral of sedentary controls is a potential source of selection bias, although we were meticulous in excluding those with medical comorbidities or adverse family history, and none reported cardiovascular symptoms. Finally, although the cross-sectional study design precludes the categorical exclusion of future RV pathology, the high prevalence of voltage RVH in asymptomatic athletes is in favour of physiological remodelling.

Conclusions

Electrocardiographic voltage criteria for RVH are frequently fulfilled in healthy young athletes, and appear to be part of the spectrum of physiological adaptations manifested in the 'athlete's heart'. Voltage RVH should not prompt further evaluation for cardiac pathology if observed in isolation. Recognition of this phenomenon has the potential to reduce the burden of additional investigations after pre-participation ECG screening without compromising sensitivity for disease.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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