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The early repolarization pattern: Echocardiographic characteristics in elite athletes

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Abstract

Background: The electrocardiographic early repolarization (ER) pattern is associated with idiopathic ventricular fibrillation and increased long-term cardiovascular mortality. Whether structural cardiac aberrations influence the phenotype is unclear. Since ER is particularly common in athletes, we evaluated its prevalence and investigated predisposing echocardiographic characteristics and cardiopulmonary exercise capacity in a cohort of elite athletes.

Methods: A total of 623 elite athletes (age 21 ± 5 years) were examined during annual preparticipation screening from 2006 until 2012 including electrocardiography, echocardiography, and exercise testing. ECGs were analyzed with focus on ER. All athletes participated in a clinical follow-up.

Results: The prevalence of ER was 17% (108/623). ER-positive athletes were predominantly male (71%, 77/108), showed a lower heart rate (57.1 ± 9.3 bpm versus 60.0 ± 11.2 bpm; $p = 0.015$) and a higher lean body mass compared to ER-negative participants ($88.1\% \pm 5.6\%$ versus $86.5\% \pm 6.3\%$; $p = 0.015$). Echocardiographic measurements and cardiopulmonary exercise capacity in male and female athletes with and without ER largely showed similar results. Only the notching ER subtype ($n = 15$) was associated with an increased left atrial diameter (OR 7.01, 95%CI 1.65–29.83; $p = 0.008$), a higher left ventricular mass (OR 1.02, 95%CI 1.00–1.03; $p = 0.038$) and larger relative heart volume (OR 1.01, 95%CI 1.00–1.01; $p = 0.01$). During a follow-up of 7.4 ± 1.5 years, no severe cardiovascular event occurred in the study sample.

Conclusions: In elite athletes presence of ER is not associated with distinct alterations in echocardiography and cardiopulmonary exercise. Athletes presenting with ER are rather male, lean with a low heart rate.

KEYWORDS

early Repolarization, echocardiography, electrocardiography, exercise, sports

1 | INTRODUCTION

The electrocardiographic pattern of early repolarization (ER) has been known for decades and was considered a benign normal variant of the surface electrocardiogram (ECG) (Grant, Estes, & Doyle, 1951; Wasserburger & Alt, 1961). However, individual case reports described ECG changes at the QRS-ST junction in young men with idiopathic ventricular fibrillation (Kalla, Yan, & Marinchak, 2000; Shinohara, Takahashi, Saikawa, & Yoshimatsu, 2006) and case-control studies reported an increased prevalence of ER in patients with a history of sudden cardiac arrest (Haissaguerre et al., 2008; Rosso et al., 2008). Subsequently, large population-based studies found an association of the ER pattern with increased risk of death from cardiac causes and all-cause mortality (Sinner et al., 2010; Tikkanen et al., 2009). Since then, the previously accepted view of ER as a benign ECG variant has been questioned.

The prevalence of ER varies between 1%–13% in the general population (Klatsky, Oehm, Cooper, Udaltsova, & Armstrong, 2003; Sinner et al., 2010; Tikkanen et al., 2009) but reaches up to 44% in young, trained athletes (Tikkanen et al., 2011). Furthermore, competitive athletes have a 2.8-fold increased risk for sudden cardiac death (SCD; Corrado, Basso, Rizzoli, Schiavon, & Thiene, 2003). Fortunately, these are rare but devastating events, with more than half being attributable to cardiac causes (Maron, Doerer, Haas, Tierney, & Mueller, 2009). However, a definite cardiovascular event cannot be confirmed in one-third of cases and an arrhythmogenic origin is most likely (Maron et al., 2009). Mechanisms by which ER confers the risk for malignant tachyarrhythmias are largely unknown, and it is unclear whether the presence of ER reflects a hazardous condition per se, or whether it only acts in combination with additional triggers (Rosso, Adler, Halkin, & Viskin, 2011).

Today, several potential high-risk subphenotypes of ER have been established including ER in the inferior leads, a high amplitude of ER (>2 mV), a notching morphology or a horizontal/descending ST segment (Cheng et al., 2016; Juntila et al., 2014; Sinner et al., 2010; Tikkanen et al., 2011). The presence of ECG variants like ER in apparently healthy, highly trained athletes remains challenging for physicians and previous work on this topic has mainly dealt with physically active amateurs or competitive collegiate athletes (Noseworthy et al., 2011), with only little data on top-level athletes (Quattrini et al., 2014). Therefore, in the present study, we investigated a large sample of exclusively highly trained elite athletes to analyze the ER pattern with respect to structural and functional echocardiographic alterations, differences in exercise tolerance, and predominance of a specific type of physical activity. Moreover, we sought to elucidate whether echocardiographic measurements in high-risk subtypes of ER can help to discriminate between benign and malignant forms of ER.

2 | METHODS

2.1 | Study sample

Participants were examined in the outpatient clinic of the Department of Prevention and Sports Medicine, Technical

University Munich, Germany. Here, elite athletes of a variety of disciplines undergo annual preparticipation screening. Participants were selected according to their status as members of national or top-level state teams. Many of those belong to the world class of their disciplines including several Olympic and World Championship medalists. Furthermore, all athletes were ≥ 16 years of age and had a complete examination including physical examination, electrocardiography, echocardiography, exercise testing (treadmill $n = 352$, bicycle $n = 271$), standardized interview, and clinical follow-up. Individuals with known cardiovascular diseases like hypertrophic or dilated cardiomyopathy, relevant valve disease and other conditions that preclude from participation on competitive sports according to the international recommendations for competitive athletes were excluded from the analysis (Drezner et al., 2017; Maron, Zipes, & Kovacs, 2015). In addition, the following ECG exclusion criteria were defined to allow unambiguous assessment of the ER pattern: QRS width >120 ms ($n = 11$), presence of pacemaker ($n = 0$), and irregular heart rhythms, for example, atrial fibrillation ($n = 0$).

Written informed consent was obtained from all subjects (parents or guardians gave written informed consent for minors), and a local ethical committee approved the analysis of the anonymized clinical data. The investigation conforms to the principles outlined in the Declaration of Helsinki.

2.2 | Anthropometric and echocardiographic measurements

Study design and methodological aspects of data collection have been described in detail elsewhere (Pressler et al., 2012). Height and body weight were assessed according to standard techniques and body surface area was calculated using the DuBois formula. Lean body mass was calculated using body weight and total body fat, which was determined using the skinfold thickness model by Jackson and Pollock (1982). In all athletes, two-dimensional echocardiography was performed by experienced physicians according to current guidelines (Lang et al., 2015). Systolic function was measured using left ventricular fractional shortening (FS). Diastolic function was assessed using pulse-wave Doppler profiles across the mitral valve leaflets and tissue Doppler velocities of the septal and lateral mitral valve annulus. Left ventricular mass (LVM) was calculated using the formula by Devereux et al. (1986) and indexed to body surface area (LVM_{BSA}) and height (LVM_{height} ; Pressler et al., 2012). Relative wall thickness was calculated as $2 \times$ posterior wall thickness at end-diastole/left ventricular end-diastolic dimension. Left ventricular hypertrophy was defined as $LVM_{BSA} > 115 \text{ g/m}^2$ in men and $> 95 \text{ g/m}^2$ in women (Finocchiaro et al., 2017; Lang et al., 2006). An abnormal relative wall thickness was defined as > 0.42 (Lang et al., 2015, 2006). The heart volume of each athlete was calculated according to the formula by Dickhuth, Nause, Staiger, Bonzel, and Keul (1983) and is also provided as relative heart volume in ml per kg bodyweight.

2.3 | ECG recording and definition of ER

At baseline, study participants received 12-lead resting ECGs (Custo ECG system, Ottobrunn, Germany) recorded at a paper speed of 50 mm/s after ten minutes rest in a supine position. Routine ECG parameters were obtained from automated measurements. ER was assessed retrospectively according to the definition by Haissaguerre et al. (2008) and Macfarlane et al. (2015). In brief, ER was defined as J-point elevation above the level of QRS onset of ≥ 0.1 mV in ≥ 2 corresponding leads. Leads V1 to V3 were not interpreted to avoid confusion with the original ECG phenotype of Brugada syndrome as a right bundle branch block configuration with persistent ST-segment elevation (Brugada & Brugada, 1992). Two trained cardiologists, blinded to clinical data, independently analyzed all ECGs for J-point elevation. ECGs with ER were reevaluated by a third blinded cardiologist and final decision on ER status was achieved by consensus. In the presence of ER, region, either inferior (leads II, III, aVF), antero-lateral (leads I, aVL, V₄-V₆), or both, and the amplitude of J-point elevation was recorded. The ST segment after the J-point was analyzed according to Tikkanen et al. (2011) as either concave/rapidly ascending (>0.1 mV elevation 100 ms after J-point peak or persistently elevated ST segment >0.1 mV) or horizontal/descending (≤ 0.1 mV elevation within 100 ms after J-point peak) (Macfarlane et al., 2015; Tikkanen et al., 2011). High-risk subtypes of ER were defined as previously described

including inferior region, amplitude >2 mV, notching morphology, and horizontal/descending ST segment (Cheng et al., 2016; Junttila et al., 2014; Sinner et al., 2010; Tikkanen et al., 2011).

2.4 | Statistical analysis

Means or proportions of baseline demographic and clinical characteristics were compared using Student *t* test, Mann-Whitney *U* test, or Fisher's exact test and are expressed as means or proportions as appropriate. Trend testing for a linear association was performed using the Chi-Square test. In age- and sex-adjusted logistic regression models, continuous variables were individually tested for their associations with ER. For each continuous variable in the model, odds ratios (OR) were calculated for an increase of 1 unit of the value. For all analyses a *p*-value <0.05 was considered statistically significant. All statistical evaluations were performed using the IBM SPSS Statistics software package (Version 21, IBM Corp).

3 | RESULTS

3.1 | Baseline characteristics and prevalence of ER

Clinical characteristics of the study sample are depicted in Table 1. The overall prevalence of ER was 17.3% (108/623) with significantly

TABLE 1 Baseline characteristics of the study population

	All (n = 623)	ER + (n = 108)	ER- (n = 515)	p-Value
Anthropometry				
Age (years)	21.0 $\pm$ 4.9	21.4 $\pm$ 5.2	20.9 $\pm$ 4.8	0.402
Men, n (%)	378 (60.7)	77 (71.3)	301 (58.4)	0.013
Height (m)	1.76 $\pm$ 0.1	1.76 $\pm$ 0.1	1.76 $\pm$ 0.1	0.896
Weight (kg)	72.8 $\pm$ 13.2	72.6 $\pm$ 11.5	72.9 $\pm$ 13.6	0.820
Body mass index (kg/m ²)	23.3 $\pm$ 2.9	23.2 $\pm$ 2.4	23.3 $\pm$ 3.0	0.745
Lean body mass (kg)	63.2 $\pm$ 12.3	63.9 $\pm$ 10.9	63.0 $\pm$ 12.6	0.499
Lean body mass (% of weight)	86.7 $\pm$ 6.2	88.1 $\pm$ 5.6	86.5 $\pm$ 6.3	0.015
BSA (m ²)	1.88 $\pm$ 0.2	1.88 $\pm$ 0.2	1.89 $\pm$ 0.2	0.952
Systolic blood pressure (mmHg)	119.9 $\pm$ 12.1	121.3 $\pm$ 11.9	119.6 $\pm$ 12.1	0.180
Diastolic blood pressure (mmHg)	75.0 $\pm$ 7.8	74.7 $\pm$ 7.5	75.1 $\pm$ 7.9	0.635
ECG characteristics				
Heart rate (bpm)	59.5 $\pm$ 10.9	57.1 $\pm$ 9.3	60.0 $\pm$ 11.2	0.015
Heart rate ≤ 59 (bpm)	352 (56.5)	73 (67.6)	279 (54.1)	0.011
QRS duration (ms)	98.8 $\pm$ 9.3	99.5 $\pm$ 8.0	98.7 $\pm$ 9.5	0.370
QTc (ms)	413.5 $\pm$ 25.7	407.6 $\pm$ 22.0	414.8 $\pm$ 26.3	0.009
SVES, n (%)	23 (3.7)	3 (2.8)	20 (3.9)	0.781
VES, n (%)	9 (1.4)	1 (1.0)	8 (1.6)	1.000

Note. Continuous variables are expressed as mean $\pm$ standard deviation, dichotomous data as n (%). BSA: body surface area; QTc interval was calculated using Bazett formula; SVES: supraventricular extrasystole during rhythm strip; VES: ventricular extrasystole during rhythm strip.

TABLE 2 Prevalence of ER and ER subphenotypes

	All (n = 108)	Men (n = 77)	Women (n = 31)	p-Value
Region				
Inferior leads, n (%)	30 (27.8)	23 (29.9)	7 (22.6)	0.487
Antero-lateral leads, n (%)	20 (18.5)	13 (16.9)	7 (22.6)	0.585
Both regions, n (%)	58 (53.7)	41 (53.2)	17 (54.8)	1.000
Morphology				
Notching morphology, n (%)	15 (13.9)	11 (14.3)	4 (12.9)	1.000
Slurring morphology, n (%)	66 (61.1)	45 (58.4)	21 (67.7)	0.393
Both morphologies, n (%)	27 (25.0)	21 (27.3)	6 (19.4)	0.468
ST Segment				
Rapidly ascending, n (%)	54 (50)	42 (54.6)	12 (38.7)	0.201
Horizontal or descending, n (%)	54 (50)	35 (45.5)	19 (61.3)	0.201
Amplitude				
≤2 mV, n (%)	95 (88.0)	68 (88.3)	27 (87.1)	1.000
>2 mV, n (%)	13 (12.0)	9 (11.7)	4 (12.9)	1.000

Note. Data are given as n (%).

mV: millivolts

more male than female athletes presenting ER (77/108, 71.3% vs. 31/108, 28.7%; $p = 0.013$). Age, height, and weight did not differ between ER-positive (+) and ER-negative (-) athletes. ER+ athletes had a different body composition with a higher proportion of lean body mass in comparison to ER- participants ($88.1\% \pm 5.6\%$ vs. $86.5\% \pm 6.3\%$; $p = 0.015$). Furthermore, ER+ athletes showed a significantly lower heart rate compared to ER- study participants (57.1 ± 9.3 bpm vs. 60.0 ± 11.2 bpm; $p = 0.015$). In this regard, 67.6% of ER+ athletes (73/108) had a resting heart rate of 59 bpm or lower ($p = 0.011$ for comparison with ER- athletes), whereas the QTc interval was shorter in ER+ athletes compared to ER- participants (407.6 ± 22.0 ms vs. 414.8 ± 26.3 ms; $p = 0.009$). The most common ER phenotype was present in both leads (inferior and antero-lateral leads) (58/108, 53.7%) with a slurring morphology (66/108, 61.1%). The ST segment was likewise ascending or horizontally descending (54/108, 50%) and most athletes showed an amplitude of the J-point of ≤ 20 mV (95/108, 88.0%). There were no differences in the ER subphenotypes between men and women (Table 2). Examples of the different ER subphenotypes are displayed in Figure 1.

3.2 | Association of ER with type of training

Overall, athletes participated in 41 sport disciplines that are listed in detail in the Supplemental Table 1. Sport disciplines were further divided into dynamic or static physical activity according to the classification by Mitchell (Mitchell, Haskell, Snell, & Van Camp, 2005). The prevalence of ER in each category is displayed in Figure 2. There was no association of ER with a particular sport category ($p = 0.160$). However, there was a trend toward a higher prevalence of ER from low to high dynamic sport disciplines ($p = 0.074$).

3.3 | ER and echocardiographic measurements

The comparison of structural and functional echocardiographic measurements between ER+ and ER- individuals according to sex is displayed in Table 3. Overall, there were only minor differences between ER+ and ER- athletes. In men, ER+ athletes showed a higher relative heart volume than ER- athletes (12.3 ± 1.8 vs. 11.6 ± 2.0 ml/kg body weight; $p = 0.008$). In women, the ER+ group exhibited a thicker left ventricular posterior wall compared to ER- women (0.9 ± 1.0 cm vs. 0.8 ± 0.1 cm; $p = 0.025$). However, all other echocardiographic parameters including left atrial diameter, left ventricular mass, and systolic or diastolic function did not differ between ER+ and ER- male and female athletes. Comparison of left ventricular geometry between ER+ and ER- athletes is shown in Figure 3. Most athletes showed a normal left ventricular geometry, and there were no differences in the distribution of the four categories of left ventricular geometry between ER+ and ER- individuals ($p = 0.756$).

Logistic regression analyses were performed to identify echocardiographic parameters associated with high-risk ER subtypes. The only subtype that showed significant echocardiographic changes after adjusting for age and sex was the notching ER pattern ($n = 15$). Notching was associated with an increased left atrial diameter (OR 7.01 95% CI 1.65–29.83; $p = 0.008$), a higher left ventricular mass (OR 1.033, 95% CI 1.004–1.062; $p = 0.026$) and an increased relative heart volume (OR 1.01, 95% CI 1.00–1.01; $p = 0.01$) (Table 4).

3.4 | ER and exercise testing

Analysis of exercise testing either using leg cycling ($n = 271$) or a treadmill test ($n = 352$) did not show any significant difference between ER+ and ER- athletes for several variables of maximal cardio-pulmonary capacity (Table 2).

FIGURE 1 Representative examples of the ER pattern in the study sample. (a) Notching morphology of the J-point in the (antero)-lateral leads with an ascending ST segment. (b) Slurring type of ER in the inferior leads with a horizontal/descending ST segment

3.5 | ER and clinical outcome

All athletes participated in a clinical follow-up. The longest follow-up was 11.7 years and the shortest follow-up time was 5.6 years. The mean follow-up duration of athletes was 7.4 ± 1.5 years. During the follow-up time, no event of unexplained syncope or SCD was recorded.

4 | DISCUSSION

Since the first description of the ER phenotype in 1951 (Grant et al., 1951), its definition has been modulated and sharpened and was recently summarized in a consensus paper (Macfarlane et al., 2015). However, the classification of ER as a benign or a potentially harmful ECG pattern is controversial and has been under debate since the first reports of ER being associated with ventricular fibrillation and SCD (Haissaguerre et al., 2008; Rosso et al., 2008). Recently, a large meta-analysis of patients with known structural heart disease linked the ER pattern to a higher rate of ventricular arrhythmias and SCD (Cheng et al., 2017). In athletes, regular moderate-intense physical training is known to induce structural changes in the heart mostly without pathological significance (Sharma, Merghani, & Mont, 2015). Therefore, in the present study, we analyzed the ER pattern and its association with structural and functional cardiac alterations in more than 600 healthy elite athletes without any relevant cardiovascular disease prior to inclusion. Our analyses demonstrate that although the ER pattern showed a high prevalence in this cohort, the

FIGURE 2 Sport disciplines were classified according to the classification by Mitchell et al. (2005). There was a trend toward an increase in ER prevalence from low to high dynamic sport categories

ER phenotype was not invariably associated with echocardiographic changes or a distinct pattern of cardiopulmonary performance. Although there was no single sport discipline for which ER is particularly common, we could show that ER was rather associated with dynamic than static sport disciplines. There were no differences in outcome since no event of SCD or unexplained syncope were recorded within the follow-up.

The prevalence of ER in our study cohort was 17%, which is in accordance with previous studies showing a similar prevalence of 14%–32% in trained athletes. (Quattrini et al., 2014) Interestingly, a longitudinal study of athletes showed that after retirement from training the ECG phenotype only persists in 53.4% of athletes

(Serra-Grima et al., 2015). Thus, the ER pattern in athletes could reflect structural changes of the left ventricle in times of intense exercise. After training is stopped structural alterations regress and the ER phenotype may dissolve. Furthermore, a previous analysis of elite athletes by Quattrini and colleagues linked the ER pattern with an increased left ventricular mass (Quattrini et al., 2014). However, in this study sex differences were not considered, although 75% of ER+ athletes were male. We assume that this is the main reason why we were not able to reproduce this finding in our large sample of elite athletes. In our study, prevalence of ER was also significantly higher in male athletes (71%) with clearly higher left ventricular mass than in female athletes. Sex-stratified analyses did not show differences

TABLE 3 Echocardiographic characteristics of the study population

	Male (n = 378)			Female (n = 245)		
	ER positive (n = 77)	ER negative (n = 301)	p-Value	ER positive (n = 31)	ER negative (n = 214)	p-Value
Echocardiographic characteristics						
Left atrial diameter (mm)	35.3 ± 4.0	34.9 ± 3.9	0.424	32.6 ± 3.3	31.5 ± 3.9	0.150
FS (%)	35.7 ± 5.8	35.7 ± 5.9	0.980	36.6 ± 6.1	37.3 ± 5.8	0.554
Aortic root diameter (cm)	2.9 ± 0.3	3.0 ± 0.3	0.142	2.6 ± 0.3	2.6 ± 0.3	0.907
IVSD (cm)	1.0 ± 0.1	1.0 ± 0.1	0.332	0.9 ± 0.1	0.9 ± 0.1	0.891
LVPWd (cm)	1.0 ± 0.1	1.0 ± 0.1	0.353	0.9 ± 0.1	0.8 ± 0.1	0.025
LV end-diastolic diameter (cm)	5.2 ± 0.4	5.2 ± 0.4	0.869	4.8 ± 0.4	4.7 ± 0.4	0.272
LV end-systolic diameter (cm)	3.4 ± 0.4	3.4 ± 0.4	0.865	3.1 ± 0.4	3.0 ± 0.4	0.166
E/E' lateral	5.0 ± 1.1	4.9 ± 1.2	0.701	5.5 ± 1.0	5.2 ± 1.2	0.283
E/E' medial	6.9 ± 1.7	7.0 ± 1.7	0.624	7.6 ± 1.5	7.3 ± 1.6	0.477
E/A	2.1 ± 0.6	2.1 ± 0.8	0.815	2.4 ± 1.0	2.3 ± 0.8	0.540
Deceleration time (ms)	213 ± 49	204 ± 52	0.211	216 ± 55	208 ± 52	0.453
LV mass (g)	192.3 ± 40.2	195.7 ± 40.0	0.503	145.1 ± 35.3	134.8 ± 30.3	0.085
LV mass/BSA (g/m ²)	98.9 ± 18.7	98.3 ± 18.7	0.794	83.0 ± 17.7	77.7 ± 16.9	0.107
LV mass/height (g/m)	107.1 ± 21.4	107.8 ± 21.4	0.794	85.5 ± 19.7	79.6 ± 17.6	0.087
Relative wall thickness	0.37 ± 0.05	0.38 ± 0.06	0.292	0.37 ± 0.06	0.36 ± 0.06	0.184
Relative heart volume ml/kg	12.26 ± 1.77	11.60 ± 1.98	0.008	11.19 ± 1.38	10.79 ± 1.81	0.243
Exercise testing						
Leg cycling, n (%)	35 (45.5)	130 (43.2)	0.797	15 (48.4)	91 (42.5)	0.565
Treadmill, n (%)	42 (54.5)	171 (56.8)	0.797	16 (51.6)	123 (57.5)	0.565
METs	15.6 ± 2.7	15.5 ± 2.8	0.759	13.8 ± 2.1	14.0 ± 2.1	0.488
Heart rate peak (bpm)	186.3 ± 13.6	186.9 ± 14.1	0.718	186.5 ± 10.0	190.0 ± 11.4	0.109
VO ₂ peak (ml kg ⁻¹ min ⁻¹)	54.6 ± 9.5	54.2 ± 9.7	0.759	48.2 ± 7.3	49.1 ± 7.3	0.488
P _{peak} adjust kg (W)	3.8 ± 0.7	3.8 ± 0.7	0.448	3.3 ± 0.5	3.4 ± 0.6	0.639

Note. Continuous variables are expressed as mean ± standard deviation, dichotomous data as n (%).

BSA: body surface area; FS: Fractional shortening; IVSD: Interventricular septum thickness at end-diastole; LBM: lean body mass; LV: left ventricular; LVPWd: Left ventricular posterior wall thickness at end-diastole; METs: estimated metabolic equivalents of task; P_{peak}: power at peak effort; kg: kilogram bodyweight; VO₂ peak: oxygen uptake at peak effort.

in left ventricular mass or diameters between ER+ and ER- athletes. Hence, this is the first report examining ER and echocardiographic metrics and function accounting for these gender differences. In male athletes, ER was only associated with one parameter namely an increased relative heart volume. This suggests that structural changes may not be the only cause for the occurrence of ER in athletes.

A different hypothesis for the high prevalence of ER in trained athletes could be a training-induced increase in vagal activity which in turn promotes the presence of the ER pattern. This theory is supported by the significantly lower heart rate in ER+ individuals and a significantly higher proportion of athletes with sinus bradycardia (<60 bpm) in our cohort, which is a well-established risk factor for the presence of ER (Olson, Viera, Soliman, Crow, & Rosamond, 2011; Tikkanen et al., 2009). Furthermore, in individuals without structural heart disease, the ER pattern was independently associated with

an increased vagal activity and this was likewise linked to a higher amplitude of ER (Baek et al., 2015). Sinus bradycardia is mainly present in highly trained endurance athletes (Brosnan et al., 2014) who also usually demonstrate lower body fat (Pressler et al., 2012). In our study, ER+ athletes also showed a body composition with less body fat and a higher percentage of lean body mass. Furthermore, we were the first to show that there is a trend toward an increase in ER prevalence in high dynamic versus low dynamic disciplines. Taken together this suggests that the ER pattern is rather present in lean, male athletes performing highly dynamic endurance disciplines and presenting with low heart rates.

Regarding stress testing, we could not show a difference in performance between ER+ and ER- athletes whereas a previous analysis of ER and exercise testing in nonathletes showed that ER+ individuals had a higher aerobic capacity (Haydar, Brantley, Gittings, Wright, & Fleg, 2000). Also, there was no difference in supraventricular or ventricular extrasystole between ER+ and ER- athletes. This is in accord with our previous analysis of ER in the general population showing no association of ER with ventricular or supraventricular ectopy (Trenkwalder et al., 2017).

We did not detect any severe cardiovascular event during the clinical follow-up. However, given the low incidence of ER-associated idiopathic ventricular fibrillation (Rosso et al., 2008) and arrhythmia death (Wu, Lin, Cheng, Qiang, & Zhang, 2013) our study was not designed to detect significant differences in such events. A previous study by Cappato and colleagues detected a higher frequency of ER in athletes with cardiac arrest or sudden death compared to control athletes (Cappato et al., 2010), whereas in a study with the so far longest follow-up of 24 years, no event of SCD occurred in ER+ athletes (Serra-Grima et al., 2015). Looking at the high prevalence of ER in trained athletes and the comparatively low number of SCD in this cohort the sole presence of ER may not be considered a high-risk phenotype.

Therefore, we also analyzed subtypes of ER, which have been linked to a poorer outcome. Here, a horizontal/descending ST segment, presence of ER in the inferior leads and a high amplitude of J-point elevation (>2 mV) have been described as potentially malignant

FIGURE 3 Common classification of left ventricular geometry depending on the relation of left ventricular mass (hypertrophy: males >115 g/m², females >95 g/m²) to relative wall thickness (concentric: >0.42). Overall there were no differences in the distribution of the four categories of left ventricular geometry between ER+ and ER- individuals

TABLE 4 Association of high-risk ER subtypes with left atrial and left ventricular structure

	ER region: Inferior (n = 30)		ER amplitude: >2 mV (n = 13)		ER type: Notching (n = 15)		ER ST segment: Horizontal/descending (n = 54)	
	OR (95% CI)	p ^a	OR (95% CI)	p ^a	OR (95% CI)	p ^a	OR (95% CI)	p ^a
Left atrial diameter	0.62 (0.24–1.61)	0.325	0.75 (0.18–3.15)	0.691	7.01 (1.65–29.83)	0.008	1.35 (0.64–2.83)	0.428
LV mass	0.99 (0.98–1.00)	0.246	1.00 (0.99–1.02)	0.744	1.02 (1.00–1.03)	0.038	1.00 (0.99–1.01)	0.417
LV mass/BSA	0.995 (0.98–1.02)	0.64	1.018 (0.99–1.05)	0.207	1.033 (1.00–1.06)	0.026	0.999 (0.98–1.01)	0.861
LV mass/height	0.99 (0.97–1.01)	0.401	1.01 (0.98–1.04)	0.44	1.03 (1.00–1.06)	0.03	1.00 (0.98–1.01)	0.619
Relative heart volume	1.08 (0.87–1.35)	0.478	1.22 (0.91–1.64)	0.19	1.01 (1.00–1.01)	0.01	1.12 (0.95–1.32)	0.171

Note. Analyses are adjusted for age and gender.

95% CI: 95% confidence interval; BSA: body surface area; LV: left ventricular; OR: Odds ratio.

^aCompared to early repolarization negative athletes.

subtypes (Junttila et al., 2014; Rosso et al., 2012; Sinner et al., 2010; Tikkanen et al., 2011). Recently, the notching configuration was also described as a high-risk variant (Cheng et al., 2016). Interestingly, in our study, only the notching subtype was associated with echocardiographic alterations showing an increased atrial diameter, higher left ventricular mass and relative heart volume. However, it is important to emphasize that this subgroup consisted of 15 athletes and future studies are needed to confirm this observation.

Overall, in elite athletes functional and structural echocardiographic measurements were similar between athletes with ER and those without. Therefore, the addition of echocardiographic characteristics does not help to discriminate between benign and potentially harmful forms of ER. Future studies including genetic analyses are needed to identify individuals with ER at risk.

4.1 | Strengths and limitations

Our study is the first analysis of ER in highly trained athletes taking gender differences into account. In the investigation of left ventricular metrics in a phenotype that occurs predominantly in men, it is of utmost importance to perform sex-stratified analyses to avoid any gender-related bias. Moreover, as comparison of various sport disciplines is difficult we tried to overcome this issue by classifying sports into static and dynamic subgroups and thereby could show that ER is rather associated with highly dynamic endurance sport types.

However, there are some limitations that should be considered. Compared to population-based studies the size of 623 individuals is small and particularly in the subtype analysis of ER, group sizes are very low. Therefore, results must be interpreted carefully. In addition, the follow-up time of seven years is comparably short, especially as severe events in a young and healthy study sample are rare. We therefore focused on the morphological analyses in this unique cohort of elite athletes including several Olympic and World Championship medalists with a detailed clinical examination including echocardiography. The prevalence of ER highly depends on its definition. We invariably used the definition by Haissaguerre (Haissaguerre et al., 2008) and Macfarlane (Macfarlane et al., 2015) which excludes leads V1–V3. Therefore, repolarization variants like the black athlete repolarization variant (Sharma et al., 2017) might have been missed. However, of seven black athletes in our study, only one presented with the black athlete repolarization variant. This athlete was also classified as ER-positive following our definition. Another limitation is that we did not correct for multiple testing in our analyses.

5 | CONCLUSION

Presence of ER in elite athletes is not associated with distinct structural or functional echocardiographic changes or a typical pattern in cardiopulmonary exercise capacity. The prototype of an athlete presenting with ER is male, lean, has a low heart rate or sinus bradycardia and is predominantly involved in high dynamic endurance sport disciplines.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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