Early Repolarization

Electrocardiographic Phenotypes Associated With Favorable Long-Term Outcome

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Background**—**Early repolarization (ER) in inferior/lateral leads of standard ECGs increases the risk of arrhythmic death. We tested the hypothesis that variations in the ST-segment characteristics after the ER waveforms may have prognostic importance.

Methods and Results**—**ST segments after ER were classified as horizontal/descending or rapidly ascending/upsloping on the basis of observations from 2 independent samples of young healthy athletes from Finland (n=62) and the United States (n=503), where ascending type was the dominant and common form of ER. Early repolarization was present in 27/62 (44%) of the Finnish athletes and 151/503 (30%) of the US athletes, and all but 1 of the Finnish (96%) and 91/107 (85%) of US athletes had an ascending/upsloping ST variant after ER. Subsequently, ECGs from a general population of 10 864 middle-aged subjects were analyzed to assess the prognostic modulation of ER-associated risk by ST-segment variations. Subjects with ER ≥0.1 mV and horizontal/descending ST variant (n=412) had an increased hazard ratio of arrhythmic death (relative risk 1.43; 95% confidence interval 1.05 to 1.94). When modeled for higher amplitude ER (>0.2 mV) in inferior leads and horizontal/descending ST-segment variant, the hazard ratio of arrhythmic death increased to 3.14 (95% confidence interval 1.56 to 6.30). However, in subjects with ascending ST variant, the relative risk for arrhythmic death was not increased (0.89; 95% confidence interval 0.52 to 1.55).

Conclusions**—**ST-segment morphology variants associated with ER separates subjects with and without an increased risk of arrhythmic death in middle-aged subjects. Rapidly ascending ST segments after the J-point, the dominant ST pattern in healthy athletes, seems to be a benign variant of ER. **(*Circulation*. 2011;123:2666-2673.)**

Key Words: arrhythmia ■ electrocardiography ■ epidemiology ■ follow-up studies ■ risk factors

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Early repolarization (ER) patterns in standard 12-lead ECGs recorded from normal subjects was considered a benign variant[1] before recent case-control reports associated vulnerability with idiopathic ventricular fibrillation (VF) with ER patterns in the inferolateral leads.[2–7] Subsequently, J-point elevation in leads other than V1–V3 has been identified as a predictor of cardiac and arrhythmic deaths in 2 independent general population cohorts, especially when present in the inferior ECG leads.[8–9] These observations have alerted physicians to the potential significance of such ECG variations in apparently healthy subjects, but it is not yet clear whether specific variants of ER in inferior and/or lateral leads are associated with an increased risk of life-threatening arrhythmias, either alone or in conjunction with acquired structural disease states.

Clinical Perspective on p 2673

Besides the general population and those with documented idiopathic VF, ER and ST segment changes in precordial leads are known to be common in trained athletes.[10–14] In addition, ER patterns in the inferior and lateral leads with a rapidly ascending slope of the ST segment after the J-point, which resemble those observed in leads V1–V3 in athletes, are common in young healthy subjects.[1] Therefore, we hypothesized that this ER ST-segment pattern may be a benign variant of ER and performed a pilot study in young healthy athletes in Finland and in college athletes in the United States to assess the prevalence and patterns of ER in these subjects. Subsequently, we reanalyzed the ECGs from a sample of 10 957 subjects from our general population with a long follow-up[8] to assess the prognostic significance of different ST-segment patterns in the presence of ER.

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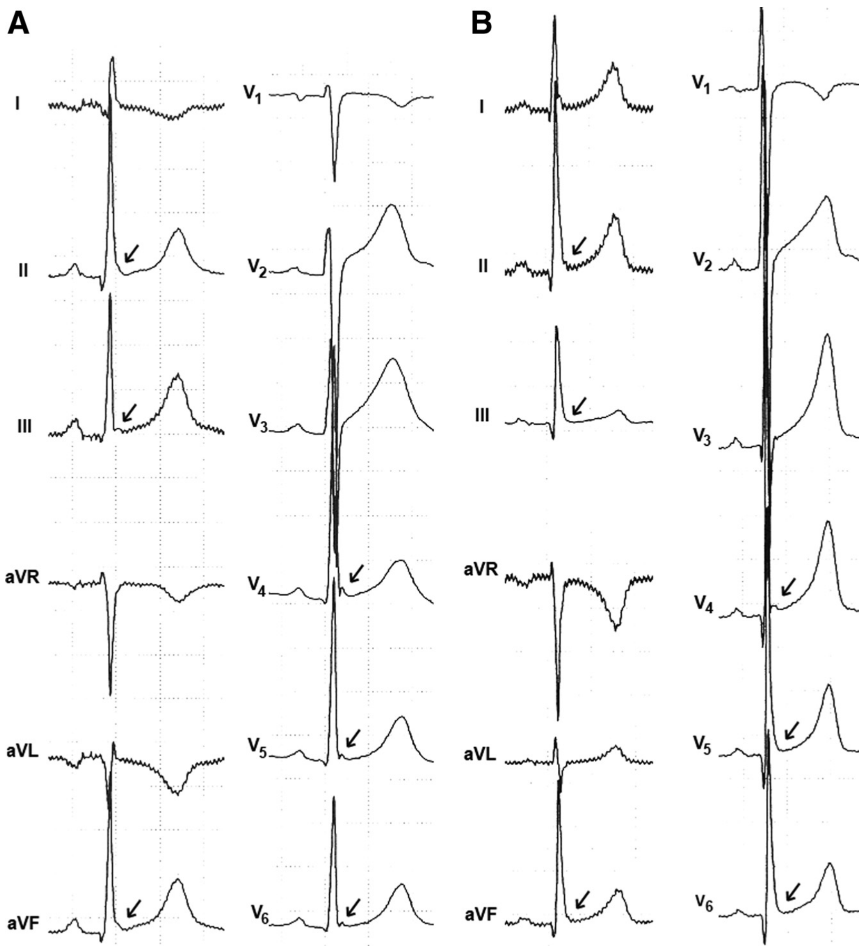

Figure 1. ECGs (**A** and **B**) of 2 young athletes with early repolarization and rapidly ascending/upsloping ST-segment morphology. All but one subject presenting early repolarization pattern in the Finnish athlete population had similar rapidly ascending ST segment after the J point. Both terminal QRS notching and slurring were present (arrows), but only 1 of the 27 cases with early repolarization had dominant ST segment categorized as horizontal/descending. Black arrows indicate terminal QRS notching or slurring.

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Methods

Study Populations

Pilot Study in Athletes in Finland

ECG tracings were recorded from 62 volunteer Finnish young male athletes, aged 13 to 15 years (mean age 13.4±0.6). The tracings were analyzed for general ECG c features, and for the presence of ER and patterns of ST segments after ER by 2 readers independently. Early repoloarization in the inferior and/or lateral leads was observed in 27 of the 62 subjects (43.5%), with uniform agreement of the ER status. In all but 1 of the subjects with ER, the ST-segment patterns after J-point elevations, defined as >0.1 mV elevation of ST segment 100 ms after the J point (Figure 1), were characterized by rapidly ascending/upsloping ST segments. This definition was used in subsequent analysis of prognostic significance of ER (see General Middle-Aged Population).

Athlete Population in the United States

The results in the Finnish athletes were validated in a population of 503 competitive athletes from the University of Miami (Miami, FL). Fifty-one percent were men, with ages ranging from 17 to 24 years, and 34% were black, compared with 100% men and no athletes of African descent in the Finnish athletes (see Tables 1 and 2).[14] The US ECG tracings were read by a single reader.

General Middle-Aged Population

This study population consists of subjects participating in the Finnish Social Insurance Institution's Coronary Heart Disease Study (CHD Study) who had undergone clinical baseline examinations between 1966 and 1972. The CHD Study was part of the large prospective Mobile Clinic Health Survey. This cohort consisted of 10 957 men and women, aged 30 to 59 years (52.3% men) at entry, drawn from 35 different geographical areas of Finland, and was a representative sample of the middle-aged Finnish population. We excluded 93 ECGs that had missing data or were otherwise unreadable. Thus, our final study group included 10 864 subjects (52% of whom were men; mean age, 44.0±8.5 years) from the original cohort. A detailed account of the study rationale and procedures performed at the baseline examination has been described previously in detail.[15]

ECG Measurements

The presence of ER was analyzed from standard resting 12-lead ECGs, recorded at a paper speed of 50 mm/s and calibration of 1 mV

Table 1. Characteristics of the Subjects in the Pilot Finnish Athlete Population

	No ER	ER+	*P*
No. of subjects	35	27	
Age	13.3±0.6	13.4±0.6	0.59
Men, %	100	100	1.00
Heart rate, bpm	71±17	68±11	0.34
QRS duration, ms	88±8	84±12	0.02
QTc interval, ms	405±17	417±22	0.02
PR interval, ms	145±25	142±20	0.62
Sokolow-Lyon index, mV	3.1±0.7	3.6±0.7	0.01
QRS angle, degrees	71±21	74±47	0.75
J-point amplitude, mV	0	0.13±0.03	<0.001

Values are mean±SD unless otherwise specified.

Table 2. Characteristics of the Athletes in the Miami Validation Population

	No ER	ER With Horizontal/ Descending ST	ER With Ascending/ Upsloping ST	*P*
No. of subjects	352	16*	91*	
Men, %	48†	62	62†	0.043
Heart rate, bpm	62±11	59±8	60±9	0.166
QTc interval, ms	393±29	398±22	390±26	0.602
Sokolow-Lyon index, mV	2.5±0.8‡	2.8±1.2	3.1±0.9‡	<0.001

Values are mean±SD unless otherwise specified.

*Missing ER-type information on 44 ER carriers.

†Bonferroni post-hoc analysis for multiple comparisons; $P=0.060$ between No ER and ER with ascending/upsloping ST.

‡Bonferroni post-hoc analysis for multiple comparisons; $P<0.001$ between No ER and ER with ascending/upsloping ST.

per 10 mm, using the criteria of J-point elevation ≥0.1 mV in at least 2 inferior or lateral leads.[2,8] Each ECG positive for ER was classified according to specific ER patterns, with coding as (1) notched, (2) slurred, or (3) undetermined (no dominant form). Notching was defined as a positive J deflection at the end of the QRS complex, and slurring as a terminal slower waveform transitioning from QRS J point to the ST segment (Figure 2).

ST-segment patterns after the J point were coded as follows: (1) horizontal/descending or (2) concave/rapidly ascending. The concave/rapidly ascending ST segment was defined as >0.1 mV elevation of ST segment within 100 ms after the J point or a persistently elevated ST segment of >0.1 mV throughout the ST segment. These criteria were derived from the findings in the ER ST-segment patterns in the healthy athletes described above. Horizontal/descending type was defined as ≤0.1 mV elevation of the ST segment within 100 ms after the J point (Figure 3). The isoelectric line (baseline) was defined as the level between 2 T-P intervals. J-point or ST-segment patterns had to be present in at least 2 inferior or lateral leads for positive grading.

Figure 2. ECG leads II and aVF of 2 Finnish athletes with inferior early repolarization. Subject **A** presented notching, and subject **B** slurring of the terminal QRS (arrows). Notching was defined as a distinct positive deflection ≥1 mm inscribed in or after the R wave, and slurring as gradual transforming of R wave to ST segment. J-point amplitude was measured from the time point of QRS offset drawn from another lead, and the ECG was scored positive for early repolarization if the J-point amplitude was at least 0.1 mV.

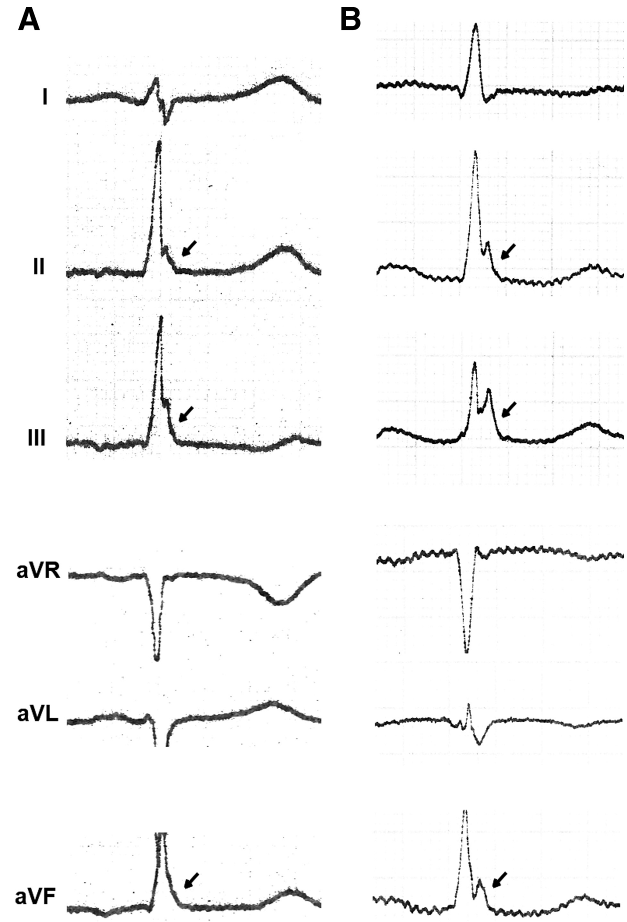

Figure 3. Horizontal/descending ST-segment patterns from 2 subjects in the general population. Subject **A** presented horizontal/descending ER (dominant horizontal ST segment in leads II and aVF and descending ST segment in lead III). Subject **B** presented ER with horizontal/descending ST segments (dominant horizontal ST segment in leads II, III, and aVF). In the middle-aged general population, only ER with horizontal/descending ST segment predicted arrhythmic death. Black arrows indicate terminal QRS notching or slurring.

Follow-Up

The general population subjects were followed up for a mean of 30±11 years (until December 31, 2007) after the baseline examinations performed between 1966 and 1972. The mortality data were determined from the Causes of Death Register maintained by Statistics Finland. Less than 2% of subjects were lost to follow-up as a result of moving abroad, but even in this group the survival status could still be determined for a majority of subjects. Because of extensive administrative registers in Finland, every death in the country is recorded, and the quality and reliability of these registers have been validated previously.[16] To identify cases of sudden death from arrhythmia, all deaths from cardiac causes were reviewed by experienced cardiologists (O.A. and H.V.H.) on the basis of the definitions presented in the Cardiac Arrhythmia Pilot Study,[17] as described by our group previously.[8] The end point of this study was arrhythmic death.

Statistical Analysis

All continuous data are presented as mean±SD. Two-sided *t* test and χ^2 analyses were performed for comparisons between 2 groups in the Finnish athlete and general population samples. One-way ANOVA test was used to compare the values between the three groups, and Bonferroni post hoc analysis was used for multiple comparison tests in the US athlete and general population samples. The general linear

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Table 3. Adjusted Characteristics of Subjects With ER and Different ST-Segment Patterns

	No ER (n=10 288)	ER With Ascending/ Upsloping ST (n=164)	ER With Horizontal/ Descending ST (n=412)	*P*, No Versus ER With Ascending/ Upsloping ST)	*P*, No Versus ER With Horizontal/ Descending ST)	*P*, Between Groups
Men, %*	51.5	88.1	57.1	<0.001	0.03	<0.001
Age, y†	44.0±8.5	42.6±7.9	45.5±8.2	0.04	<0.001	<0.001
Current smokers, %‡	33.8	38.4	36.4	0.17	0.20	0.19
Cholesterol, mmol/L‡	6.50±1.32	6.48±1.32	6.58±1.21	0.84	0.22	0.46
BMI, kg/m^2‡	25.9±3.9	25.0±2.9	25.7±3.6	0.001	0.15	0.002
Heart rate, bpm‡	76±15	70±12	75±14	<0.001	0.09	<0.001
Systolic blood pressure, mm Hg‡	138±22	134±16	138±21	0.01	0.62	0.04
Diastolic blood pressure, mm Hg‡	82±12	79±12	83±13	<0.001	0.61	<0.001
Chronotropic medication, %‡	4.3	3.2	4.2	0.46	0.89	0.77
Cardiovascular disease, %‡	8.1	8.7	7.2	0.75	0.49	0.74
Electrocardiographic LVH, %‡	30.8	60.6	33.2	<0.001	0.27	<0.001
QTc duration, ms‡	408±28	400±22	409±28	<0.001	0.86	<0.001
QRS duration, ms‡	87±8	87±7	89±7	0.31	<0.001	<0.001
ECG signs of coronary artery disease, %‡	9.6	12.2	14.9	0.28	<0.001	0.001
History of prior myocardial infarction, %‡	1.1	0.3	1.3	0.35	0.71	0.59
History of angina pectoris, %‡	2.3	2.5	1.6	0.85	0.33	0.60

Values are mean±SD unless otherwise specified.

*Adjusted for age; †Adjusted for sex; ‡Adjusted for age and sex.

model was used to compare the age- and sex-adjusted mean values for continuous variables and the prevalence of categorical variables between the groups. The hazard ratios (HRs) and 95% confidence intervals (CIs) for arrhythmic death were calculated using the Cox proportional hazards model, in which the ER subgroups were each compared with the reference group with no ER. The primary adjustments to these models were age and sex. The multivariate model included age, sex, body mass index, heart rate, QRS duration, QTc duration, ECG signs of left ventricular hypertrophy and ECG signs of coronary artery disease. Kaplan–Meier survival curves were plotted for different ER types. For the general population sample, statistical analyses were performed with SAS software, version 9.1.3 (SAS Institute), and for the Finnish and US athlete populations with PASW 17.0 software (SPSS, Chicago, IL). $P<0.05$ was considered statistically significant.

Results

Early Repolarization and ST-Segment Patterns in Healthy Athletes

Early repolarization in the inferior and/or lateral leads was present in 27 of the 62 subjects (43.5%) in the pilot study of young Finnish athletes. Other ECG characteristics of these subjects are presented in Table 1. As anticipated, there were no outcome events in this group, for the reason that this study was intended to seek only cross-sectional observations of ER prevalence and ST-segment patterns. In all but 1 of the subjects with ER (96%), the ST-segment patterns appearing after J-point elevations were ascending/upsloping, defined as >0.1 mV elevation of the ST segment 100 ms after the J point with an ascending slope (Figure 1).

In the US population, 151 of the 503 athletes (30%) had inferior or lateral ER in primary analysis for ER prevalence. Of the 151 ER positive athletes, 107 ECGs were later available for the ST-segment morphology reanalysis). In the ST-segment analysis 91/106 subjects (85%) had rapidly ascending ST segments after J-point elevation. Detailed results are described in Table 2.

Prevalence and Patterns of Early Repolarization in the Middle-Aged General Population

Early repolarization in inferior and/or lateral leads was present in 576 subjects (5.3%) in the general middle-aged population. The distribution of J-point types was notched in 228 subjects (39.6% of those with ER), slurred in 292 (50.7% of those with ER), and undetermined in 56 subjects (9.7% of those with ER). Distribution of ST segments was as follows: (1) horizontal/descending in 412 subjects (71.5%), and (2) rapidly ascending/upsloping in 164 subjects (28.5%).

Characteristics of General Population Subjects With Early Repolarization Based on ST-Segment Patterns

The baseline characteristics of general population subjects, based on the specific ER ST-segment patterns, are presented in Table 3. A subtle male dominance was present among the subjects with horizontal/descending ST segments. This group was older, had higher prevalence of ECG signs of coronary artery disease, and had a longer QRS duration in ECG compared with those without ER. Other characteristics did not differ significantly between these groups. In contrast, subjects with rapidly ascending/upsloping ST segments were younger, more often men, had lower body mass index, lower heart rate, lower blood pressure, shorter QTc duration, and higher prevalence of ECG left ventricular hypertrophy, and were more commonly smokers, compared with those without ER.

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Table 4. HRs, 95% CIs, of Sudden Arrhythmic Death in Different ER ST-Segment Groups

According to ST Segment	No. of Subjects	No. of Arrhythmic Deaths	Unadjusted HR (95% CI)	Adjusted HR (95% CI)*	Adjusted HR (95% CI)†
No ER	10 288	739	1	1	1
ST segment, horizontal/descending					
Any J-point–type ER ≥0.1 mV in inferior/lateral leads	412	43	1.62 (1.19–2.21)	1.43 (1.05–1.94)	1.39 (1.02–1.89)
Any J-point type ER >0.2 mV in inferior/lateral leads	50	9	3.37 (1.75–6.51)	2.61 (1.35–5.04)	2.42 (1.25–4.69)
Inferior, any J-point–type ER ≥0.1 mV	265	35	2.01 (1.43–2.82)	1.72 (1.22–2.41)	1.73 (1.22–2.44)
Inferior, any J-point–type ER >0.2 mV	33	8	4.28 (2.13–8.58)	3.14 (1.56–6.30)	3.13 (1.55–6.32)
Inferior notched ER ≥0.1 mV	133	19	2.38 (1.51–3.76)	1.60 (1.01–2.53)	1.70 (1.08–2.69)
Inferior slurred ER ≥0.1 mV	127	15	1.63 (0.98–2.72)	1.76 (1.06–2.94)	1.82 (1.09–3.03)
Inferior slurred ER >0.2 mV	13	4	4.72 (1.77–12.61)	5.26 (1.97–14.07)	5.51 (2.05–14.82)
Lateral, any J-point–type ER ≥0.1 mV	142	8	0.92 (0.46–1.85)	0.84 (0.42–1.70)	0.81 (0.40–1.62)
ST segment, rapidly ascending					
Any J-point type ER ≥0.1 mV in inferior/lateral leads	164	13	1.15 (0.67–2.00)	0.89 (0.52–1.55)	0.87 (0.50–1.52)
Any J-point type ER >0.2 mV in inferior/lateral leads	10	1	1.66 (0.23–11.84)	1.08 (0.15–7.69)	0.96 (0.13–6.83)
Inferior any J-point type ER ≥0.1 mV	90	8	1.31 (0.65–2.63)	1.01 (0.50–2.03)	1.05 (0.52–2.11)
Inferior any J-point type ER >0.2 mV	3	0	No deaths	No deaths	No deaths
Inferior notched ER ≥0.1 mV	23	2	1.55 (0.39–6.17)	1.34 (0.33–5.39)	1.47 (0.37–5.92)
Inferior slurred ER ≥0.1 mV	41	4	1.53 (0.57–4.10)	1.02 (0.38–2.74)	1.16 (0.43–3.26)
Lateral any J-point type ER ≥0.1 mV	124	9	1.02 (0.52–1.95)	0.84 (0.43–1.60)	0.79 (0.40–1.52)
According to J-point type (independent of ST segments)					
J-point notched type					
Notched type ER ≥0.1 mV in inferior/lateral leads	215	27	2.00 (1.37–2.94)	1.58 (1.07–2.32)	1.53 (1.03–2.26)
Inferior notched ER ≥0.1 mV	158	21	2.23 (1.45–3.44)	1.54 (1.00–2.38)	1.70 (1.07–2.56)
Inferior notched ER >0.2 mV	22	4	3.44 (1.29–9.18)	2.10 (0.79–5.62)	2.05 (0.76–5.51)
J-point slurred type					
Slurred type ER ≥0.1 mV in inferior/lateral leads	290	26	1.31 (0.89–1.94)	1.19 (0.81–1.76)	1.18 (0.79–1.74)
Inferior slurred ER ≥0.1 mV	171	19	1.56 (1.01–2.50)	1.50 (0.95–2.37)	1.59 (1.00–2.51)
Inferior slurred ER >0.2 mV	14	4	4.59 (1.72–12.26)	5.14 (1.92–13.76)	5.42 (2.02–14.54)

HR indicates hazard ratio; CI, confidence interval; ER, early repolarization.

*Adjusted for age and sex; †Adjusted for age, sex, body-mass index, heart rate, QTc duration, QRS duration, ECG signs of left ventricular hypertrophy, and ECG signs of coronary artery disease.

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Risk of Arrhythmic Death With Early Repolarization Stratified for Different ST-Segment Patterns

During follow-up, 6133 subjects (56.5%) died. Of these deaths, 1969 (32.1% of all deaths) were from cardiac causes, and 795 (40.5%) of the latter were classified as sudden arrhythmic deaths. Table 4 presents unadjusted, age- and sex-adjusted, and multivariate-adjusted HRs of death from arrhythmia associated with different ER ST-segment patterns.

Subjects with ER and horizontal/descending ST segments had a higher risk of sudden arrhythmic death (age- and sex adjusted HR 1.43; 95% CI 1.05 to 1.94) than subjects without ER. In contrast, subjects with ER and rapidly ascending/upsloping ST segments (upsloping) (n=164) did not have an elevated risk for arrhythmic death (adjusted HR 0.89; 95% CI 0.52 to 1.55). The results remained essentially the same in multivariate analysis (Table 4).

A separate analysis of inferior ER subjects demonstrated the same trend. Among subjects with inferior ER and horizontal/descending ST segments (n=265), the HR was 1.72 (95% CI 1.22 to 2.41) for arrhythmic death after adjustments for age and sex. By contrast, inferior ER and rapidly ascending/upsloping ST segment (n=90) was not associated with adverse outcome (Table 4). Figure 4 shows the Kaplan–Meier survival curves for death from arrhythmia in subjects with different inferior ER ST-segment patterns.

Assessment of Mortality According to Early Repolarization Pattern

Analysis of outcomes among subjects with notched ER ≥0.1 mV, independent of ST-segment patterns, had an age- and sex-adjusted HR of 1.58 (95% CI 1.07 to 2.32; P=0.05) for arrhythmic death. The HR of arrhythmic death in subjects with slurred ER patterns ≥0.1 mV, independent of ST-segment patterns, was 1.19 (95% CI 0.81 to 1.76; P=0.41). In subjects with >0.2 mV ER, independent of ST-segment patterns, the numbers were conflicting: Notched >0.2 mV ER had an adjusted HR of 2.14 (95% CI 0.89 to 5.16), and slurred >0.2 mV ER had a very high HR of 5.14 (95% CI 1.92 to 13.76). Before adjustments, both notching and slur-

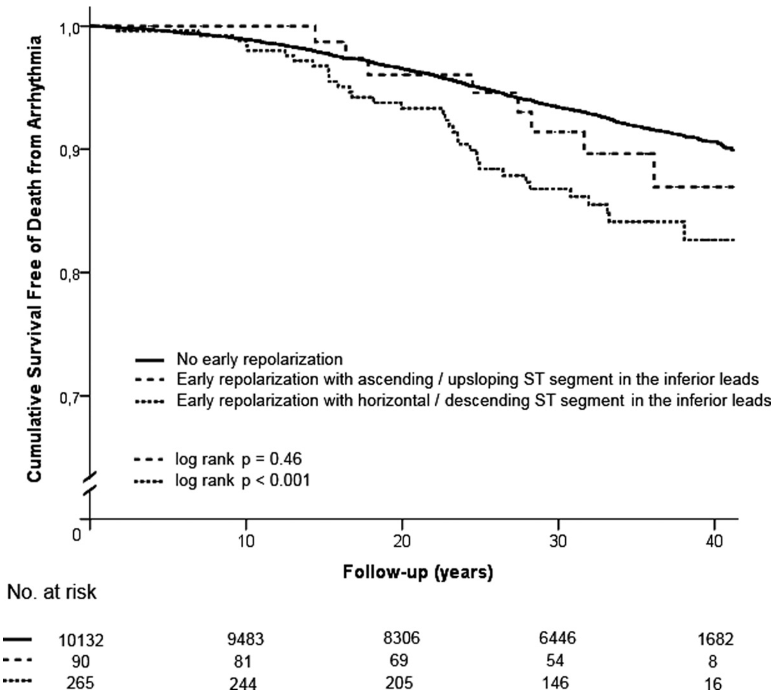

Figure 4. Unadjusted Kaplan–Meier estimates.

ring of the terminal QRS conveyed significantly increased risk. When only inferior location was included, subjects with notched ER had an adjusted HR of 1.54 (95% CI 1.00 to 2.38) and subjects with slurred ER had an adjusted HR of 1.50 (95% CI 0.95 to 2.37), with borderline significance. In the rest of the comparisons, the results were contradictory: No clear difference between notching and slurring of the terminal QRS was observed. It should, however, be acknowledged that the small sample size precludes any strong conclusions drawn from the analyses between notching and slurring of the terminal QRS despite the statistical significance reached by some of the HRs (Table 4).

Discussion

The results of this study show that ER patterns in the inferior or lateral leads of a standard 12-lead ECG are not associated with uniformly increased risk of arrhythmic death in a middle-aged general population. Early repolarization patterns associated with horizontal or descending ST segments after the J point are accompanied by an increased risk for arrhythmic death, but ER followed by rapidly upsloping ST segments after the J point is not associated with such risk. The highest risk occurred with the combination of ER in the inferior limb leads, high amplitude (>0.2 mV) J-point waveforms, and a dominant horizontal or descending ST segment after the J point. None of the lateral patterns of ER without concomitant J-point elevation in inferior leads was associated with increased mortality.

In addition to different prognostic impact, the subjects with various types of ST-segment after the ER had certain differences in the baseline characteristics. Those with a rapidly ascending ST-segment pattern in the general middle-aged population were younger, their heart rate and blood pressure were lower, and they more commonly had ECG signs of left ventricular hypertrophy. In contrast, subjects with horizontal or descending ST-segment pattern with ER were somewhat older and had longer QRS durations than those without ER. Overall, these characteristics suggest that those subjects with rapidly ascending ST segments were healthier and likely more physically active than the others, leading to the presumption that the ascending ST-segment ER variant might be a reflection of athlete ECG changes such as left ventricular hypertrophy voltage in lateral precordial leads.

The rapidly upsloping ST-segment pattern was less common than the horizontal/downsloping ST-segment patterns in a random sample of middle-aged subjects, and it was not associated with an increased risk of arrhythmic death. This pattern associated with a low HR in the general population with long-term follow-up dominated in prevalence in both athlete datasets. This finding is consistent with the notion that ER in athletes is generally benign, although exceptions may exist.[18] Specifically, the distribution of different ST-segment characteristics in conjunction with ER was similar, and low prevalence of ER with horizontal/descending ST segment was nearly identical between the 2 athlete populations and to that of the general population in the present study.

Terminal left precordial QRS notching has been previously reported to be more prevalent in malignant than benign variants of ER (idiopathic ventricular tachycardia/VF).[7] Additionally, Rosso et al have reported J-point elevation, defined as notched ER, to be more prevalent in ER patients with idiopathic VF than in matched control subjects whereas slurred ER pattern did not differ between the groups.[4] However, in the present population, definite differences between prognostic significance of notching and slurring of ER pattern did not emerge. When all ER cases were pooled together, subjects with a notched J point had worse prognosis, but in other comparisons the results were not unambiguous. Slurred morphology with a high J-point amplitude in inferior localization was associated with the highest risk of arrhyth-

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mic death in combination with the horizontal/descending ST segment.

Several physiological modulators are known to influence early repolarization patterns, and it is possible that the different ST-segment types after ER defined in this study are a spectrum of the same electrophysiological abnormality manifested in various forms at different times, similar to that observed in the Brugada syndrome, where benign Brugada ECG types II and III can convert spontaneously to a more malignant type I (eg, during fever or by some drugs blocking the sodium channels).[19] For example, a recently described case report illustrated a temporal relationship between hypothermia and exacerbation of J-point elevation, followed by increased frequency of ventricular arrhythmias.[20] The similar prevalence of the malignant form of ER in the athlete populations and in the middle-aged population in this study suggests that the malignant ER form may be more stable and independent of age. The cellular electrophysiological basis for the formation of Brugada ECG has been described as due to the heterogeneous repolarization during phase 2 of the action potential. Particularly, the regional loss of the plateau dome in the epicardium of the right ventricle has been associated with the type I Brugada ECG finding.[21] The similarities in the surface ECG of the different Brugada ECG manifestations and the ER ECG manifestations presented in this study would suggest also a similar dynamic electrophysiological basis, but further basic studies are needed to test these speculations. The observed ER patterns in this population might not apply in a straightforward fashion to familial ER syndrome but suggest that the malignant type of ER with horizontal/descending ST segment plays a modifying role as a trigger of fatal arrhythmias in acute events in middle-aged subjects.

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Study Limitations

We used a specific predefined measuring point (100 ms at baseline level after J point) for coding of ST segment on the basis of observations from the athlete populations. This point may not be optimal for separating the malignant and benign forms of ER syndrome, and should be tested also in other populations, such as those with documented VF. Despite the arbitrary empirical measuring point, the results confirm the primary hypothesis of the study. A recent study also partly confirms the present observations showing that the presence of J wave with no ST-segment elevation ($>$0.05 mV) was more prevalent in athletes with cardiac arrest or sudden death than in control healthy athletes.[18] Actually, the examples provided by Cappato et al[18] illustrate horizontal/descending ST segment in the ECG of an athlete who had cardiac arrest during practice and upsloping ST segment in the ECG of a control male. We recognize the fact that we do not have any follow-up data available of the athlete populations, and thus the conclusions drawn from the general population may not apply to these young subgroups. Therefore, the conclusion that ER with rapidly ascending ST-segment pattern is benign in young healthy athletes remains partly speculative.

Conclusions

The observations from the present community-based study show that the ER with rapidly ascending ST segment in inferior or lateral leads of a 12-lead ECG is a benign variant, similar to that observed in leads V1–V3, at least in middle-aged subjects. Subjects with this ECG pattern should not be profiled at high risk and do not require specific cardiovascular evaluations or treatment if they are asymptomatic without a family history of sudden cardiac death or serious arrhythmias. In contrast, a specific ER pattern in inferior leads of a standard 12-lead ECG with a horizontal/descending ST segment appears to be associated with an increased risk of arrhythmic death, and a high amplitude of J-point elevation increases the risk even further. Although these observations are novel and relieve some of the pressure from the fear of J waves,[22] further studies on the pathophysiological mechanisms of this ECG pattern and strategies to treat the subjects with this ECG abnormality are needed in the future. Among the questions to be explored are whether the high-risk ER ST-segment pattern reflects a primary arrhythmic syndrome or whether it is a modifying factor for specific arrhythmic risk in patients with acquired structural heart disease. The temporal distribution of risk observed in our original general population study[8] suggests the possibility of the latter.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Previous reports have characterized inferior early repolarization (ER) as a harbinger of increased risk for sudden death. In the present study, the investigators analyzed ER from 12-lead ECGs of 10 864 randomly selected middle-aged subjects and tested the hypothesis that variations in the ST-segment characteristics after the ER waveforms may have prognostic importance. The novel observations from the present community-based study suggest that ER with rapidly ascending ST segment in inferior or lateral leads of a 12-lead ECG, which is frequently observed in young healthy athletes, is a benign variant, similar to that observed in leads V1–V3, at least in middle-aged subjects. Subjects with this ECG pattern should not be profiled as high risk, and would not require specific cardiovascular evaluations or treatment if they are asymptomatic without a family history of sudden cardiac death or serious arrhythmias. In contrast, a specific ER pattern in inferior leads of a standard 12-lead ECG with a horizontal/descending ST segment appears to be associated with an increased risk of arrhythmic death and a high amplitude of J-point elevation increases the risk even further. The pathogenesis, background, and treatment of such subjects with high-amplitude ER and horizontal/downsloping ST segment warrant further research.

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Early Repolarization: Electrocardiographic Phenotypes Associated With Favorable Long-Term Outcome

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