Early repolarization as a predictor of arrhythmic and nonarrhythmic cardiac events in middle-aged subjects

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BACKGROUND Early repolarization (ER) in the inferior/lateral leads predicts mortality, but whether ER is a specific sign of increased risk for arrhythmic events is not known.

OBJECTIVE The purpose of this study was to study the association of ER and arrhythmic events and nonarrhythmic morbidity and mortality.

METHODS We assessed the prognostic significance of ER in a community-based general population of 10,846 middle-aged subjects (mean age 44 ± 8 years). The end-points were sustained ventricular tachycardia or resuscitated ventricular fibrillation (VT-VF), arrhythmic death, nonarrhythmic cardiac death, new-onset atrial fibrillation (AF), hospitalization for congestive heart failure, or coronary artery disease during mean follow-up of 30 ± 11 years. ER was defined as ≥0.1-mV elevation of J point in either inferior or lateral leads.

RESULTS After including all risk factors of cardiac mortality and morbidity in Cox regression analysis, inferior ER (prevalence 3.5%) predicted VF-VT events (n = 108 [1.0%]) with a hazard ratio (HR) of 2.2 (95% confidence interval [CI] 1.1–4.5, P = .03) but not nonarrhythmic cardiac death (n = 1235 [12.2%]), AF (n = 1659 [15.2%]), congestive heart failure (n = 1752 [16.1%]), or coronary artery disease (n = 3592 [32.9%]) (P = NS for all). Inferior ER predicted arrhythmic death in cases without other QRS complex abnormalities (multivariate HR 1.68, 95 % CI 1.10–2.58, P = .02) but not in those with ER and other coexisting abnormalities in QRS morphology (HR 1.30, 95% CI 0.86–1.96, P = .22).

CONCLUSION ER in the inferior leads, especially in cases without other QRS complex abnormalities, predicts the occurrence of VT-VF but not nonarrhythmic cardiac events, suggesting that ER is a specific sign of increased vulnerability to ventricular tachyarrhythmias.

KEYWORDS Sudden death; Electrocardiogram; J waves; Early repolarization; QRS abnormality

ABBREVIATIONS AF = atrial fibrillation; **CAD** = coronary artery disease; **CHF** = congestive heart failure; **CI** = confidence interval; **ER** = early repolarization; **HR** = hazard ratio; **LVH** = left ventricular hypertrophy; **VF** = ventricular fibrillation; **VT** = ventricular tachycardia

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Introduction

Early repolarization (ER) syndrome, consisting of a specific ECG pattern of J-point elevation in the inferior or lateral leads among subjects with otherwise unexplained ventricular fibrillation (VF), has been described recently by independent investigators.[1–3] Most of the recent studies in general, middle-aged population samples have shown that the same type of ER ECG pattern is a sign of increased mortality during a long follow-up period.[4,5] We also previously showed that the inferior ER ECG pattern predicts sudden arrhythmic death.[4] These findings have not been confirmed in all studies, some of which have suggested that the ER ECG pattern may be a sign of depolarization abnormality caused by an underlying structural heart disease.[6,7] To further elucidate this topic, we analyzed the various fatal and nonfatal cardiac events from our middle-aged mobile clinic population with a long follow-up. We tested the hypothesis that the ER ECG pattern is specifically related to an increased risk of documented sustained ventricular tachycardia (VT) or VF leading to aborted cardiac arrest but not to nonarrhythmic cardiac death, atrial fibrillation (AF), or other nonfatal cardiovascular events. Furthermore, we studied separately the prognostic significance of ER with and without other QRS complex abnormalities to determine whether the risk associated with ER is simply a reflection of

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other abnormalities in the QRS morphology as a sign of underlying structural cardiac disease.

Methods

Study population, follow-up, and end-points

The study population consisted of 10,957 subjects from the general population enrolled in the Coronary Heart Study, which was part of the larger Mobile Clinic Heart Survey. Baseline examinations were carried out between 1966 and 1972 in 4 different areas in Finland. Details of this study population have been described previously.[4] After excluding 93 subjects because of unreadable ECGs, the study consisted of 10,864 subjects with ECGs (52% male, mean age 44.0 ± 8.5 years).

Mean follow-up was 30 ± 11 years. Less than 2% of the attendees were lost to follow-up as a result of moving abroad, but even in this group, the survival status for most could still be determined. Mortality data were obtained from the Causes of Death Register maintained by Statistics Finland, which records every death in the country. Death certificates were obtained for each deceased person. The relevant International Classification of Diseases (ICD) codes were used to define cardiac death. The procedure to identify cases of sudden cardiac death has been described in detail by our group previously.[4,8] Briefly, every death from cardiac causes was reviewed using death certificates, hospital records, and necropsy reports, if available. Cardiac mortality and arrhythmic death were determined by 2 experienced cardiologists (OA, HVH) according to the definitions presented in the Cardiac Arrhythmia Pilot Study as previously described by our group.[4,8] All hospital visits because of symptomatic VT, either monomorphic or polymorphic, resuscitated ventricular fibrillation (VF), AF, coronary artery disease (CAD), and congestive heart failure (CHF) were obtained from the Finnish Hospital Discharge Register, which includes complete nationwide data on all inpatient episodes in Finland at an individual level.[9]

ECG analysis

We previously described the methods of analyzing the inferolateral ER ECG pattern from this population.[4] The criteria for ER ECG pattern was J-point elevation $\geq$0.1mV of either notched or slurred morphology in at least 2 consecutive inferior or lateral leads. Another cutoff value was $\geq$0.2-mV J-point elevation. In cases with slurring, we measure the amplitude of the J point from the inclination point where the slurring starts. In cases of notching, we measure the amplitude from the top of the notch. In additional analysis, the ST-segment morphology in adjunct with the ER ECG pattern was divided into rapidly ascending (100 ms after J-point elevation $\geq$0.1mV) and horizontal/descending (100 ms after J-point ST-segment elevation $<$0.1mV) as described previously.[10]

In this study, all ECGs with ER ECG pattern were also reclassified according to any other QRS abnormality present on the ECG. Subjects with ER ECG pattern with Q waves or q waves, and/or QRS axis deviation (axis outside 0º–90º) and/or QRS duration $\geq$110 ms, including left anterior and posterior hemiblocks, incomplete or complete left bundle branch block or right bundle branch block, and intraventricular conduction delay, or left ventricular hypertrophy according to Sokolow-Lyon criteria were classified as ER ECG pattern with QRS abnormalities; all other subjects were classified as ER ECG pattern without QRS abnormalities (Table 1).

Statistical analysis

All continuous data are presented as mean ± SD. Cox proportional hazards model was used to determine hazard ratios (HRs) and 95% confidence intervals (CIs) for VT-VF events, sudden arrhythmic death, nonsudden cardiac death, and hospital visit because of AF, CHF or CAD. In the multivariate model, we adjusted the analysis with gender, age, smoking status, body mass index, systolic blood pressure, and prior cardiovascular disease. Analyses were repeated separately for those with ER ECG pattern with and without other QRS complex abnormalities. Cumulative hazard curves were generated for subjects with and those without inferior ER, and log-rank test was used for comparison between the curves with and those without the event. SPSS Statistics (version 19.0, SPSS, Inc. Chicago, IL) was used to analyze all statistics. All tests were 2-sided, and $P < .05$ was considered significant.

Results

The clinical characteristics of this study population were described earlier in detail. The results of the prevalence of ER ECG pattern (ie, 5.8%; 3.5% in inferior leads and 2.8% in

Table 1 Definitions of QRS abnormalities

QRS abnormality	Definition
Q waves	Any Q wave in leads V_2–V_3 $\geq$20 ms or QS complex in leads V_2 and V_3 Q wave $\geq$30 ms and $>$0.1 mV deep or QS complex in inferolateral leads
q waves	Same as Q wave, but in inferolateral leads q-wave duration $<$30ms
Complete or incomplete bundle branch block	QRS $\geq$120 ms and QRS morphology of LBBB or RBBB
Intraventricular conduction defect	QRS $\geq$110 ms without bundle branch block QRS morphology
Hemiblocks and QRS axis deviation	QRS axis $<0^\circ$ or $>90^\circ$
Left ventricular hypertrophy Sokolow-Lyon index	V_2 S amplitude + $V_5/_6$ R amplitude $\geq$35mm or R amplitude in aVL $\geq$11 mm

LBBB = left bundle branch block; RBBB = right bundle branch block.