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Prevalence and prognostic value of early repolarisation syndrome in the Yazd province: a single-centre study

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A – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

Summary **Background.** Early repolarisation (ER) pattern is defined as a QRS-ST junction (J point) elevation of ≥ 0.1 mV in two adjacent leads with either a slurred or a notched morphology in surface electrocardiography. Although it was first considered a benign finding, recent studies have shown a correlation between idiopathic ventricular fibrillation and ER pattern.

Objectives. The main objective of this study is to evaluate the prevalence of ER and its different types in healthy Iranian subjects in the city of Yazd.

Material and methods. This was a cross-sectional study from a large cohort enrolling 2,704 healthy adults between 35–75 years of age. All participants underwent 12 lead standard ECGs. One cardiologist and one electrophysiologist interpreted the ECGs and defined the presence or absence of ER and different ER types.

Results. ER pattern was present in 43 subjects (1.6%). There was a significant male preponderance in the ER positive group (97.7%). The most prevalent types of early repolarisation according to electrocardiography pattern was type I (53.5%) in all age groups, followed by type IV (30.2%), type III (11.6%) and type II (4.7%).

Conclusions. Knowing ER prevalence, its different types and high-risk patterns in a special population will help physicians guide patients with incidental ER pattern in their electrocardiography.

Key words: Brugada syndrome, electrocardiography, prevalence.

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Background

Early repolarisation (ER) is defined as a QRS-ST junction (J point) elevation of ≥ 0.1 mV in two adjacent leads with either a slurred or a notched morphology in surface electrocardiography [1]. Grant et al. first described this electrocardiographic pattern in 1951. Its general prevalence ranged between 1% and 13% in various studies [2]. The J point elevation is dynamic, and about 20% of the population with > 0.1 mV did not present this pattern in the follow-up [3].

This finding was previously thought to be completely benign, but the benign nature of this pattern was challenged in 2001. Since then, multiple studies have shown that some ER variants result in enhanced vulnerability to ventricular fibrillation and, rarely, sudden cardiac death (SCD) [4].

This ECG pattern is an inherited trait, at least in some families, compatible with an autosomal dominant pattern. Mutations in the inward sodium channel, which results in loss of function, have been linked to patients with ER [5]. When ER is associated with aborted cardiac arrest or ventricular arrhythmia in the absence of structural heart disease, ER is referred to as early repolarisation syndrome (ERS) [6].

ER in the lateral leads is considered benign and can be found in healthy persons. ER in the inferior or inferolateral leads is associated with moderate risk. The highest risk is related to ER in the inferolateral and right precordial leads. J point elevation in the right precordial leads is also known as the Brugada pattern. A horizontal or downsloping ST-segment following ER indicates a higher risk [7].

Objectives

Though ER is rarely associated with sudden cardiac death, it is advisable to investigate its prevalence in our population, be aware of its different types and follow up with patients to look for signs of rare but catastrophic consequences. We performed this study to find out the prevalence of ER and its types among healthy adult subjects in our region.

Material and methods

This was a cross-sectional study from a large cohort in the city of Yazd Shahedieh from March 2016 to March 2017. Healthy adults between 35–75 years of age were enrolled. Patients with low ECG quality, history of congenital or structural heart diseases, bundle branch blocks, arrhythmias, such as frequent PVC or AF, history of pacemaker implantation and wolf Parkinson white syndrome were excluded.

Data about the patient's gender, age and clinical history were collected. A physical examination was performed for

R/o structural heart disease. All participants underwent 12 lead standard ECGs (Avicenna ECG machine) in a resting supine position.

One cardiologist and one electrophysiologist interpreted the ECGs and defined the presence or absence of ER and different ER types. According to current criteria, the amplitude of the J point elevation should be at least 1 mm (0.1 mV) above the baseline level in two adjacent leads for diagnosis of ER. We classified patients with ER into five classes according to the ECG pattern (Figure 1). Type 1: Classic early repolarisation without J wave; Type 2: Notched J wave with ascending ST-segment; Type 3: Notched J wave with horizontal/descending ST-segment; Type 4: Slurred J wave with ascending ST-segment; Type 5: Slurred J wave with horizontal/descending ST segment [8].

The study was approved by the ethics committee. All patients completed an informed consent form. Data was analysed using SPSS for Windows (version 21, Chicago, Inc.). Data was presented as mean ± SD and percent (%). A value of $p < 0.05$ was considered statistically significant.

Ethical considerations

In this study, except for maintaining the anonymity of the patient in accordance with the Helsinki Treaty, it was assured to patients that their information would be confidential and would be used only for the purposes of the research. In addition, no additional costs were imposed upon the patients. This study was approved by the Ethics Committee of Sadoughi University of Medical Sciences, Yazd, Iran.

Results

2,704 Iranian individuals with a mean age of 49.4 years were enrolled in our study. Among them, 47.4% were men, and 52.3% were women. ER pattern was present in 43 subjects (1.6%), including 42 men and 1 woman. 2,661 subjects were without evident ER pattern, consisting of 1,247 men and 1,414 women during the study period (Table 1).

Table 1. Baseline characteristics of the study population

	Number (*n*)	Percent (%)
Gender		
male	1,289	47.7
female	1,415	52.3
Age		
> 50 years of age	1,507	55.7
≤ 50 years of age	1,197	44.3
ER pattern		
yes	43	1.6
no	2,661	98.4

There was a noticeable predominance of males in the ER-positive group (97.7%), especially in men below 50 years of age and who were physically active.

Type I was the most frequent ER pattern (53.5%) in all age groups, followed by type IV (30.2%), type III (11.6%) and type II (4.7%) (Figure 2).

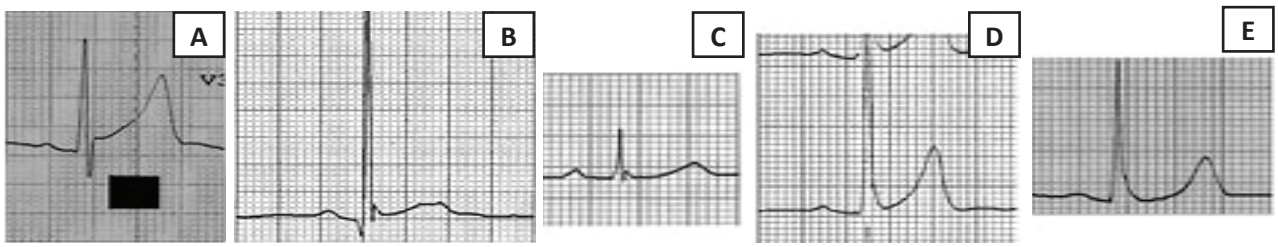

Figure 1. Type of ER classification according to the ECG pattern

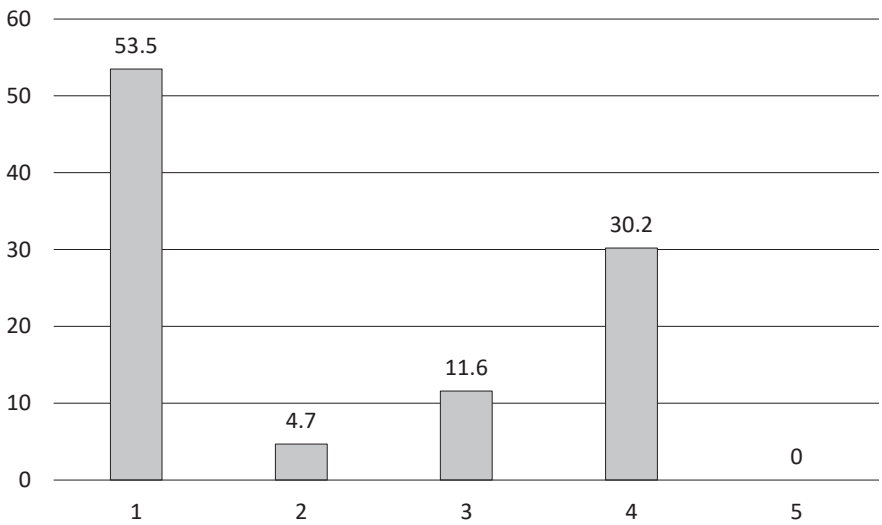

Figure 2. Prevalence of different early repolarisation syndrome (%)

A. early repolarisation without J wave. B. notched J wave with ascending ST segment. C. notched J wave with horizontal/descending ST segment. D. slurred J wave with ascending ST-segment. E. slurred J wave with horizontal/descending ST segment.

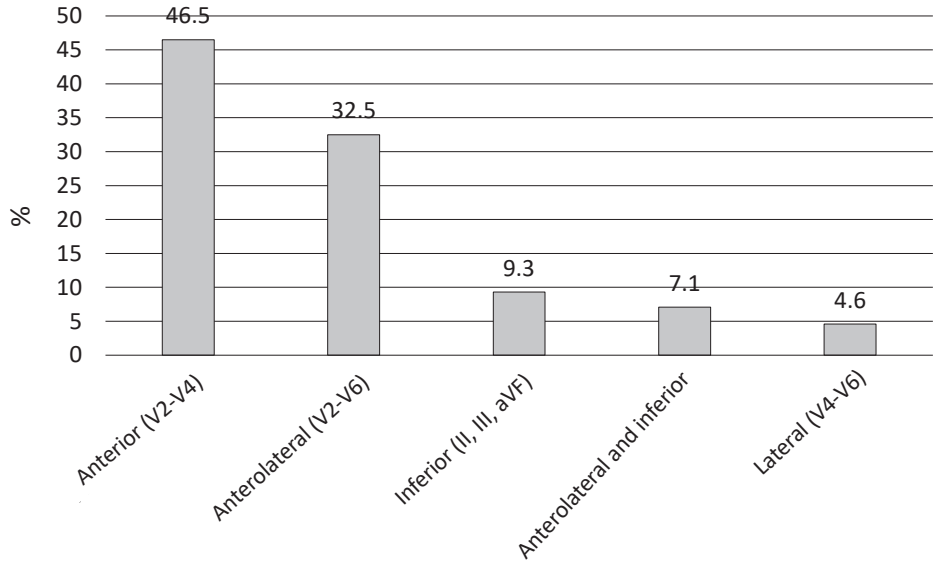

Figure 3. Leads with early repolarisation pattern (%)

At baseline, ER was predominantly positive in anterior leads (46.5%), followed by anterolateral (32.5%) and inferior leads (9.3%). Lateral leads showed the least frequent ER pattern (4.6%) (Figure 3).

During 40 months of follow up, we did not observe any hard event, including ventricular tachycardia or fibrillation and sudden cardiac arrest.

Discussion

Most patients with sudden cardiac arrest do not survive despite improvements in the medical system. The majority of these arrests are due to ventricular arrhythmia, including idiopathic ventricular fibrillation in a subject with a structurally normal heart. In a study conducted by Hissaguerre, ER pattern was more frequent among patients with idiopathic ventricular fibrillation than in control subjects (31% vs 5%; $p < 0.001$) [9].

The prevalence of ER pattern was 1.6% in the present study, whereas in recent literature, this prevalence varied from 3 to 24%. In a study by Mollazadeh et al., 9.6% of the healthy Iranian population had an ER pattern [10]. The overall prevalence of early repolarisation in the Nepalese population was 2.82% [11]. In another study involving 6,213 patients in Central Europe, the prevalence of ER was 13.3% [12]. This wide spectrum of estimated prevalence is probably due to the difference in population demographics (age, gender, race…) and ER definition.

Our results showed a predominance of males (97.7%) between ER-positive groups, which was observed in previous studies. It is noticeable that nearly all previous studies showed early repolarisation most frequently in males. In other studies, 75% of patients with early repolarization were male [13]. Haruta et al. proposed that outward repolarisation potassium current, such as IK1, IKr, IKs and Ito, are influenced by testosterone [14].

Previous data suggests that ER prevalence is age dependant and decreases with increasing age. We found that most ER-positive subjects were below 50 years of age, with a mean age of 44 years, which is far higher than in other studies. For example, in Klatsky's research, 60% of patients were younger than 40 years of age [15]. In another study performed by Barakoti, ER was much more common in men and in the age group 18–24 years, where the incidence was 8.64% [11]. This difference was due to the higher mean age of our participants (49 years of age), as we considered only subjects between 35–75 years of age.

ER pattern was mainly present in anterior leads (46.5%), followed by anterolateral leads (32.5%). In a study of 10,864 middle-aged subjects, Tikkanen et al. showed that ER was present in the inferior leads (3.5%) and in the lateral leads (2.4%) [16]. In another study performed by Mollazadeh et al. among the Iranian population, ER was predominantly positive in inferior leads (47.8%), followed by lateral leads (30.1%) [10]. These results show that ER patterns are different in various regions of one country. As shown in previous studies, each ER pattern carries a different risk of ventricular arrhythmia; thus, diagnosing ER types in different regions may help to discern and prevent sudden cardiac death.

Previous trials showed a higher risk of arrhythmic death in the population with early repolarisation syndrome. For example, in a 2010 investigation by Sinner et al., during a follow-up period of approximately 19 years, there was a higher risk of death from arrhythmia in subjects with inferior ERS [12]. We did not observe arrhythmic death during the 3.3 years that followed. This could be due to the higher prevalence of anterior ERS in our population, which has a more benign course, but a longer follow up is needed to confirm the exact nature of ERS in our region.

Conclusions

ERS is an infrequent cause of SCD among the general population, especially in young healthy adults without structural heart disease. Although there is no definite algorithm for risk stratification and preventive strategies in ERS, knowing ER prevalence, its different types and high-risk patterns in our population will help physician guide patients with incidental ER pattern in their electrocardiography. Large population-based research and follow-up cohorts are needed to provide exact information.

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Conflicts of interest: The authors declare no conflicts of interest.

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