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Characteristics of Early Repolarization Pattern in the Iranian Population

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Abstract

Background: The early repolarization pattern (ERP) has been considered a normal variant in electrocardiography (ECG) for a long time. Nevertheless, increasing evidence has demonstrated its association with adverse outcomes.
Objectives: The present study aimed to evaluate the prevalence of ERP in the Iranian general population and demonstrate its clinical and ECG correlates.
Methods: A cross sectional study, comprising 1424 consecutive healthy adult individuals, was conducted at two university based hospitals in Tehran, Iran in 2012-2013. The ERP prevalence, clinical characteristics and ECG morphology were investigated in volunteers.
Results: ERP was present in 136 out of 1,424 people (9.6%). Slurring comprised the most frequent morphology (41.2%) followed by notching. ERP was predominantly positive in inferior leads (47.8%) followed by lateral leads (30.1%). There was also a significant male preponderance in the ERP positive group (81.6%). The mean diastolic pressure was significantly lower in the ERP positive group versus the ERP negative group (77.3 + 7.9 mmHg vs. 78.8 + 10.5 mmHg) (P = 0.03). However, despite a lower systolic blood pressure in the ERP positive subjects (120.9 + 12.6 mmHg vs. 123.1 + 14.8 mmHg), the difference was not statistically significant (P = 0.06).
Conclusions: ERP was present in 9.6% of healthy Iranian individuals with a higher frequency in inferior leads and slurring as the most prevalent morphology. Additionally, there was a male preponderance and middle-aged trend for ERP.

Keywords: Electrocardiography, Sudden Cardiac Death, Ventricular Fibrillation

1. Background

Since its description, the early repolarization pattern (ERP) has been identified a normal electrocardiographic (ECG) variant (1-3). It is a common finding in normal populations, with general prevalence ranging between 1% and 25% (4-6). For a long time, ERP was only listed as a differential diagnosis for other heart conditions associated with ST elevation (7-9). However, data demonstrating a relationship between ERP and other serious conditions such as ventricular arrhythmia or sudden cardiac deaths are increasing (10, 11).

ERP has been defined as an elevation of the QRS-ST junction (J point) in at least two contiguous leads. The amplitude of J-point elevation should be at least 1 mm (0.1 mV) above the baseline level either as QRS slurring (a smooth transition from the QRS segment to the ST segment) or notching (a positive J deflection inscribed on the S wave) in the inferior leads (II, III, and aVF), lateral leads (I, aVL, and V4 to V6) or both (12). Its diagnosis could be challenging due to the effect of other variables such as age, sex, heart rate and the amplitude of the QRS complex (13-15). It is noteworthy that the presence of ERP in the inferior leads has been recently linked to ventricular fibrillation (10) and several mechanisms have been suggested as the underlying electrophysiologic pathology (7).

To our knowledge, there is no single study regarding ERP in the Iranian population. This is just an observational study and we tried to compare our findings with different studies that were done in other nationalities.

2. Objectives

The aim of this study was to determine the prevalence and characteristics of ERP in an Iranian healthy adult population and to investigate its clinical and electrocardiographic correlates.

3. Methods

A cross sectional study, recruiting a total of 1,424 consecutive healthy adults attending the health maintenance clinic for routine medical visits, was conducted in 2 university based Imam Khomeini medical complex and Shariati hospital in Tehran, Iran from May 2012 to September 2013. Health Iranian adults between the ages of 20 and 60 years old were included in the study. Patients with a history of congenital/structural heart diseases, any arrhythmia on electrocardiogram (ECG), Wolff-Parkinson-White syndrome, QRS $\geq$ 120 msec, and critical illness such as fever or signs of systemic infections were excluded. The Institutional Review Board of Tehran University of Medical Sciences approved the study protocol. Informed consent was taken from all subjects before the study.

Detailed clinical history was obtained from all the cases followed by physical examination; if necessary, echocardiography and exercise test were also performed to rule out any cardiovascular condition. All participants underwent a standard 12-lead ECG (Kenz-cardico 1210) in a resting supine position (paper speed: 25 mm/s, amplification: 10 mm/mV). The patients' baseline clinical variables such as history of hypertension (HTN), smoking, cardiac arrest, or familial history of sudden cardiac death (SCD) were recorded in data sheaths. Blood pressure was recorded with the digital sphygmomanometer Omron).

2 independent cardiologists interpreted ECGs and if a consensus was not reached or if the ECG record was not of high quality a digitized ECG was analyzed by a trained mechanical engineer using plot digitizer software.

According to the Haissaguerre criteria (10), the amplitude of J-point elevation should be at least 1 mm (0.1 mV) above the baseline level in the inferior leads (II, III, and aVF), lateral leads (I, aVL, and V4 to V6) or both (Figures 1 and 2). Variations in the ERP morphology are divided into notching (positive J point deflection over the S wave) and slurring (mild transition between QRS and ST segment).

Data were analyzed using SPSS for windows (version 21, Chicago, Inc.). Student t-test and Chi-square were used for continuous and categorical variables, respectively. Data was presented as mean $\pm$ SD and n (%). A $P < 0.05$ was considered statistically significant.

4. Results

The study population consisted of 1,424 Iranian individuals with a mean age of 43.6 $\pm$ 8.7 years (37.4% female and 62.6% male). HTN and cigarette smoking were present in 14.3% and 20.8% of the subjects, respectively. Five patients (0.35%) had a family history of SCD. ERP was present in 136 subjects (ERP+) (9.6%) in comparison with the ERP negative (ERP-) subjects (n = 1288). Slurring was the most frequent ERP morphology followed by notching. ERP was predominantly positive in inferior leads followed by lateral leads. All baseline characteristics of the study population (age, sex distribution, HTN, Cigarette smoking, mean systolic and diastolic blood pressure, Family history of SCD and ERP findings) are summarized in Table 1.

The mean age of ERP+ patients was higher than ERP- subjects (45 $\pm$ 8.4 vs. 43.4 $\pm$ 9 years, P = 0.05). Meanwhile, there was a significant male preponderance in the ERP positive group as compared with the ERP negative group (81.6% vs. 60.5%, $P < 0.0001$). The mean diastolic pressure was lower in the ERP positive group versus the ERP negative group (77.3 $\pm$ 7.9 mmHg vs. 78.8 $\pm$ 10.5 mmHg, P = 0.03). However, despite the lower systolic blood pressure in the ERP positive group than the ERP negative group, the difference was not statistically significant (P = 0.06). Other variables did not significantly differ between the two ERP + and ERP- groups (Table 2).

5. Discussion

5.1. Population Characteristics

5.1.1. Prevalence

The present study showed that the prevalence of ERP was 9.6% in the Iranian healthy adult population. There was also a male preponderance (12.5% of men vs. 4.5% of women had ERP in their ECG) and the ERP prevalence increased with age. Our demonstrated prevalence settles in a wide spectrum of estimates ranging from 2% to 31%, which is probably due to differences in the population demographics and ERP definition (4-6). In 2013, Maury P et al. (4) reviewed 30 studies conducted on subjects with early repolarization. They divided the studies to before and after awareness of a possible link between ERP and sudden death. They reported the prevalence to be between 0.9 and 31%. They attributed the great variation in the ERP prevalence to factors such as gender, age, race and level of activity in different studies. Macfarlane et al. (16) reviewed different ERP definitions and proposed an agreed definition, which requires the peak of an end-QRS notch and/or the onset of an end-QRS slur as a measure, denoted Jp, to be determined when an interpretation of early repolarization is being considered. He believed that the absence of a common universal definition led to the differences in various studies.

5.1.2. Gender

Our study, in accordance with previous findings, showed male preponderance of subjects who had ERP. Antzelevitch et al. (7) showed that Ito channel was the main

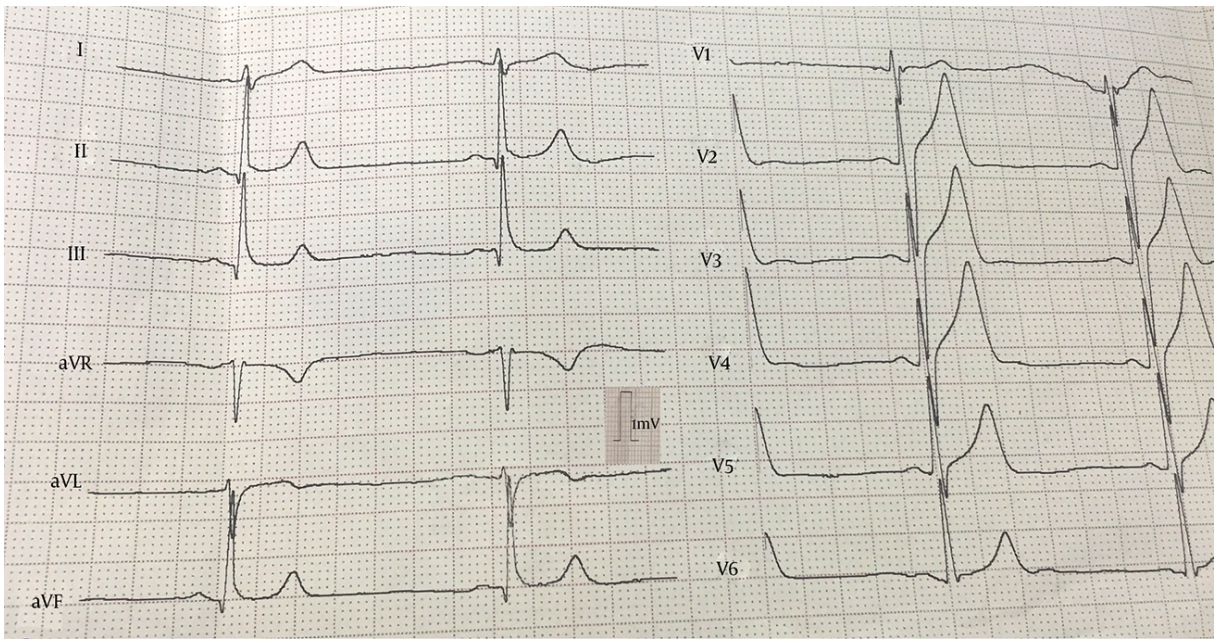
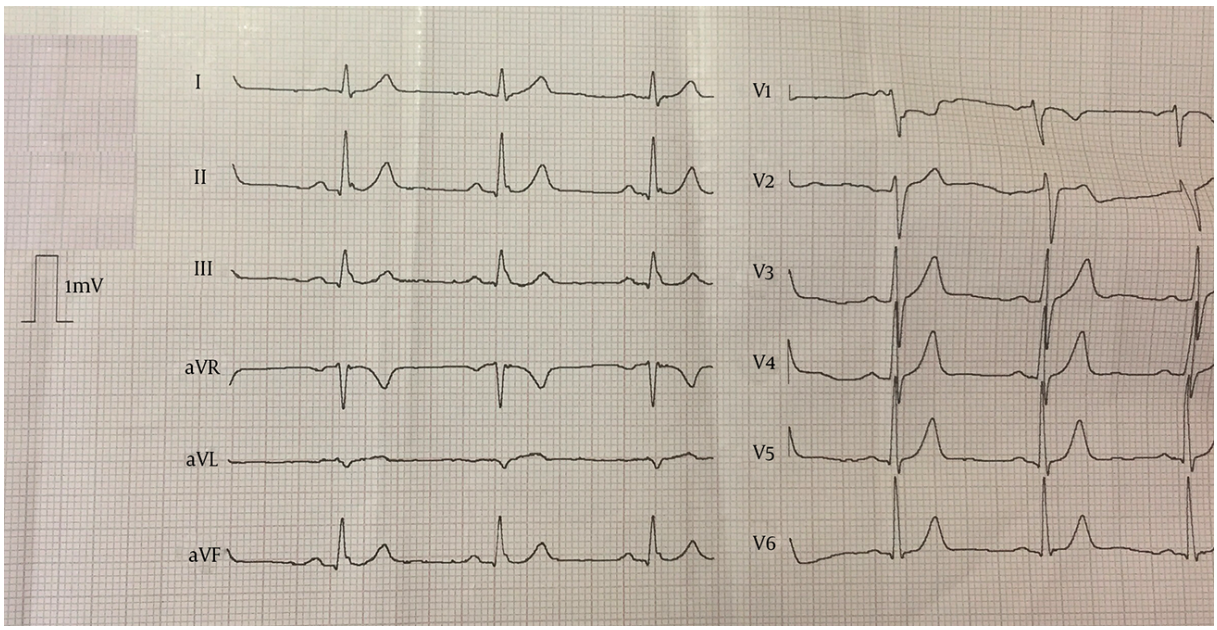


Figure 1. A 20-Year-Old Male Whose ECG Shows ERP (QRS Slurring) in the Inferior Leads

Figure 2. An 18-year-Old Male Whose ECG Shows ERP (QRS Notching) in the Leads II, avF and Slurring in Lead III



This patient was categorized in the notching group.

contributor for ERP in ECG. This channel is more prominent in young men and this finding is in accordance with our findings. Haruta et al. (15) proposed that testosterone might increase the outward repolarizing potassium currents such as IK1, IKr, IKs and Ito while inhibiting the inward L-type calcium current.

Table 1. Baseline Demographics, Clinical and Electrocardiographic Characteristics of Study

Variables	Patients (%)
Age, y	43.7 ± 8.9
Sex	
Female	533 (37.4)
Male	891 (62.6)
Hypertension	203 (14.3)
Cigarette smoking	296 (20.8)
Mean systolic blood pressure, mmHg	122.9 ± 14.7
Mean diastolic blood pressure, mmHg	78.7 ± 10.3
Family history of SCD	5 (0.35)
ERP morphology	n = 136
Slurring	56 (41.2)
ECG leads with ERP	n = 136
lateral	41 (30.1)
Inferior	65 (47.8)

Table 2. Comparison of Study Variables Between ERP and Non-ERP Groups

	ERP Positive Group (n=136)	ERP Negative Group (n=1288)	P
Age, y	45 ± 8.4	43.4 ± 9	0.05
Sex			< 0.0001
Male	111 (81.6)	780 (60.5)	
Female	25 (18.4)	508 (39.5)	
Hypertension	13 (9.6)	190 (14.8)	0.09
Cigarette smoking	33 (24.3)	263 (20.4)	0.30
Mean systolic blood pressure, mmHg	120.9 ± 12.6	123.1 ± 14.8	0.06
Mean diastolic blood pressure, mmHg	77.3 ± 7.9	78.8 ± 10.5	0.03

5.1.3. Age

The results of many studies suggest that the ER prevalence also depends on age, decreasing as age increased (4, 14, 15). In our study, the ERP+ subjects were older (although with a borderline statistical significance: P = 0.05). This can be interpreted as the age distribution of ERP in the Iranian population does not follow the age rule as many other countries. Another point is that the mean age of our study population was 43 years old, which is far higher than the mean age of the participants in other studies; for example, in a study done by Klatsky (12), only 30% of the patients were older than 40 years of age.

5.1.4. Race/ Nationality

Mansi et al. (17) studied 597 healthy adults (58% men, 15 - 60 years) and found that 3.5% of them had ERP on ECG without a significant difference amongst the ethnic groups (Arabs, Indians and Caucasians). The rate of ERP in healthy young men of northeastern Thailand was 10.3 (18). ERP pattern was prevalent in 9.6% of our patients in Iran. ERP prevalence in normal populations, as historically published, ranged from 1%-34%; our finding is in the middle of this range. Our study did not evaluate the ERP in immigrants to Iran. Our study presented the first report of the rate of ERP in Iran and the Middle East region.

5.2. Associated Factors

In a large population-based cohort, Noseworthy et al. (5) showed that a higher ERP prevalence was seen in subjects with lower systolic and diastolic blood pressure. Multivariate regression model showed that only a lower systolic blood pressure was an independent predictor of ERP+.

In our study, the mean systolic blood pressure was lower in ERP+ patients although the difference was not statistically significant. However, a lower diastolic blood pressure was associated with a higher ERP prevalence. We think that it may be due to the heightened vagal tone that increased the Ito current and lead to ERP in ECG and lower blood pressure in this healthy population.

Consistent with the literature, we did not find a significant relationship between ERP and a history of smoking, cardiac arrest, SCD and a family history of SCD (3, 5), which could result from the low prevalence of these variables in our study population.

5.3. ECG Morphology

ERP was mainly present in the inferior leads followed by lateral leads (47.8% vs. 30.1%). Moreover, slurring was observed in 41.2% of all ERP cases followed by notching seen in 33.1% of the individuals. In a study of 10,864 middle-aged subjects, similar to our study population, Tikkanen et al. (14) assessed the prevalence of ERP. Their analysis showed that ERP was present in 5.8% of the subjects, 3.5% in the inferior leads and 2.4% in the lateral leads. Klatsky et al. (12) discovered that slurring was the most common ECG finding.

5.4. Limitation of Study

Although we evaluated 1,424 patients, many population-based studies have assessed about 5000 to 10000 subjects. Nevertheless, as the first report of the ERP prevalence in Iranian adults, this study paved the way for future studies in this population to more concisely evaluate the long-term outcome(s) associated with ERP. Although inter-observer variability was shown to be acceptable, measurements of ER sometimes remain difficult and probably sometimes unreliable especially at 25 - mm/second-paper speed on ECG. If more reliability would be reached using higher paper speed (100 mm/second) or automated interpretation deserve further studies. Considering that there were two observers in our study, it would be more accurate to use agreement indices such as Kappa coefficient in cases of discordance between the two observers.

5.1. Conclusion

Our study showed ERP in 9.6% of the healthy Iranian individuals, with a higher frequency in inferior leads and slurring as the most prevalent morphology. Additionally, there was a male preponderance and middle-aged trend for ERP. These patients had a lower systolic and diastolic blood pressure. Early repolarization pattern is a common finding in ECGs of many subjects and its prevalence is needed to be identified in the Iranian population. Its association with sudden cardiac death is proved; however, SCD occurs just in minority. This benign pattern should be differentiated from the more important patterns such as myocardial infarction or Brugada pattern.

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