Research Article

Interventional Cardiology

Heart rate variability in children and adolescents with incidentally found early repolarization pattern

Ahmet Fatih Arinc[1*], Sule Arici[2], Figen Akalin[2]

[1]Department of Pediatrics, Cengiz Gokcek Obstetrics, Gynecology and Children's Hospital, Gaziantep, Turkey;

[2]Department of Pediatric Cardiology, Marmara University, Istanbul, Turkey

*Author for correspondence:
Ahmet Fatih Arinc, Department of Pediatrics, Cengiz Gokcek Obstetrics, Gynecology and Children's Hospital, Gaziantep, Turkey, E-mail: arincahmetfatih@gmail.com

Received date: 04-Mar-2024, Manuscript No. FMIC-24-128422;
Editor assigned: 06-Mar-2024, PreQC No. FMIC-24-128422 (PQ);
Reviewed date: 21-Mar-2024, QC No. FMIC-24-128422;
Revised date: 29-Mar-2024, Manuscript No. FMIC-24-128422 (R);
Published date: 05-Apr-2024, DOI: 10.37532/1755-5310.2024.16(S22).555

Abstract

Aim: Early Repolarization (ER) on Electrocardiogram (ECG) was considered as a benign finding until the emergence of patients with fatal arrhythmia and sudden death. Its importance in childhood is unknown. We investigated the risk of premature death and arrhythmia in children with incidentally found early repolarization using ECG and heart rate variability parameters.

Method: The study group consisted of healthy children between 6-18 years of age with early repolarization and the control group without early repolarization. All the children were evaluated by medical history, physical examination, echocardiography, 12-lead ECG, and 24-hour Holter. ECG parameters; P wave, QTc, JT, Tp-e dispersion; "Time-domain" parameters, SDANN, SDNN-i, r-MSSD, pNN50 and "Frequency-domain" parameters HF, LF, LF/HF were obtained.

Results: Heart rate was lower in the study group (p=0.020). There was no difference between the groups regarding P, QTc, and Tp-e dispersion. JT dispersion was high in the study group (p=0.025). The interventricular septum was thicker in the study group (p=0.030). LF/HF (p=0.045), awake HF, and LF/HF (p=0.046, p=0.036) were higher in the study group. Heart rate variability has increased in favor of parasympathetic activity in males. Those with J waves in the inferolateral leads had higher heart rates and lower SDNN and VLF during sleep than those with only in the inferior lead (p=0.049, p=0.040, and p=0.040).

Conclusion: Incidental early repolarization in children did not indicate increased risk for cardiac events. It was related to parasympathetic activity, inferolateral early repolarization may be relatively riskier.

Keywords: Early repolarization • Dysrhythmia • Heart rate variability

Highlights

1. There were no significant differences in P wave dispersion, QT dispersion, QTc dispersion, or Tp-e dispersion between the study and control groups. This suggests that healthy children with incidentally discovered ERP do not have an increased risk of atrial or ventricular arrhythmia, ventricular fibrillation, or sudden death.

2. Findings in boys mirror those in the adult age group in the literature, indicating that parasympathetic system dominance is more pronounced in boys. This dominance in HRV may be linked to physical activity, sports, and a reduced risk of sudden death.

3. Inferior ER patterns are associated with higher parasympathetic activity dominance compared to inferolateral ER patterns, as indicated by our study's HRV data. Evidence in the literature suggests that the inferior ER pattern is associated with a higher malignancy.

4. We found no evidence of increased arrhythmia or sudden cardiac death risk in healthy children who were coincidentally diagnosed with an ER pattern.

Introduction

Early Repolarization (ER) was considered as a benign Electrocardiography (ECG) finding previously, however, due to reported cases with fatal arrhythmias and sudden death, Early Repolarization Syndrome (ERS) has been defined and draw attention to this finding. It is even more controversial in children and young adults in which ER is more common. It is not known whether it is an indication of increased risk for cardiovascular disease, arrhythmia or sudden death; or just a benign ECG change with no clinical importance [1].

ER is also called as J point elevation or J wave. ER is defined as a prominent and well-defined positive deviation at the beginning of the ST segment following the positive QRS complex, a notch found just after the QRS complex, or elevation of the J-point for at least 1 mm (0.1 mV) in two consecutive leads relative to the isoelectric line [2]. The prevalence of ER in adults varies between 1% to 30%, depending on age, race, gender, and the intensity of physical activity. Very few studies are available in childhood, however, Maury, et al., has reported a frequency of 23.6% [3].

Electrocardiographic parameters such as QT dispersion, T wave dispersion, P wave dispersion, or Heart Rate Variability (HRV) obtained from 24-hour Holter recordings are used to evaluate the risk of arrhythmia and sudden death in many disease groups [4]. Decreased HRV is generally accepted as an indication of increased risk for cardiac death.

In our study, we evaluated the children with ER who admitted to our outpatient clinics with any complaints and found to have no cardiac disease by history, physical examination, telecardiography, echocardiography and 24-hour-Holter recordings; and compared to their peers without ER. We searched for an increased risk for arrhythmia or sudden death using ECG criteria and HRV in both groups.

Materials and Methods

The study group consisted of healthy children between 6 and 18 years of age, admitted to outpatient clinics with ER on ECG. The control group consisted of healthy children of the same age group who did not have ER on ECG. In both groups; medical history, physical examination, ECG, and Echocardiography were performed, and 24-hour Holter recordings were obtained. None of the children in either group had any chronic disease or abnormal physical examination findings. Children with any cardiac, neurological, or systemic disease, who were taking any medication, or whose parents didn't agree to participate in the study were excluded. The study was approved by the local ethical committee (Date 02.10.2020, number 09.2020.1127).

Clinical evaluation

A detailed medical history was taken of the children included in the study, including their reasons for admission, exercise capacity (NYHA classification), whether they had palpitations, fainting, chest pain, and their level of physical activity or sports participation. Family history was taken for heart diseases (early coronary artery disease, myocardial infarction, and congenital heart disease), sudden death, and arrhythmia history.

In addition to a detailed full body examination, weight, height, heart rate, and blood pressure were also checked. Body Surface Area (BSA) and Body Mass Index (BMI) were calculated, and abnormal heart sounds or murmurs were recorded.

Electrocardiography

In both groups, 12-lead ECG was obtained using the GE MAC 2000 ECG machine at rest at 25 mm/sec speed and 10 mm/mV amplitude.

Heart rate, P wave axis, QRS axis, P wave maximum duration, P wave minimum duration, P wave dispersion, QTc interval, QTc maximum duration, QTc minimum duration, QTc dispersion, JT minimum and maximum durations, JT dispersion, Tp-e interval, Tp-e interval maximum, Tp-e interval minimum, Tp-e dispersion were calculated. The Bazett formula was used to calculate the QTc [5]. In the study group, those with J waves only in leads DII, DIII and aVF were considered inferior, those with J waves only in leads V4-5-6 were considered lateral, and those with J waves in all of the leads mentioned above were considered inferolateral ER.

Initially, the electrocardiographic parameters were compared between the study and the control groups. In order to investigate the effect of puberty, the study and the control groups were divided into two groups; the patients and controls between 6 to 12 years of age were accepted as prepubertal and the children between 13 to 18 years of age as postpubertal. These two groups were also compared to their healthy peers separately in terms of the ECG parameters. To evaluate the effect of gender, the boys and girls in the study group were compared. In addition, the ECG parameters of the children with J waves in inferior leads and those with J waves in inferolateral leads were compared with each other to investigate the differences according to the leads with J waves.

Echocardiography

Transthoracic echocardiography was performed using a Philips EPIC7 Echocardiography Machine (Philips Medical Systems, Andover, MA, USA, serial number US318B0028) equipped with an S5-2 transducer to exclusion of underlying structural heart disease. Interventricular Septum diastolic thickness (IVSd), Left Ventricular End-Diastolic diameter (LVDd), Left Ventricular

Posterior Wall diastolic thickness (LVPWd), Aortic root (Ao), diastolic Left Atrial Diameter (LAD) were measured by M-mode. The Shortening and Ejection Fractions (SF and EF) were calculated. E wave velocity (mitral E), a wave velocity (mitral A), Deceleration Time (DecT), and Isovolumetric Relaxation Time (IVRT) were measured using PW Doppler mitral inflow. Flow velocities of the aorta, pulmonary artery, and descending aorta were measured.

24-hour Holter ECG

In both groups, the highest and lowest heart rate, mean heart rate, number of supraventricular premature beats, number of ventricular premature beats, presence or absence of supraventricular or ventricular tachycardia, AV block, and sinus pause detected throughout the day were recorded.

Time domain parameters SDNN, SDANN, SDNNi, rMSSD, and pNN50 and frequency domain parameters LF, HF, VLF, LF/HF ratio were obtained from 24-hour-Holter recordings after careful removal of artifacts and early beats using cardio scan software system (Powered by DM Software Inc. USA, version 11.5.0076a).

HRV parameters obtained from 24-hour-Holter ECG findings were compared between the study and the control groups, in the study and the control groups between the ages of 6 and 12 years (including 12 years), in the study and the control groups between the ages of 13-18 years, between the boys and the girls in the study group, and between the patients with inferolateral ER and the patients with inferior ER in the study group. HRV parameters were also obtained during awake and sleeping hours (awake was accepted as between 08:00 am to 12:00 pm; and sleep between 00:00 to 08:00 am); SDNN, rMSSD, pNN50 from time-domain measurements and LF, HF, VLF, and LF/HF parameters from frequency-domain measurements were examined. In addition, minimum, maximum, and average heart rate and SDNN-i parameters were also compared.

Statistical analysis

Statistical analysis was performed using SPSS software (version 22.0, SPSS, Inc, Chicago, IL, USA). After a variance analysis test; Man-Whitney-U test was used for comparing the data without homogeneous distribution such as P wave axis, PR interval, P wave duration, P wave duration maximum, P wave duration minimum, P wave dispersion, QRS duration, JT dispersion, Tp-e interval time, Tp-e interval maximum, Tp-e interval minimum, Tp-e dispersion; Unpaired T-test was used for the rest of the parameters showing homogeneous distribution. Man-Whitney-U test was used for comparing the groups with small number of subjects such as the prepubertal and postpubertal patients and the boys and the girls. The study data were transferred to the tables as mean and standard deviation, range, and p values for those groups which underwent the parametric tests and as median, percentile 25-75, and p values for those in which the non-parametric tests were applied. P ≤0.05 were considered as statistically significant. Artificial intelligence (AI) assisted technologies didn't used in this study.

Results

The ECGs of 332 healthy children between the ages of 6 to 18 who were admitted to the pediatrics or pediatric cardiology outpatient clinics without any cardiac or systemic chronic disease were scanned. Early repolarization was detected in 32 of them (9.6%) and they were included in study group. The mean age of the study group was 14.09 ± 3.0 years, there were 13 girls (40.6%) and 19 boys (59.4%). The control group consisted of 30 healthy children between 7 and 18 years of age, without ER on ECG. The mean age of the control group was 13.4 ± 3.4 years, there were 12 girls (40%) and 18 boys (60%). There was no statistically significant difference between the study and control groups in terms of gender or age (p>0.05).

The reason for admission was a routine check-up in 21.8% (n=7) of the study group and 56.6% (n=17) of the control group. The other children admitted mostly non-cardiac non-specific complaints.

Exercise capacity was normal (NYHA Class I) in all the subjects in both groups. History revealed, palpitation in 4 children (12.5%) in the study group and 2 children (6.7%) in the control group; chest pain in 7 children (21.9%) in the study group and 8(26.7%) children in the control group; syncope in 4 and 2 children respectively. There was no significant difference in terms of symptoms between the groups. None of the children were elite athletes, however, the number of children performing physical training at least for three days in a week lasting more than one hour was 5(15.6%) in the study group and 3(10%) in the control group.

Family history of heart disease among the groups significantly differed (p=0.029). The study group (9.4%, n=3) had a lower family history of heart disease than the control group (33.3%, n=10).

There was no significant difference between the study and control groups in terms of family history of arrhythmia, defibrillator implantation, and congenital deafness (p>0.05).

No statistically significant difference was found in terms of weight, height, BMI, BSA, heart rate, systolic and diastolic Blood Pressure (BP) (p>0.05) between the groups (Table 1).

The 12-lead surface ECG was normal in all children except the ERP. Heart rate was significantly lower in the study group (p=0.020). QRS axis has turned rightward in the study group (p=0.001); however, it was within the normal range for age in both groups. JT interval dispersion was longer in the study group than in the control group (p=0.025). There was no significant difference between the groups regarding other ECG findings (Table 2).

J wave was observed only in inferior leads in 10 (31.3%) children, only in lateral leads in two (6.3%), and in both lateral and inferior leads (inferolateral) in 10 (62.5%). Elevated ST segment was in ascending form in all children, none of them had a descending ST segment.

In comparison of prepubertal and postpubertal children; the children with ER between 6-12 years had a significant p-axis deviation towards the left, higher JT dispersion, and lower Tp-e dispersion comparing the control group (p=0.008, p=0.035, p=0.043 respectively). However, all were within the normal range. In children between 13-18 years of age; the study group had significantly lower heart rate (p=0.021) and the QRS axis turned towards the right (p=0.006), however, the QRS axis was within the normal range in both groups.

None of the ECG parameters differed between the boys and girls. Similarly, no significant difference was found in terms of these ECG parameters between the children with J waves on inferior leads or inferolateral leads (p>0.05).

Echocardiography measurements of all children in the study and control groups were within normal range. However; Interventricular Septum Diastolic Thickness (IVSd) was significantly thicker in the study group (0.84 ± 0.19 cm in the study and 0.75 ± 0.13 cm in the control group, p=0.030).

24-hour Holter ECG findings showed LF/HF ratio was significantly higher in the study group (p=0.045) (Table 3). When day (awake) and night (sleep) HRV values were analyzed separately, a significantly lower awake HF (p=0.046) and a higher awake LF/HF ratio (p=0.036) were found in the study group. No significant difference was found in terms of other sleep and awake HRV parameters (p>0.05) (Table 4).

24-hour Holter ECG parameters of children between 13-18 years of age revealed a significantly lower minimum heart rate in the study group (p=0.044); LF/HF ratio during daytime (awake) was significantly higher in the study group (p=0.028). 24 hour Holter findings and HRV parameters during awake and sleeping hours did not differ between study and control groups in younger children.

In comparison of boys and girls; minimum heart rate and mean heart rate were significantly lower in boys (p=0.049 and p=0.008). In addition, SDNN-i, LF, and VLF were significantly higher in boys (p=0.022, p=0.030, and p=0.010). Also; in boys SDNN, LF, and VLF were higher during day-time (awake) (p=0.037, p=0.016, and p=0.016); SDNN and VLF were higher during sleep (p=0.014 and p=0.032) comparing the girls (Table 5).

When the children with inferior J waves to the children with inferolateral J waves were compared; the mean heart rate was higher in children with inferolateral J waves (p=0.049). SDNN and VLF increased in children with inferior J waves (p=0.040 and p=0.040).

Table 1: Comparison of clinical findings between study and control groups.

Parameters	Study (n=32)		Control (n=30)		P
	Mean ± SD	Range	Mean ± SD	Range	
Weight (kg)	54.5 ± 18.7	19-121	50.9 ± 18.1	19-98	0.438
Length (cm)	158 ± 5.0	112-184	154.7 ± 18.6	110-189	0.413
BMI (kg/m²)	21.2 ± 4.9	12.6-42.9	20.5 ±4.2	14.4-31.2	0.548
BSA (m²)	1.53 ± 0.32	0.77-2.26	1.45 ± 0.32	0.76-2	0.323
Heart rate (/pm)	85.8 ± 14.4	55-155	91.8 ± 16	65-130	0.125
Sistolic BP (mmHg)	112.3 ± 11	93-139	114 ± 9.5	100-140	0.521
Diastolic BP (mmHg)	72.8 ± 8.1	60-90	74.9 ± 7.6	60-90	0.3
Cardiothoracic index	0.4 ± 0.04	0.33-0.48	0.4 ± 0.04	0.32-0.49	0.916

Note: BMI: Body Mass Index; BSAL: Body Surface Area; BP: Blood Pressure; n: Number; SD: Standart Deviation; p<0.05: statistically significant.

Table 2: Comparison of electrocardiography parameters between study and control groups.

Parameters	Study (n=32)			Control (n=30)			P
	Median	p(25)	p(75)	Median	p(25)	p(75)	
P axis (°)	45	45	60	60	45	60	0.134
PR interval (msec)	125	120	140	120	120	140	0.379
P duration (msec)	80	80	80	80	60	80	0.067
P duration (max) (msec)	80	80	81.65	80	80	80	0.085
P duration (min) (msec)	60	46.6	60	60	40	60	0.882

P dispersion (msec)	20	20	33.3	20	20	20	0.319
QRS duration (msec)	80	80	80	80	80	90	0.974
	Mean ± SD		**Range**	**Mean ± SD**		**Range**	
QRS axis (°)	69.9 ± 7	55-87	63.1 ± 8.5	46-79	0.001	65-130	65-130
QTc (msec)	376.3 ±26.1	330-433	382 ± 24.3	333-428	0.35	65-130	65-130
QTc (max) (msec)	384.9 ± 26.8	345-440.6	393.8 ± 26.5	343-438	0.196	65-130	65-130
QTc (min) (msec)	355.6 ± 25.7	320-410	361.1 ± 27.3	300-410	0.419	65-130	65-130
QTc dispersion (msec)	29.2 ±12.9	7.6-56	32.7 ± 15.2	Aug-81	0.343	65-130	65-130
Heart rate (/pm)	77.8 ± 14.6	48-115	87.5 ± 16.9	55-128	0.02	65-130	65-130
JT (msn)	268.7 ± 31.6	200-360	268 ± 25.5	24-320	0.919	65-130	65-130
JT (max) (msec)	286.5 ± 40	200-400	280 ± 27.2	240-340	0.458	65-130	65-130
JT (min) (msec)	254.6 ± 41.3	160-360	255.5 ± 25.5	220-320	0.941	65-130	65-130
	Median	**p(25)**	**p(75)**	**Median**	**p(25)**	**p(75)**	
JT dispersion (msec)	33.3	20	40	20	20	20	0.025
Tp-e (msec)	60	60	80	60	60	80	0.659
Tp-e (max) (msec)	66,6	60	80	60	60	80	0.7
Tp-e (min) (msec)	60	40	60	40	40	60	0.147
Tp-e dispersion (msec)	20	18.3	20	20	20	20	0.158

Note: P axis: P wave axis; QRS axis: QRS wave axis; QTc: Corrected QT interval; JT: JT interval; Tp-e: Tp-e interval; max: Maximum; min: Minimum; n: number; SD: Standard deviation; p (25): 25th percetile; p (75): 75th percentile; p<0.05: Statistically significant.

Table 3: Comparison of 24-hour Holter's parameters between study and control groups.

Parameters	Study (n=32)		Control (n=30)		P
	Mean ± SD	**Range**	**Mean ± SD**	**Range**	
Minimum heart rate (bpm)	47.8 ± 9.9	30-82	49.2 ± 6.7	37-74	0.525
Maximum heart rate (bpm)	155.2 ± 16.4	114-183	161.8 ± 15.2	137-192	0.109
Average heart rate (bpm)	82 ± 12	56-117	82.8 ± 9.2	63-99	0.771
SDNN	157.3 ± 46.9	72-227	161.4 ± 47.4	94-260	0.732
SDANN	140.3 ± 48.3	62-208	140.9 ± 44.5	80-236	0.961
SDNN-i	70.3 ± 19.1	31-112	73.2 ± 16.7	46-115	0.54
r-MSSD	43.9 ± 14.6	Oct-76	47.2 ± 16.5	25-103	0.405
PNN50	19.6 ± 10.4	0-44	21.5 ± 9.9	May-50	0.472
LF (Hz)	1082 ± 453.9	192.7-1911.4	1164.8 ± 466.4	431.3-2227.2	0.482
HF (Hz)	562.4 ± 265.3	33.7-1116.6	701.8 ± 316	189-1376.4	0.064
LF/HF	2.2 ± 1.00	0.77-5.71	1.79 ± 0.62	0.99-3.96	0.045
VLF (Hz)	3463.6 ± 1966.7	687.5-9368.4	3387 ± 1584.9	1245.8-7557.6	0.867

Note: SDNN: Standart deviation of the interbeat intervals of normal sinüs beats; SDANN: Standart deviation of the average NN intervals for each 5 minute segment of the 24-hour HRV recording; SDNN-i: The mean of the standart deviations of all the NN intervals for each 5 minutes segment of 24-hour HRV recording; r-MSSD: Root mean square of the successive differences between normal heartbeats; pNN50: Proportion of the adjacent R-R intervals differing by more than 50 ms; LF: Low frequency; HF: High frequency; LF/HF: Low frequency/High frequency ratio; VLF: Very low frequency; Hz: Hertz; bpm: beats per minute; n: number; SD: Standart deviation; p<0.05: Statistically significant.

Table 4: Comparison of sleep-awake Holter ECG parameters of study and control groups.

Parameters	Study (n=31)		Control (n=29)		P
	Mean ± SD	**Range**	**Mean ± SD**	**Range**	
Awake SDNN	129.3 ± 3.9	74-191	139.3 ± 43.8	76-243	0.33
Awake r-MSSD	37.8 ± 13.5	15-71	41.4 ±15.1	22-89	0.33
Awake LF(Hz)	990.2 ± 433.9	250.2-1849.6	1092 ± 461.2	398.1-2225	0.374
Awake HF (Hz)	423.2 ± 224.4	74.4-964.2	549 ± 260.4	122.3-1105.5	0.046

Awake LF/HF	2.76 ± 1.25	0.71-6.22	2.17 ± 0.89	1.16-5.61	0.036
Awake VLF (Hz)	2888.2 ± 1769.7	567-9042.7	3022.7 ± 1503.7	1122.1-7092.8	0.749
Sleep SDNN	144.9 ± 51.8	50-236	129.1 ± 50.9	55-283	0.241
Sleep r-MSSDc	58 ± 20.6	17-96	58.9 ± 23.3	29-134	0.871
Sleep PNN50	32.3 ± 15.9	Jan-60	32.7 ± 15.3	Aug-68	0.921
Sleep LF (Hz)	1289.1 ± 542.3	250.1-2229.6	1306 ± 567.6	412.3-2747.3	0.907
Sleep HF (Hz)	848.4 ± 429.8	73.9-1969.5	997.5 ± 546.6	277.9-2279.5	0.244
Sleep LF/HF	1.79 ± 0.84	0.71-4.54	1.47 ± 0.57	0.66-2.74	0.097
Sleep VLF (Hz)	4640.3 ± 2693.2	938.4-9990.3	4063.7 ± 2069.2	986.3-9268.5	0.355

Note: SDNN: Standart deviation of the interbeat intervals of normal sinus beats; r-MSSD: Root mean square of the successive differences between normal heartbeats; pNN50: proportion of the adjacent R-R intervals differing by more than 50 ms; LF: Low frequency; HF: High frequency; LF/HF: Low frequency/High frequency ratio; VLF: Very low frequency; Hz: Hertz; n: number; SD: Standart deviation; p<0.05: Statistically significant.

Table 5: Comparison of 24-hour Holter ECG parameters between genders in the study group.

Parameters	Boys (n=19)			Girls (n=13)			P
	Median	p(25)	p(75)	Median	p(25)	p(75)	
Minimum heart rate (bpm)	43	39	51	51	43	59	0.049
Maximum heart rate (bpm)	154	144	163	163	154	173	0.099
Average heart rate (bpm)	77	71	83	86	82	94	0.008
SDNN	161	134	204	142	88	184	0.136
SDANN	134	116	194	123	78	185	0.158
SDNN-i	77	62	94	64	57	66	0.022
r-MSSD	47	38	57	43	26	48	0.195
PNN50	21	14	28	20	6	23	0.362
LF (Hz)	1350.4	835.9	1559.2	883.9	641.3	1028.8	0.03
HF (Hz)	596.2	489.3	817.1	548.2	266.7	564.2	0.136
LF/HF	2.11	1.71	2.53	1.82	1.65	2.4	0.596
VLF (Hz)	3985.3	2378.2	5713	2488.5	1251.1	2884.4	0.01

Note: SDNN: Standard deviation of the interbeat intervals of normal sinus beats; SDANN: Standard deviation of the average NN intervals for each 5 minute segment of the 24-hour HRV recording; SDNN-i: The mean of the standard deviations of all the NN intervals for each 5 minutes segment of 24-hour HRV recording; r-MSSD: Root mean square of the successive differences between normal heartbeats; pNN50: Proportion of the adjacent R-R intervals differing by more than 50 ms; LF: Low frequency; HF: High frequency; LF/HF: Low frequency/High frequency ratio; VLF: Very low frequency; Hz: Hertz; bpm: beats per minute; n: number; SD: Standard deviation; p<0.05: Statistically significant.

None of the patients or controls had rhythm abnormalities other than rare isolated supraventricular or ventricular premature beats.

Discussion

Early repolarization is defined as the presence of a J wave in two or more consecutive leads or elevation of the J point on the ECG. The "Early Repolarization Pattern (ERP)" was previously considered as benign. The recent discovery of cases with polymorphic ventricular tachycardia and idiopathic ventricular fibrillation has led to the definition of "Early Repolarization Syndrome (ERS)" [6]. After the discovery of Brugada syndrome with similar ECG changes in anterior precordial leads; it became even more controversial. Furthermore, some studies showed an association between early repolarization and sudden cardiac death in the adult population.

Most studies are community-based and conducted in adults, and some cases with sudden death had comorbid conditions. Although ERP is more frequent in children, adolescents, young adults, and athletes; the importance of an incidentally found ER in terms of cardiovascular disease, sudden death, or fatal arrhythmia is unknown. This is the first study investigating cardiac risk using ECG and HRV in this group.

The frequency of the ERP varies according to study design, population recruited, and ER definition. The prevalence in adults ranges between 1% to 13% [7]. Maury, et al., [3], have found the incidence as 23.6% in children and 22%-44% in athletes. The rate of ER on ECGs in our study was 9.6%. This may be due to the exclusion of patients with findings suggestive of cardiac disease in our study. The study of Maurym, et al., [3] included African-Americans in which ER is more prevalent. ER is most common in the second decade of life [8]; which was the case in our study (Mean age=14.09 ± 3.0).

ER is more common in boys, reported up to 75%. Similarly, the ratio of boys was higher in our study (59%). Experimentally, testosterone has been shown to increase outward potassium currents and decrease ICaL current in myocytes, which may increase the size of the action potential notch, and cause a voltage difference between the endocardium and epicardium; the ST segment and J point are elevated [9,10].

Cardiac complaints were very rare and exercise capacity was normal in our group (28.2%) as a result of the study design; since the patients with cardiac findings were excluded. This rate is about 55% in other studies [11].

The heart rate was lower and interventricular septal thickness was higher in the study group. These may be due to increased physical fitness. Elite athletes were not included, however, 15% of the patients performed regular exercise, which was similar in c the control group. There may be a difference in their activity levels. It is known that ER is more common in athletes. Çetin S, et al., [12] found no cardiac structural difference in children with ER. Decreased heart rate is associated with appearance of ER. In patients with ventricular fibrillation, an increased rate of ER was observed during bradycardia. Tachycardia may normalize the ECG in patients with ER.

Increased P wave dispersion, QT dispersion, and Tp-e dispersion are indicators of heterogenous depolarization and their increase indicates atrial or ventricular arrhythmia risk. No difference in terms of P wave dispersion, QT dispersion, QTc dispersion, or Tp-e dispersion was found between the study and control groups. Therefore, we may conclude that there is no increased risk for atrial or ventricular arrhythmia, ventricular fibrillation, or sudden death in healthy children with accidentally found ERP. Only JT dispersion had increased in children with ER, which was possibly due to J wave which complicate the measurement of JT interval. The absence of a J wave in each lead and its different magnitudes may cause an overestimation of the JT dispersion.

The autonomic nervous system consisting of the sympathetic and parasympathetic systems, the intrinsic cardiac nervous system, respiration, and reflexes regulate the heart rate by affecting the contractility and conduction system of the heart. Physical, mental, and hemodynamic factors play a role in irregularity of heart rate. The temporal variation between consecutive heartbeats is called Heart Rate Variability (HRV) [13]. In general, decreased HRV indicates an increased risk of sudden death and arrhythmia. By using 24-hour Holter ECG recordings, time domain and frequency domain measurements, are calculated [14].

SDNN, SDANN, and SDNNi show both sympathetic and parasympathetic effects; rMSSD and pNN50 indicate vagal control. Since SDNN, SDANN, and SDNNi are calculated with the absolute value of the R-R interval, an increase in these values means an increase in HRV, that is, the dominance of the parasympathetic system. A decrease in values indicates a decrease in HRV, the dominance of the sympathetic system. A decreased HRV means a heart with a relatively higher rate and a loss of day-night heart rate differential. In other words, it indicates that sympathetic tone is dominant in the autonomic nervous system of the heart and is associated with increased cardiovascular risk [15].

Frequency domain measurements LF, were mainly associated with sympathetic activity; HF was associated with vagal activity [16]. The LF/HF ratio reflects the balance between the sympathetic and parasympathetic autonomic nervous systems. An increase in this ratio suggests the dominance of sympathetic activity, and a decrease in this ratio indicates the dominance of parasympathetic activity [17].

There are very few studies where HRV analysis is performed in patients with early repolarization. In a study conducted on adults, the mean heart rate and minimum heart rate were lower in cases with an ER pattern. In addition, SDNN, rMSSD, and pNN50 parameters were higher, and the LF/HF ratio was lower in patients with ER. These findings suggest that there may be a strong connection between parasympathetic activity and ER. The increase in parasympathetic activity may be one of the mechanisms in the pathophysiology of ER [18]. In our study, the LF/HF ratio was higher in cases with ER than in the control group. This finding shows that sympathetic activity is more dominant in the cases, unlike the above-mentioned study. However, there was no finding supporting sympathetic activation in terms of other HRV parameters. One of the reasons causing this discrepancy may be the physiologic dominance of sympathetic tone in childhood. No study has been found investigating HRV in children with ER. Our study is the first study in this aspect.

HRV measurements in the study and control groups were also compared separately during sleeping and awake hours. The hours between 08:00 a.m. and 00:00 were considered as awake and between 00:00 and 08:00 a.m. as asleep. The awake HF was significantly lower, and awake LF/HF ratio was higher in the study group. Suggesting more dominant sympathetic activity during daytime in cases with ER patterns. However, there was no difference between the study and control groups regarding HRV values obtained during sleep. According to the literature, in individuals who do not have ER during the daytime hours when the sympathetic system is dominant, ER may become evident at night by activation of the parasympathetic system. There may be similarities between malignant forms of ER and Brugada Syndrome. In Brugada Syndrome, characterized by ST changes in the anterior precordial leads, ventricular fibrillation, and sudden death typically occur during nighttime sleeping hours [19].

However, no such increased risk was observed in our study group.

The study group was divided into subgroups according to age (6 to 12 years as prepubertal; 13 to 18 years as postpubertal), gender, and the leads in which the J wave was observed. Compared to the controls, the P axis was relatively shifted to the left in prepubertal children (p=0.008) but was within normal limits, JT dispersion was higher (p=0.035), and Tp-e dispersion was lower (p=0.043). The difference in JT dispersion is thought to be related to measurement difficulties in the whole group. The low Tp-e dispersion in the study group, on the contrary, indicates that the risk of arrhythmia and sudden cardiac death is low. The results of the postpubertal group were in accordance with the general study group and the heart rate was significantly lower in the study group.

In a comparison of HRV measurements in prepubertal and postpubertal patients separately; no significant difference was found HRV in total 24-hour; asleep or awake in prepubertal children with and without ER. However, in postpubertal children the minimum heart rate was lower and the LF/HF ratio higher in cases with ER; similar to the general study group. This suggests that prepubertal children should be investigated in more detail. Normally, there is sympathetic system dominance in prepubertal children and parasympathetic dominance after puberty [14]. Although pubertal age was roughly accepted as 12 in our study group, this age may show significant variations in society, and it usually occurs later in boys. This may be a limitation of our study.

It is known that gender also plays a role in early repolarization, and it is more common in males. When we compared the boys and girls in our study group in terms of ECG parameters and HRV, no difference was found between the two groups in terms of ECG parameters. In HRV parameters, minimum heart rate and mean heart rate were lower in boys, and SDNN-i, LF, and VLF were significantly higher. Findings in boys are similar to results in the adult age group in the literature and show that parasympathetic system dominance is more prominent in boys. Parasympathetic dominance in HRV may be associated with physical activity and sports and a lower risk of sudden death. In comparing asleep or awake HRV parameters, SDNN, LF, and VLF during awake hours and SDNN and VLF during sleep hours were significantly higher in boys than in girls. This shows that parasympathetic dominance is more prominent in boys compared to girls, similar to the healthy population. In all the children with early repolarization in our study, ST segment concavity was facing upward which is considered as benign ST elevation.

J waves were detected in the inferolateral leads in 62% of our cases, in the inferior leads in 31%, and in the lateral leads in 6% of our cases. Since the number of cases with J waves only in the lateral leads is too small to be evaluated statistically, the inferior and inferolateral leads were compared. When the study group was divided into two inferior and inferolateral leads according to the leads in which the ER pattern is seen, no significant difference was found between the two groups regarding ECG parameters.

In comparing HRV of children with inferior and inferolateral ER patterns, mean heart rate was found to be lower in favor of parasympathetic activity in the inferior ER pattern, and SDNN and VLF during sleep were found to be higher.

Studies have shown that sudden cardiac death and life-threatening arrhythmias increase especially in patients with an ER pattern in the inferior and inferolateral leads [20,21]. Studies in this field conducted in children are rare. It is also noteworthy that the J point elevation is at least 0.1 mV in ER patterns associated with sudden cardiac death. In our study, children with ER in the inferior leads and those with ER in the inferolateral leads were compared in terms of ECG parameters, but no statistically significant difference was found; relatively mild cases may be included in our study. In our study, the increased parasympathetic activity reported in adults was not demonstrated in children with ER patterns. On the contrary, findings of increased sympathetic tone during nighttime sleep hours were detected, which is more pronounced after 12 years of age. Parasympathetic activity is more prominent in boys who have more frequent ER patterns.

Another important finding from our study's HRV data is that parasympathetic activity dominance is higher in patients with inferior ER patterns than in patients with inferolateral ER patterns. There is evidence in the literature that the inferior ER pattern is more malignant. New studies are needed to understand whether the dominance of parasympathetic activity and the ER seen in the inferior leads is responsible for this increased risk.

Conclusion

As a result, we found no evidence of increased arrhythmia or sudden cardiac death risk in healthy children who were coincidentally diagnosed with an ER pattern. The fact that the resting heart rate is lower and the interventricular septum is thicker in children with ER suggests that ER is associated with increased physical activity. We observed that parasympathetic tone was more dominant in boys, where ER was more common. In our study group, and especially at night time, we found that the sympathetic nervous system was dominant in children, unlike in adult studies. New studies are needed to understand whether the relatively dominant sympathetic nervous system, which is effective in ER suppression, has a protective effect against arrhythmia and sudden death in the pediatric age group.

References

1. Obeyesekere MN, Klein GJ, Nattel S, et al. A clinical approach to early repolarization. Circulation. 127(15):1620-1629 (2013).

2. Ali A, Butt N, Sheikh AS, et al. Early repolarization syndrome: A cause of

sudden cardiac death. World J Cardiol.7(8):466-475 (2015).

3. Maury P, Authenac C, Rollin A, et al. Prevalence of early repolarisation pattern in children. Int J Cardiol.243:505-510 (2017).

4. Akpinar M, Ocal M, Irdem A, et al. Ventricular repolarization changes in children with breath holding spells. J Electrocardiol.55:116-119 (2019).

5. Al-Tweigeri T, Dent S, Al Sayed A, et al. Using the appropriate formula for QT measurement can save lives. Hematol Oncol Stem Cell Ther.15(1):79-82 (2022).

6. Li GL, Yang L, Cui CC, et al. J wave syndromes: A decade of progress. Chin Med J (Engl). 128(7):969-975 (2015).

7. Bourier F, Denis A, Cheniti G, et al. Early repolarization syndrome: Diagnostic and therapeutic approach. Front Cardiovasc Med.5:169 (2018).

8. Haruta D, Matsuo K, Tsuneto A, et al. Incidence and prognostic value of early repolarization pattern in the 12-lead electrocardiogram. Circulation.123(25):2931-2937 (2011).

9. Liu XK, Katchman A, Whitfield BH, et al. In vivo androgen treatment shortens the QT interval and increases the densities of inward and delayed rectifier potassium currents in orchiectomized male rabbits. Cardiovasc Res. 57(1):28-36 (2003).

10. Bai CX, Kurokawa J, Tamagawa M, et al. Nontranscriptional regulation of cardiac repolarization currents by testosterone. Circulation. 112(12):1701-1710 (2005).

11. Sridharan MR, Horan LG. Electrocardiographic J wave of hypercalcemia. Am J Cardiol.54(6):672-673 (1984).

12. Çetin S, Akgün EZ, Babaoğlu K, et al. Evaluation of early repolarization pattern in male teenage competitive athletes and association with left ventricular remodelling. Turk Arch Pediatr. 56(5):485 (2021).

13. Draghici AE, Taylor JA. The physiological basis and measurement of heart rate variability in humans. J Physiol Anthropol.35(1):22 (2016).

14. Topcu B, Akalin F. The autonomic nervous system dysregulation in response to orthostatic stress in children with neurocardiogenic syncope. Cardiol Young.20(2):165-72 (2010).

15. Patocskai B, Barajas-Martinez H, Hu D, et al. Cellular and ionic mechanisms underlying the effects of cilostazol, milrinone, and isoproterenol to suppress arrhythmogenesis in an experimental model of early repolarization syndrome. Heart Rhythm.13(6):1326-34 (2016).

16. Cenk M, Akalin F, Saylan BC, et al. P wave dispersion in assessment of dysrhythmia risk in patients with secundum type atrial septal defect and the effect of transcatheter or surgical closure. Cardiol Young.30(2):263-270 (2020).

17. Ventura R, Maas R, Zeidler D, et al. A randomized and controlled pilot trial of beta-blockers for the treatment of recurrent syncope in patients with a positive or negative response to head-up tilt test. Pacing Clin Electrophysiol.25(5):816-821 (2002).

18. Chen XM, Fan J, Cheng YJ, et al. Autonomic influences related to early repolarization in patients without structural heart disease. J Cardiovasc Transl Res.13(6):970-976 (2020).

19. Kabra N, Gupta R, Aronow WS, et al. Sudden cardiac death in brugada syndrome. Cardiol Rev.28(4):203-207 (2020).

20. Haissaguerre M, Sacher F, Nogami A, et al. Characteristics of recurrent ventricular fibrillation associated with inferolateral early repolarization role of drug therapy. J Am Coll Cardiol.53(7):612-619 (2009).

21. Macfarlane PW, Antzelevitch C, Haissaguerre M, et al. The early repolarization pattern: A consensus paper. J Am Coll Cardiol.66(4):470-477 (2015).