BMC Cardiovascular Disorders

RESEARCH

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

Ahmet F. Arinc[1,4*], Sule Arici[2] and Figen Akalin[3]

Abstract

Background Early repolarization pattern (ERP) on electrocardiogram (ECG) was long considered benign, but recent data suggest a potential association with fatal arrhythmia and sudden cardiac death. Its relevance in pediatric populations remains unclear. This study investigated the risk of premature death and arrhythmia in children with incidentally found early repolarization using ECG and heart rate variability parameters.

Methods This cross-sectional study included healthy children aged 6–18 years with incidentally detected ERP (study group) and age- and sex-matched controls without ERP. All participants underwent medical history evaluation, physical examination, 12-lead ECG, transthoracic echocardiography, and 24-h Holter monitoring. ECG parameters (P wave, QTc, JT, Tp-e, and their dispersions), time-domain (SDNN, SDANN, SDNN-i, r-MSSD, pNN50), and frequency-domain (HF, LF, LF/HF) HRV parameters were analyzed.-i, r-MSSD, pNN50 and "Frequency-domain" parameters HF, LF, LF/HF were obtained.

Results The study group had lower heart rates ($p=0.020$) and increased JT dispersion ($p=0.025$). Interventricular septal thickness was significantly greater in the ERP group ($p=0.030$). LF/HF ratio ($p=0.045$), awake HF ($p=0.046$), and awake LF/HF ($p=0.036$) were significantly higher in ERP patients. Parasympathetic activity predominance was more evident in males. ERP localized in inferolateral leads was associated with higher heart rate and lower SDNN and VLF during sleep ($p=0.049$, $p=0.040$, $p=0.040$, respectively).

Conclusion Incidental ERP in children was not associated with arrhythmic events but correlated with increased parasympathetic tone. Inferolateral ERP may indicate a relatively higher autonomic imbalance risk.

Keywords Early repolarization, Dysrhythmia, Heart rate variability

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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-h 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 (h)-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

This prospective cohort study, conducted from October 2020 to October 2021, was approved by the ethical committees of Marmara University, in compliance with the Declaration of Helsinki. Written informed consent was obtained from parents or caregivers of pediatric patients, with patient assent. The study group consisted of healthy children between 6 and 18 years of age, admitted to Marmara University Pediatrics or Pediatric Cardiology 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-h 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. A schematic representation of the study design and workflow was generated using BioRender (agreement number: QJ286LFHFN) and is provided in Fig. 1.

Clinical evaluation

A detailed medical history was taken of the children included in the study, including their reasons for admission, exercise capacity according to New York Heart Association (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, 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)

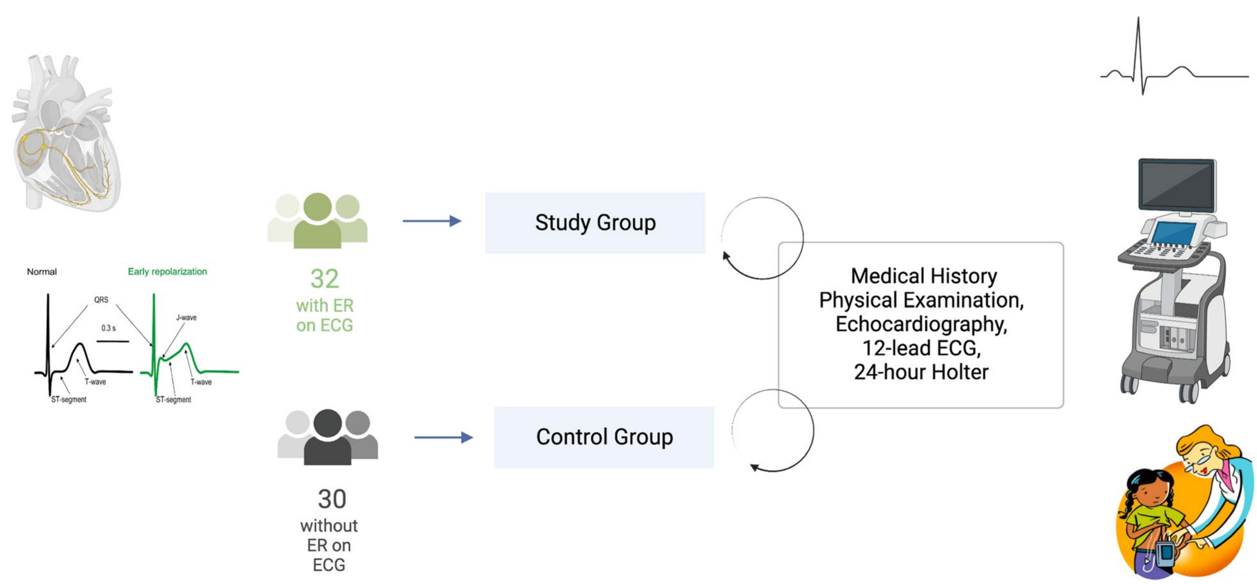

Fig. 1 Schematic representation of the study design and evaluation protocol. ECG: Electrocardiogram, ER: Early Repolarization

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-h 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, Atrioventricular (AV) block, and sinus pause detected throughout the day were recorded.

Time domain parameters, standard deviation of NN intervals (SDNN), standard deviation of the average NN intervals (SDANN), mean of the standard deviations of NN intervals in 5-min segments (SDNNi), root mean square of successive differences (rMSSD), and percentage of NN intervals differing by more than 50 ms from the previous one (pNN50) and frequency domain parameters low frequency (LF), high frequency (HF), very low frequency (VLF), LF/HF ratio were obtained from 24-h-Holter recordings after careful removal of artifacts and early beats using Cardioscan Software System (Powered by DM Software Inc. USA, version 11.5.0076a).

HRV parameters obtained from 24-h-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 SDNNi parameters were also compared.

Statistical analysis

Statistical analysis was performed using SPSS 22.0 program. 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 fort 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. $P \leq 0.05$ were considered as statistically significant.

A multivariable binary logistic regression analysis was conducted to identify clinical and autonomic predictors independently associated with ERP. The dependent variable was the presence of ERP. Clinically plausible variables were selected a priori as independent predictors, regardless of their univariate significance. These included resting heart rate, JT dispersion, LF/HF ratio, IVSd, SDNN, sex, and age. Before modeling, multicollinearity was assessed using Pearson correlations and variance inflation factors (VIF); all VIFs were <2, indicating no collinearity issues. Linearity in the logit was confirmed for continuous predictors. No variable transformations or interactions were applied. Logistic regression results were reported as adjusted odds ratios (OR) with 95% confidence intervals (CI) and p-values. Statistical significance was defined as $p < 0.05$.

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 (Fig. 2). 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 (Fig. 3).

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 ($p > 0.05$) (Fig. 1).

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 ER. 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%).

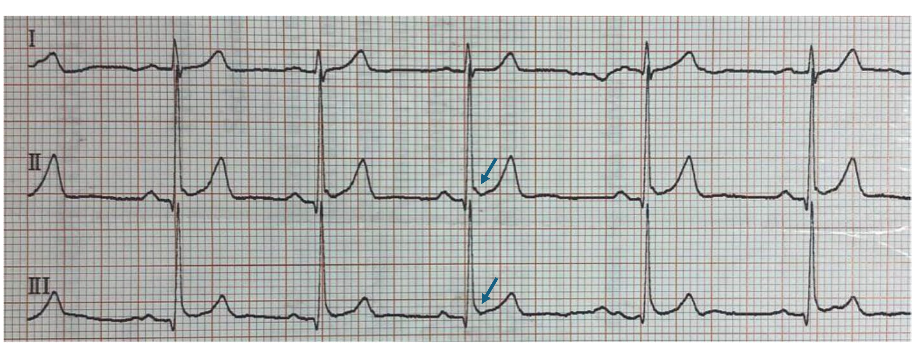

Fig. 2 Twelve-lead electrocardiogram from a participant in the study group demonstrating an early repolarization pattern. Mild J-point elevation is observed in the inferior leads (II and III), indicated by arrows

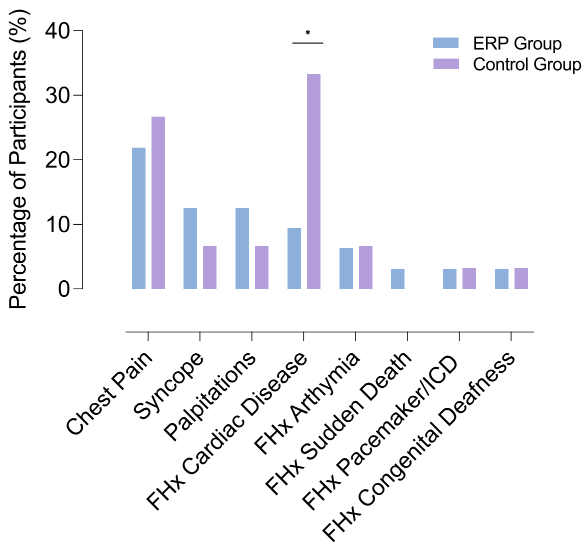

Fig. 3 Comparative distribution of self-reported cardiac symptoms and familial cardiovascular history in pediatric patients with early repolarization pattern (ERP) versus age-matched controls. (*; $p < 0.05$). (ERP; Early Repolarization Pattern, FHx; Family History, ICD; İmplantable Cardioverter-Defibrillator)

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; 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, $p = 0.030$) (Table 3).

24-h Holter ECG findings showed LF/HF ratio was significantly higher in the study group ($p = 0.045$) (Table 4). 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 5).

24-h 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 6).

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 $p = 0.040$).

The analysis of 24-h Holter ECG recordings was conducted for both the study and control groups to evaluate the presence and frequency of supraventricular premature beats (SVPB), supraventricular tachycardia (SVT), sinus pauses, ventricular premature beats (VPB), ventricular tachycardia (VT), and AV block. The frequency of any detected arrhythmias was noted throughout the 24-h monitoring period. Neither group had participants displaying SVT, sinus pauses, VT, or AV block. In the study group, 13 children (40%) showed no signs of SVEA or VEA. One participant (4%) had 119 isolated VEA episodes. The remaining children (56%) had infrequent

Table 1 Comparison of clinical findings between study and control groups

Parameters	Study group ($n = 32$)	Control group ($n = 30$)	p
Age (years)	14 ± 3	13.4 ± 3.4	0,401
Weight (kg)	54.5 ± 18.7	50.9 ± 18.1	0.438
Length (cm)	158 ± 5.0	154.7 ± 18.6	0.413
BMI (kg/m^2)	21.2 ± 4.9	20.5 ± 4.2	0.548
BSB (m^2)	1.53 ± 0.32	1.45 ± 0.32	0.323
Heart rate (/pm)	85.8 ± 14.4	91.8 ± 16	0.125
Sistolic BP (mmHg)	112.3 ± 11	114 ± 9.5	0.521
Diastolic BP (mmHg)	72.8 ± 8.1	74.9 ± 7.6	0.300
Cardiothoracic index	0.4 ± 0.04	0.4 ± 0.04	0.916

Data are expressed as mean ± SD (standart deviation). Normality was confirmed prior to parametric analysis. $p < 0.05$, statistically significant

BMI Body mass index, *BSA* Body surface area, *BP* Blood pressure, *n* number, *SD* Standart deviation

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
QTc (msec)	376.3 ± 26.1	330–433		382 ± 24.3	333–428		0.350
QTc (max) (msec)	384.9 ± 26.8	345–440.6		393.8 ± 26.5	343–438		0.196
QTc (min) (msec)	355.6 ± 25.7	320–410		361.1 ± 27.3	300–410		0.419
QTc dispersion (msec)	29.2 ± 12.9	7.6–56		32.7 ± 15.2	8–81		0.343
Heart rate (/pm)	77.8 ± 14.6	48–115		87.5 ± 16.9	55–128		0.020
JT (msn)	268.7 ± 31.6	200–360		268 ± 25.5	24–320		0.919
JT (max) (msec)	286.5 ± 40	200–400		280 ± 27.2	240–340		0.458
JT (min) (msec)	254.6 ± 41.3	160–360		255.5 ± 25.5	220–320		0.941
	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	0.700
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

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* Standart deviation, *p (25)* 25 th percetile, *p (75)* 75 th percentile

$p < 0.05$, statistically significant

isolated SVEA (from 0 to 9 beats) and/or isolated unifocal VEA (from 0 to 4 beats). In the control group, 16 children (53%) showed no evidence of SVEA or VEA. One subject (4%) recorded 119 isolated SVEA episodes. The rest of the children (56%) exhibited infrequent isolated SVEA (0 to 9 beats) and/or isolated unifocal VEA (0 to 6 beats).

In the multivariable logistic regression model, three variables emerged as independent predictors of ERP. Resting heart rate was inversely associated with ERP, with each bpm increase corresponding to a 6% lower odds of ERP (OR: 0.94, 95% CI: 0.89–0.99, $p = 0.012$). JT dispersion was positively associated with ERP (OR: 1.10 per 1 ms, 95% CI: 1.03–1.18, $p = 0.004$), suggesting increased repolarization heterogeneity in ERP patients. IVSd also showed a significant positive association (OR: 1.78 per 1 mm, 95% CI: 1.11–2.87, $p = 0.018$). In contrast, LF/HF ratio, SDNN, sex, and age were not significantly associated with ERP in the adjusted model ($p > 0.05$ for all) (Table 7).

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 [2]. The 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 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 ER 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.

Table 3 Comparison of echocardiography parameters between study and control groups

Parameters	Study Group ($n = 32$)	Control Group ($n = 32$)	p
IVSd (cm)	0.84 ± 0.19	0.75 ± 0.13	**0,030**
LVDd (cm)	4.42 ± 0.48	4.43 ± 0.45	0,954
LVDs (cm)	2.64 ± 0.42	2.68 ± 0.42	0,723
LVPWd (cm)	0.71 ± 0.19	0.71 ± 0.15	0,948
FS (%)	39.3 ± 5.6	39.6 ± 4.8	0,831
EF (%)	70.1 ± 5.8	70.0 ± 6.4	0,921
Aortic Root Diameter (cm)	2.35 ± 0.42	2.29 ± 0.37	0,561
Left Atrial Diameter (cm)	2.90 ± 0.48	2.76 ± 0.45	0,266
Mitral E Velocity (m/s)	1.00 ± 0.14	1.00 ± 0.13	0,484
Mitral A Velocity (m/s)	0.62 ± 0.14	0.66 ± 0.20	0,344
DecT (ms)	154.8 ± 48.9	148.4 ± 44.0	0,593
IVRT (ms)	68.1 ± 14.7	68.9 ± 12.8	0,826
Aortic Flow Velocity (m/s)	1.39 ± 0.29	1.33 ± 0.22	0,362
Pulmonary Artery Flow Velocity (m/s)	1.18 ± 0.16	1.16 ± 0.18	0,657

Data are expressed as mean ± SD (standart deviation). Normality was confirmed prior to parametric analysis. $p < 0.05$, statistically significant

cm centimeter, *DecT* Deceleration Time, *EF* Ejection Fraction, *FS* Fractional Shortening, *IVRT* İsovolumetric Relaxation Time, *IVSd* Interventricular Septum Diastolic Thickness, *LVDd* Left Ventricular End-Diastolic Diameter, *LVDs* Left Ventricular End-Systolic Diameter, *LVPWd* Left Ventricular Posterior Wall Diameter, *m* meter, *ms* millisecond, *s* second

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 (1). 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 Maury 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.

ER is more common in boys, reported up to 75% [7]. 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 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 VF, an increased rate of ER was observed during bradycardia. Tachycardia may normalize the ECG in patients with ER.

Table 4 Comparison of 24-h Holter's parameters between study and control groups

Parameters	Study ($n = 30$)		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	0.540
r-MSSD	43.9 ± 14.6	10–76	47.2 ± 16.5	25–103	0.405
PNN50	19.6 ± 10.4	0–44	21.5 ± 9.9	5–50	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

SDNN Standart deviation of the interbeat intervals of normal sinüs beats, *SDANN* Standart deviation of the average NN intervals for each 5 min segment of the 24-h HRV recording, *SDNN-i* the mean of the standart deviations of all the NN intervals for each 5 min segment of 24-h 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 5 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	0.330
Awake r-MSSD	37.8 ± 13.5	15–71	41.4 ± 15.1	22–89	0.330
Awake PNN50	15.6 ± 10.2	1–45	17.5 ± 9.5	3–43	0.444
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-MSSD	58 ± 20.6	17–96	58.9 ± 23.3	29–134	0.871
Sleep PNN50	32.3 ± 15.9	1–60	32.7 ± 15.3	8–68	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

SDNN standard 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

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, VF, 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

Table 6 Comparison of 24-h 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	**0.030**
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	2.40	0.596
VLF (Hz)	3985.3	2378.2	5713.0	2488.5	1251.1	2884.4	**0.010**

SDNN standard deviation of the interbeat intervals of normal sinus beats, *SDANN* Standart deviation of the average NN intervals for each 5 min segment of the 24-h HRV recording, *SDNN-i* the mean of the standart deviations of all the NN intervals for each 5 min segment of 24-h 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 7 Multivariable binary logistic regression analysis of clinical and autonomic predictors of early repolarization pattern (ERP)

Variable	OR (95% CI)	*p*-value
Resting heart rate (per 1 bpm)	0.94 (0.89–0.99)	**0.012**
JT dispersion (per 1 mm)	1.10 (1.03–1.18)	**0.004**
LF/HF ratio (per 1 unit)	1.35 (0.65–2.81)	0.43
IVSd (per 1 mm)	1.78 (1.11–2.87)	**0.018**
SDNN (per 1 ms)	0.98 (0.97–1.00)	0.078
Sex (female vs male)	1.09 (0.31–3.82)	0.90
Age (per 1 year)	1.07 (0.83–1.37)	0.62

Odds ratios (ORs) are presented with corresponding 95% confidence intervals (CI) and p-values. An OR > 1 indicates increased odds of ERP presence per unit increase in the predictor; OR < 1 indicates decreased odds. Variables with p < 0.05 were considered statistically significant

CI Confidence Interval, *ERP* Early Repolarization Pattern, *IVSd* Interventicular Septal Diameter in Diastole, *OR* Odds Ratio, *SDNN* Standart Deviation of the Interbeat Intervals of Normal Sinus Beats, *LF/HF* low-frequency to high-frequency ratio

temporal variation between consecutive heartbeats is called HRV [13]. In general, decreased HRV indicates an increased risk of sudden death and arrhythmia. By using 24-h 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 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, VF, 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-h; 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 [14].

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.

Both ERP and Brugada syndrome fall under the broader spectrum of J-wave syndromes, characterized by terminal QRS notching or slurring and a propensity for repolarization abnormalities. Our study demonstrated that in children with incidentally identified ERP, HRV analysis revealed a parasympathetic-dominant autonomic profile, with lower resting heart rate and increased HRV indices—findings consistent with a benign phenotype. In contrast, Brugada syndrome—especially drug-induced cases—presents a more malignant profile. As shown in the study by Călburean et al., patients with Brugada syndrome who experienced ventricular arrhythmias during follow-up exhibited significant autonomic shifts during ajmaline provocation, including reduced low-frequency HRV power and increased microvolt T-wave alternans (mTWA), both serving as independent predictors of arrhythmic events [22]. Such dynamic ECG changes were not observed in asymptomatic Brugada patients or our ERP cohort. Moreover, whereas ERP in children was not associated with ventricular arrhythmias or sudden cardiac death during follow-up, Brugada syndrome maintains a measurable annual event rate. These differences highlight the prognostic divergence within J-wave syndromes: ERP in children represents a benign autonomic variant. In contrast, Brugada syndrome—particularly under pharmacologic challenge—unveils latent substrate vulnerability linked to arrhythmic outcomes [23].

Bradycardia has consistently been linked to ERP in both adult and pediatric populations. Slower heart rates may reflect increased parasympathetic tone, which has been proposed as a potential underlying mechanism facilitating J-point elevation and early repolarization [2]. In line with this, previous studies demonstrated that ERP is more frequent in athletes and individuals with high vagal tone [3, 12].Our finding that each one bpm increase in resting heart rate was associated with a 6% reduction in ERP odds (OR: 0.94, $p = 0.012$) reinforces the association between vagal predominance and ERP.

JT dispersion, which reflects heterogeneity in ventricular repolarization, has also been implicated in arrhythmic risk stratification. Increased dispersion of repolarization has been shown to predispose to ventricular arrhythmias in various contexts, including J-wave syndromes [6]. In our study, JT dispersion was a strong independent correlate of ERP (OR: 1.10 per ms, $p = 0.004$), suggesting that children with ERP may exhibit subclinical abnormalities in myocardial repolarization, even without clinical arrhythmias.

Interestingly, IVSd, while within the physiological range in our cohort, was also significantly greater in children with ERP. This could reflect early structural adaptation, possibly due to higher levels of physical activity—ERP is known to be more prevalent among physically trained individuals [7, 12]. Alternatively, this observation might suggest shared electrophysiological and morphological traits in ERP carriers, though further studies incorporating cardiac MRI or genetic profiling would be needed to explore this hypothesis.

Contrary to expectations, other HRV parameters, such as LF/HF ratio and SDNN, were not independently associated with ERP in multivariable analysis. Prior studies in adults have shown that ERP may be related to increased vagal indices (e.g., higher HF power, lower LF/HF) [1, 21]; however, the autonomic regulation in children, particularly during puberty, is more dynamic and may obscure these associations. Additionally, neither sex nor age reached statistical significance in our model, possibly due to the limited sample size.

Our findings support the hypothesis that ERP in children is associated with distinct autonomic and electrophysiological characteristics, particularly increased vagal activity and repolarization dispersion. While not indicative of acute risk in our asymptomatic cohort, these parameters may help characterize ERP as a meaningful ECG phenotype in pediatric populations. Larger, longitudinal studies are warranted to determine the'clinical significance and prognostic value of these findings.

This study has several limitations. The relatively small sample size reduces statistical power and limits the generalizability of the findings. Due to its cross-sectional design, causality cannot be inferred, and no arrhythmic events occurred during follow-up, precluding clinical risk assessment. Pubertal status was estimated by age rather than clinical staging, which may have introduced misclassification bias. Additionally, subtle structural or electrical abnormalities could not be fully excluded, as advanced imaging or electrophysiological testing was not performed. HRV was the sole method used to assess autonomic tone, which, despite its validity, is susceptible to external influences. Multicenter, prospective studies are needed to validate and expand upon these findings.

Conclusion

In this observational study, ERP identified in otherwise healthy children was not associated with documented arrhythmic events or sudden cardiac death. Although the limited sample size and absence of long-term follow-up limit definitive risk assessment, our findings suggest that ERP may reflect a physiological variant rather than a pathological substrate in the pediatric population. Children with ERP exhibited lower resting heart rates and increased interventricular septal thickness, possibly indicating a higher level of physical conditioning. HRV analysis revealed a complex autonomic profile: parasympathetic dominance was more pronounced in males, where ERP was more prevalent; sympathetic predominance during nighttime hours was also observed, a pattern distinct from adult studies. These findings imply age-specific autonomic regulation and raise the possibility that enhanced sympathetic tone in childhood may contribute to ERP suppression and protection from arrhythmogenic events. Further large-scale, prospective studies are needed to validate these observations and clarify the prognostic implications of ERP in children across developmental stages.

Abbreviations

Ao	Aortic Root
AV	Atrioventricular
BMI	Body Mass Index
BSA	Body Surface Area
DecT	Deceleration Time
ECG	Electrocardiography
EF	Ejection Fraction
ER	Early Repolarization
ERP	Early Repolarization Pattern
ERS	Early Repolarization Syndrome
HF	High Frequency
HRV	Heart Rate Variability
IVRT	Isovolumetric Relaxation Time
IVSd	Interventricular Septum Diastolic Thickness
LAD	Diastolic Left Atrial Diameter
LF	Low Frequency
LF/HF Ratio	Ratio of Low Frequency to High Frequency
LVPWd	Left Ventricular Posterior Wall Diastolic Thickness
NYHA	New York Heart Association
pNN50	Percentage of NN intervals differing by more than 50 ms from the previous one
rMSSD	Root Mean Square of Successive Differences
SDANN	Standard Deviation of the Average NN intervals
SDNN	Standard Deviation of NN intervals
SDNNi	Mean of the Standard Deviations of NN intervals in 5-minute segments
SF	Shortening Fraction
SVPB	Supraventricular Premature Beats
SVT	Supraventricular Tachycardia
VPB	Ventricular Premature Beats
VLF	Very Low Frequency
VT	Ventricular Tachycardia

Acknowledgements
None.

Clinical trial number
Not applicable.

Authors' contributions
F.A conceptualized and supervised the study. A.F.A, S.A. and F.A. provided patient care and collected clinical data. A.F.A and F.A wrote the paper. All authors reviewed and approved the final version of the manuscript.

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability
All data generated or analysed during this study are included in this published article.

Code availability
Not applicable.

Declarations

Ethics approval and consent to participate
The study was approved by the local ethical committee of Marmara University Research and Training Hospital, in compliance with the Declaration of Helsinki. (Date 02.10.2020, number 09.2020.1127).
Informed consent for participation was obtained from all individuals, in compliance with the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 12 February 2025 Accepted: 5 May 2025
Published online: 08 May 2025

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