Clinical Research

Normal Distribution of Ventricular Early Repolarization Times in Healthy Children

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ABSTRACT

Objective: This study aimed to evaluate the normal ranges of ventricular early repolarization intervals in healthy children according to age and sex.
Material and Method: Patients were divided into seven groups: 0-3 months, 3 months to 1 year, 1-3 years, 3-5 years, 5-9 years, 9-13 years, and 13-18 years. All patients underwent transthoracic echocardiography and 12-lead electrocardiography (ECG). The following parameters were evaluated: left ventricular mass (LV mass), ejection fraction (EF), mitral E and A velocities, E velocity deceleration time (DT), E/A ratio, mean heart rate (HR), repolarization intervals (QT, QTc, JT, JTc, JTp, JTpc), and repolarization dispersion intervals and rates (Tpe, Tpe/QT, Tp/QTc, Tpe/JT, Tpe/JTc).
Results: The median patient age value was 8.75 years (0.96 months-19.71 years). Heart rate (HR), JTp, JTpc, JT, JTc, QT, QTc, Tpe, Tpe/QT, Tpe/QTc, Tpe/JT, Tpe/JTc values are respectively 92 min-1 (54.60-141), 184 ms (98.33-249), 225.60 ms (162.04-279.90), 240 ms (141.67-316), 295.63 ms (240.25-336.76), 322 ms (216.67+398), 398.36 ms (350.69-454.93), 57 ms (27.50- 92), 0.18 (± 0.02), 0.14 (± 0.02), 0.24 (± 0.03), 0.19 (± 0.03).
Conclusion: Intervals such as repolarization times and repolarization dispersion are used to predict arrhythmias. We believe that in cases where it is difficult to determine the endpoint of the T wave, the evaluation of JTp and JTpc can provide useful information, and knowing the normal ranges of JTp and JTpc according to age and sex can provide useful information.
Keywords: *Repolarization Time, Early Repolarization Time, Transmural Repolarization Dispersion, JTp, Tpe.*

ÖZ

Sağlıklı Çocuklarda Erken Ventriküler Repolarizasyon Sürelerinin Normal Dağılımı
Amaç: Çalışmamızda sağlıklı çocuklarda ventriküler erken repolarizasyon intervallerinin normal aralıklarının yaş ve cinsiyetlere göre değerlendirilmesi amaçlandı.
Gereç ve Yöntem: Hastalar 0-3 ay, 3ay-1 yaş, 1-3 yaş, 3-5 yaş, 5-9 yaş, 9-13 yaş, 13-18 yaş olarak 7 gruba ayrıldı. Tüm hastalar transtorasik ekokardiyografi ve 12-lead elektrokardiyografi (EKG) ile değerlendirildi. Sol ventrikül kütlesi (LVmass), ejeksiyon fraksiyonu (EF), mitral E ve A velositeleri, E velositesi deselerasyon zamanı (DT), E/A oranı, ortalama kalp hızı (HR), repolarizasyon intervalleri (QT, QTc, JT, JTc, JTp, JTpc), transmural repolarizasyon dispersiyonu intervalleri ve oranları (Tpe, Tpe/QT, Tp/QTc, Tpe/JT, Tpe/JTc) değerlendirildi.
Bulgular: Yaş ortanca değeri 8.75 yıl (0.96 ay-19.71 yıl) idi. Kalp hızı (HR), JTp, JTpc, JT, JTc, QT, QTc, Tpe, Tpe/QT, Tpe/QTc, Tpe/JT, Tpe/JTc değerleri sırasıyla 92 min-1 (54.60-141), 184 ms (98.33-249), 225.60 ms (162.04-279.90), 240 ms (141.67-316), 295.63 ms (240.25-336.76), 322 ms (216.67+398), 398.36 ms (350.69-454.93), 57 ms (27.50-92), 0.18 (± 0.02), 0.14 (± 0.02), 0.24 (± 0.03), 0.19 (± 0.03) idi.
Sonuç: Aritmileri öngörmede repolarizasyon süreleri ve repolarizasyon dispersiyonu gibi intervaller kullanılmaktadır. T dalgasının sonlanma noktasının tayininin zor olduğu durumlarda JTp ve JTpc'nin değerlendirmesinin faydalı bilgiler verebileceğini ve JTp, JTpc'nin yaş ve cinsiyetlere göre normal aralıklarının bilinmesi faydalı bilgiler sağlayabileceği kanısındayız.
Anahtar Sözcükler: *Repolarizasyon Süresi, Erken Repolarizasyon Zamanı, Transmural Repolarizasyon Dispersiyonu, Jtp, Tpe.*

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Electrocardiography (ECG) is the gold standard for evaluating cardiac rhythm problems. Repolarization is expressed as early, late, and total repolarization time (1-3). Increasing the repolarization time and dispersion creates a substrate for increased repolarization heterogeneity, especially for the formation of reentrant arrhythmias (4).

The most important point in determining the intervals in an ECG is determining the starting and ending points of the intervals. Using QT interval to determine the repolarization time may cause incorrect evaluations as the interval includes ventricular depolarization time. The endpoint of the T wave will be intertwined with the P wave, especially when the heart rate increases, making the evaluation of intervals such as JT, QT, and Tpe difficult. In these cases, assessment of the early repolarization interval may provide important clues. Knowing the early repolarization interval, JTp, and normal values in healthy children will provide important information. For this purpose, we aimed to determine the normal range values of early repolarization and heart-rate-corrected early

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repolarization time in healthy children according to age and sex.

MATERIAL AND METHOD

The participants in this retrospective study consisted of patients who applied to the Pediatric Cardiology Outpatient Clinic and had no cardiac pathology detected as a result of the evaluation. Ethics committee approval for the study was received from Gazi Yaşargil Training and Research Hospital ethics committee (decision no:77/2024).

In this study, the participants were divided into seven groups according to their ages: under 3 months, between 3 months and 1 year, between 1 and 3 years, 3 to 5 years, 5 to 9 years, 9 to 13 years, and 13 to 18 years.

Patients with palpitations, a family history of myocardial infarction at an early age, or a family history of sudden death at a young age were excluded from the study.

The patients' ages were expressed in months for those under 1 year of age and in years for those over 1 year of age. Body surface area (BSA) was expressed in square meters (5). Body weight was expressed in kilograms, and body height was expressed in centimeters.

After a detailed physical examination of all patients, transthoracic echocardiography (ECHO) (Vivid S60, General Electric Healthcare, GE, Vingmed, Norway) and 12-lead electrocardiographic (ECG) evaluations were performed (Econet Cardio M Plus, Germany; filtered 0.5–150 Hz, 25 mm/s, 10 mm/mV).

ECHO evaluations were made using a 1.5-4 Mhz transducer, with the patients lying on their left side. Left ventricular mass (LVmass) was obtained using the formula derived from left ventricular wall thickness and diastolic diameter obtained from the left ventricular long-axis M-mode measurements (6).

In 12-lead electrocardiography (ECG), JTp, JT, QT, and Tpe values and their heart rate-corrected states, JTpc, JTc, QTc, Tpe/QT, Tpe/QTc ratio, Tpe/JT, and Tpe/JTc ratios were measured in the V5 lead (3, 7-11). JTp and Tpe intervals were not evaluated in cases where the intervals had artifacts and the T wave was less than 1 mV and biphasic.

JT interval, is defined as the duration from the beginning of the J wave to the end of the T wave, JTp; from the beginning of the J wave to the peak of the T wave, QT interval; from the beginning of the Q wave to the end of the T wave, Tpe interval; from the peak of the T wave to the end of the T wave was measured as time (3, 12, 13). JT, QT, and JTp intervals were corrected according to heart rate using the Bazett formula (11). Measurements were performed manually by enlarging the ECG recordings 200 times on a computer (12).

Analyses were performed using IBM SPSS (SPSS, Chicago, version 27). The Kolmogorov–Smirnov test evaluated normal distribution. Continuous variables were represented as mean±standard deviation or median (minimum, maximum), based on whether they followed a normal distribution, while categorical variables were shown as percentages. The chi-square test compared categorical variables, and either the Student t-test or Mann-Whitney U test was applied to compare continuous variables, depending on the normality of the parameters. For correlation analysis, both Pearson and Spearman's correlation tests were utilized according to the distribution of the parameters. Statistical significance was set at $p < 0.05$.

RESULTS

A total of 975 healthy children (495 boys and 480 girls) were evaluated. In the 0-3 month group, there were 34 boys and 30 girls; in the 3 month to 1 year group, there were 31 boys and 26 girls; and in the 1-3 year group, there were 31 boys and 27 girls. The 1-5 year group included 42 boys and 45 girls, while the 5-9 year group had 126 boys and 127 girls. In the 9-13 year group, there were 112 boys and 110 girls, and finally, the 13-18 year group consisted of 119 boys and 115 girls. The average age of the patients was 8.99 (0-17.91) years.

Left ventricular ejection fraction (EF) was 69% (57-87), left ventricular mass (LVmass) was 47.35 g (9.27-147.23), left ventricular mass index (LVmass-i) was 44.80 g/m² (23.81-125.60), mitral E velocity was 1.00 m/s (0.73-1.61), A velocity was 0.62 m/s (0.40-1.36), the E/A ratio was 1.63 (0.84-3.00), and DT was 122 ms (52-164).

The median heart rate (HR) was 92 min^{-1} (54.60-181), JTp was 184 ms (98.33-249), JTpc was 225.6 ms (162.04-279.90), JT was 240 ms (141.67-316), JTc was 295.63 ms (240.25-344.72), QT was 322 ms (216.67-398), QTc was 398.36 ms (350.69-454.93), Tpe value was 57 ms (27.50-92), the Tpe/QT ratio was 0.17 (0.11-0.27), the Tpe/QTc ratio was 0.14 (0.06-0.23), the Tpe/JT ratio was 0.23 (0.15-0.39), and the Tpe/JTc ratio was 0.19 (0.09-0.35) (Table 1).

Table 1. *Table of demographic findings, mean, SD, median and range values of transthoracic echocardiography and 12-lead electrocardiography parameters in all age groups.*

Parameters	Mean (n =971)	SD	Median	Range
Age (year)	8.99	5.00	8.75	0.08-17.91
BSA (m^2)	1.06	0.42	1.04	0.24-2.14
EF (%)	69.76	6.00	69	57-87
LVmass (g)	50.80	26.15	47.35	9.27-147.23
LVmass-i (g/m^2)	47.10	14.09	44.80	23.81-125.60
E velocity (m/s)	1.02	0.16	1.00	0.73-1.61
A velocity (m/s)	0.63	0.15	0.62	0.40-1.36
E/A ratio	1.70	0.44	1.63	0.84-3.00
DT (ms)	119.96	16.33	122	52-164
HR (min^{-1})	96.67	23.92	92	54.60-181
JTp (ms)	181.48	27.57	184	98.33-249
JTpc (ms)	225.21	20.74	225.6	162.04-279.90
JT (ms)	238.84	30.84	240	141.67-316
JTc (ms)	296.75	18.87	295.63	240.25-336.76
QT (ms)	319.93	33.65	322	216.67-398
QTc (ms)	398.45	20.41	398.36	350.69-454.93
Tpe (ms)	57.36	9.87	57	27.50-92
Tpe/QT ratio	0.18	0.02	0.17	0.11-0.27
Tpe/QTc ratio	0.14	0.02	0.14	0.06-0.23
Tpe/JT ratio	0.24	0.03	0.23	0.15-0.39
Tpe/JTc ratio	0.19	0.03	0.19	0.09-0.35

BSA: Body surface area, EF: Ejection fraction, LV: Left ventricle, LVmass-i: Ratio of left ventricular mass to BSA, E: Left ventricle early diastolic filling velocity, A: Left ventricle late diastolic filling velocity, DT: E velocity deceleration time, HR: Heart rate.

A comparison of the various parameters is presented in table 2.

Table 2. *Comparison table of electrocardiography (ECG) parameters in boys and girls.*

Parameters	Boy (n =491)	Girl (n =480)	*p* value
HR (min^{-1})	86.70 (54.60-181)	95.40 (63.80-177.33)	**<0.001**[2]
JTp (ms)	184 (105-249)	183 (98.33-247)	0.14[2]
JTpc (ms)	222.30 (±21.06)	228.19 (±20.12)	**<0.001**[1]
JT (ms)	243.50 (141.67-316)	240 (160-308)	**<0.001**[2]
JTc (ms)	294.37 (240.25-336.76)	298.19(248.32-333.09)	**0.01**[2]
QT (ms)	325.70 (215.67-398)	320 (226.25-388.40)	**<0.001**[2]
QTc (ms)	396.20 (±20.12)	400.07 (±20.55)	**0.02**[1]
Tpe (ms)	59 (33.33-92)	55 (27.50-83)	**<0.001**[2]
Tpe/QT ratio	0.18 (0.12-0.27)	0.17 (0.11-0.27)	**<0.001**[2]
Tpe/QTc ratio	0.15 (0.08-0.23)	0.13 (0.06-0.26)	**<0.001**[2]
Tpe/JT ratio	0.24 (0.15-0.39)	0.23 (0.15-0.39)	**<0.001**[2]
Tpe/JTc ratio	0.20 (0.11-0.30)	0.18 (0.09-0.35)	**<0.001**[2]

1: Student t test, 2: Mann-Whitney test, HR: Heart rate.

Table 3 shows the mean, standard deviation, median, range, and 95th percentile values of JTp, JTpc, and Tpe for each sex and age group.

Table 3. *Table of mean, standard deviation, median, minimum, maximum, 95th percentile values of JTp, JTpc, Tpe in boys (top row) and girls (bottom row).*

Parameters	Groups	Mean	SD	Median	Min	Max	95th	*p* value
JTp (ms)	0-3m	131.86	22.59	120	105	163.33	163.33	0.62[2]
		131.83	21.59	133.33	98.33	157.50	157.50	
	3m-1y	138.33	16.66	138.33	121.67	155	155	**0.01[2]**
		152.13	27.06	161.66	121.25	191.67	191.66	
	1-3y	152.87	28.74	150	123.33	198	198	**0.008[2]**
		166.18	21.24	160	125	201.67	201.66	
	3-5y	170.37	21.32	168.20	122	209	207.95	0.65[2]
		168.73	24.12	165	122	219	213.30	
	5-9y	188.23	25.72	184	137	249	243.90	0.55[2]
		183.75	19.85	184	126	229	219.60	
	9-13y	193.12	20.81	195.50	143	237	225.05	0.59[2]
		192.49	23.54	189	142	247	235.80	
	13-18y	190.85	26.63	189	127	248	230.20	0.86[2]
		192.50	18.75	188	251	234	225	
JTp-c (ms)	0-3m	216.59	28.69	208.40	177.94	259.44	259.43	0.80[2]
		215.48	34.15	209.66	162.04	262.39	262.39	
	3m-1y	209.66	19.63	196.91	190.59	229.58	229.58	0.15[2]
		224.07	23.25	225.66	200.48	265.35	265.35	
	1-3y	207.28	22.57	194.45	185.89	251.27	251.26	**<0.001[2]**
		229.01	17.98	221.80	204.77	255.97	255.97	
	3-5y	221.07	21.02	220.32	168.92	261.32	260.13	0.30[2]
		225.79	24.57	224.24	182.03	263.16	260.45	
	5-9y	228.31	21.66	225.89	193.03	277.18	269.73	0.47[1]
		230.10	17.70	231.35	181.74	266.55	253.14	
	9-13y	228.50	18.98	227.04	196	268.69	262.06	0.13[1]
		232.44	19.88	233.63	178.60	279.90	270.06	
	13-18y	214.81	19.57	216.75	158.59	256.43	240.84	**<0.001[2]**
		227.50	17.63	230.47	187.54	255.48	255.25	
Tpe (ms)	0-3m	43.52	7.18	41.66	33.33	53.33	53.30	0.39[2]
		45.16	11.47	43.33	27.50	61.67	61.60	
	3m-1y	43.78	6.67	48.33	36.67	50	50	0.52[2]
		42.01	2.74	40	40	46.67	46.60	
	1-3y	52.37	5.60	48.33	45	60	60	**0.03[2]**
		48.12	5.78	48.33	40	58	56.80	
	3-5y	58.10	10.09	55	40.60	81	79.80	0.27[2]
		55.45	10.03	55	40	83	77.90	
	5-9y	62.84	9.35	60	46	85	82.55	**<0.001[2]**
		56.37	7.10	55	42	73	68.60	
	9-13y	58.35	7.06	58	42	79	72.50	0.25[2]
		56.88	7.20	57.50	40	75	71	
	13-18y	65.15	9.29	64.50	47	92	83.05	**<0.001[2]**
		58.56	7.56	59	38	80	69.60	

1: Student t test, 2: Mann-Whitney test, m: Month, y: Year.

The median values for JTp, JTpc, and Tpe were 184 ms (98.33-249), 225.60 ms (162.04-279.90), and 57 ms (27.50-92), respectively.

Table 4 illustrates the correlation between JTp and Tpe across various parameters.

Table 4. *Correlation relationship table of JTp and Tpe with various parameters.*

Parameters		JTp	Tpe
Age	**r value**	0.58	0.51
	p value	<0.001[1]	<0.001[1]
BSA	**r value**	0.56	0.51
	p value	<0.001[1]	<0.001[1]
Heart rate	**r value**	-0.82	-0.49
	p value	<0.001[1]	<0.001[1]
EF	**r value**	-0.17	-0.09
	p value	<0.001[1]	0.01[1]
E/A ratio	**r value**	0.42	0.32
	p value	<0.001[1]	<0.001[1]
LVmass	**r value**	0.59	0.50
	p value	<0.001[1]	<0.001[1]

1: Spearman test, BSA: Body surface area, LVmass: Left ventricle mass, EF: Ejection fraction, E: Early ventricular diastolic velocity, A: Late ventricular diastolic velocity, HR: Heart rate.

Both JTp and Tpe intervals demonstrated a negative correlation with heart rate and a positive correlation with age, body surface area, heart mass, and heart function.

DISCUSSION

Our study evaluated the normal range of early repolarization time in healthy children according to their age and sex. In cases where determining the endpoint of the T wave is difficult, evaluating the JTp interval can provide important information. JTp has different values based on age and gender. JTp interval is closely related to cardiac function.

Changes in depolarization wavelength, repolarization time, and repolarization dispersion time are the basic mechanisms that contribute to arrhythmia formation (13). In clinical practice, parameters such as depolarization time, depolarization dispersion time, repolarization time, and repolarization dispersion time are used

for this purpose (9, 14-16). The myocardium comprises layers with different electrophysiological properties. The action potential duration of the epicardial layer was the shortest, and that of the mid-myocardial layer was the longest (17). The duration of repolarization can be classified as early or late. Early repolarization corresponds to the duration of the action potential of the epicardial layer, measured from the beginning of the J wave to the peak of the T wave on the ECG (1). Late repolarization is defined as the time from the peak of the T wave to the end of the T wave and is expressed as Tpe on the ECG (9, 18, 19).

Many intervals, such as repolarization time and repolarization dispersion time, have been evaluated to predict arrhythmias. In clinical practice, QT and JT serve as repolarization times, while QTd, Tpe, Tpe/QT, and Tpe/QTc ratios act as repolarization dispersion times. Determining the starting and ending points of waves and innervations on an ECG can be challenging. Although QT, JT, QTc, and JTc provide information on repolarization time, they do not indicate repolarization heterogeneity (13).

QT dispersion (QTd) is widely used in clinical practice as a marker of repolarisation heterogeneity. It is calculated by measuring the difference between the maximum and minimum QT intervals on a 12-lead ECG. However, uncertainties in defining the endpoint of the T wave, the prolonging effects of bundle branch blocks on the timing of ventricular depolarization, and the technical details required for measurements on multi-lead ECGs are among the main problems that limit the applicability of this method.

In animal models, it has been suggested that the peak of the T-wave corresponds to the moment when epicardial repolarization ends. However, later studies have indicated that this relationship does not fully align but is relatively close to the endpoint of epicardial repolarization. Although Tpe was initially thought to reflect transmural repolarization dispersion (TDR), more recent data have shown that it represents global repolarization dispersion (13). Additionally, the lead-dependency of Tpe has been highlighted as an important limitation (20). For these reasons, it is suggested that the Tpe/QT and Tpe/QTc ratios, rather than Tpe, represent TDR more reliably (8). Challenges in determining the endpoint of the T wave and including the duration of ventricular depolarization in the QT interval complicate the clinical use of these parameters, mainly because they are affected by bundle branch block. Prolongation of repolarization duration and dispersion has been reported in genetic arrhythmias and various diseases (8, 21-24).

The predictive superiority of these parameters for arrhythmias remains debatable, as each measurement interval is associated with inherent limitations. When selecting intervals for arrhythmia prediction, challenges such as accurately defining the endpoint of the T wave, including ventricular depolarization duration within the QT interval, and prolonging the total interval in cases of extended depolarization must be considered. In this context, assessing relatively simpler intervals, such as JTp, offers notable advantages in clinical practice. Evidence from a previous study suggests that an isolated increase in the QTc interval may be benign without a corresponding prolongation of the JTp interval (25). Understanding the normal reference ranges of JTp and heart rate-corrected JTp (JTpc) is crucial for accurate clinical assessments. Therefore, this study aims to determine the age- and gender-specific normal ranges of JTp and JTpc, contributing to improved clinical evaluation strategies.

In our study, the normal value ranges of the total repolarization time in healthy children were similar to those reported in the literature (16, 19, 26-29).

In one study, it was stated that JTp depends on autonomic tone, whereas Tpe is less (3). Another study noted that there was no need to correct for heart rate in the evaluation of Tpe (26). For this purpose, normal values of JTpc, the heart rate-corrected form of JTp, were analyzed according to age and sex. In our study, the mean values of JTp and JTpc were 181.47 ms (±27.57) and 225.21 ms (±20.74), respectively. Although the JTp value was similar to that reported in a previous study, JTpc was lower (3). While the JTpc value in the literature study was 313 ms (297-329), in our study, it was 225.60 ms (162.04-279.90). While the current study was conducted on prepubertal children, it evaluated children from the neonatal period to 18 years. We cannot explain the difference in the JTpc values between the current study and ours. We believe that this finding should be confirmed in other studies.

In a study conducted in the literature, the Tpe value according to age groups is 63±10.9 ms between 0-1 years of age, 67±8.75 ms between 1-5 years of age, and 71±8.1 ms between 5-10 years, 75±8.5 ms (52–97) in those over 10 years of age (27). In a study evaluating 131 healthy children with a mean age of 9.07±3.89 and age participation between 2.3-18.5, the median Tpe value was 60 ms (40-100) (20). In another study, the Tpe value was 70.50 ms (±13.01) and 86.2 ms (±9.5) in children (<11 years old) and adolescents (11-19 years old), respectively (30). In another study, the Tpe value was 60.0 (58.0–63.0) between the ages of 10 and 19 (31). In our study, the Tpe value was 57 ms (27.50-92), slightly lower than the values in the literature.

In studies conducted in the literature, Tpe/QT ratio is 0.19 (± 0.03), 0.21 (± 0.02), 0.17 (0.16-0.18), Tpe/QTc ratio is 0.15 (0.14-0.16), Tpe/JT ratio was 0.27 (± 0.05), 0.27 (± 0.03) (20, 27, 31). No studies on Tpe/JTc ratio in healthy children have been reported in the literature. In our study, Tpe/QT, Tpe/QTc, Tpe/JT, Tpe/JTc ratio values were 0.18 (± 0.02), 0.14 (± 0.02), 0.24 (± 0.03), 0.19 (± 0.03), respectively. These rates were significantly higher in boys in our study. Our findings were parallel to the literature (20).

The JTp interval, similar to the Tpe interval, correlated with age, body surface area, heart mass, and cardiac function parameters. Tpe showed a weak correlation

with heart rate, whereas JTp showed a strong correlation with heart rate.

In conclusion, various intervals were used to evaluate the repolarization and repolarization dispersion times. There are various limitations to the evaluation of these intervals in clinical practice. We believe that in cases where Tpe evaluation is difficult, the evaluation of JTp and JTpc can provide helpful information. Knowing the normal ranges of JTp and JTpc according to age and sex can provide useful information.

Limitations of our study: Manual ECG measurements and the presence of human factors were the main limitations of our study. Another limitation was that the present study did not evaluate the repolarization dispersion time.

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