Comparison Between Cardio-Electrophysiological Balance Index and Corrected Values in Different Age Groups Among School-Age Children

Okul Çağındaki Çocuklarda Farklı Yaş Gruplarında Kardiyo-Elektrofizyolojik Denge İndeksi ve Düzeltilmiş Değerlerinin Karşılaştırılması

Ömer GÜNEŞ[1], Ahmet Yasin GÜNEY[2], Halit HALİL[3], Aylin KAYALI AKYOL[4], Özhan AKYOL[4], Fatih ÜÇKARDEŞ[5], Bahar ÖZTELCAN GÜNDÜZ[6], Yüksel Hakan AYDOĞMUŞ[6], Utku PAMUK[7], Ayhan KILIÇ[8], Bülent ÜNAY[9]

[1]Department of Pediatric Infectious Disesases, Ankara Etlik City Hospital, Ankara, Türkiye
[2]Department of Pediatric Infectious Disesases, Tekirdağ City Hospital, Tekirdağ, Türkiye
[3]Department of Pediatrics, Yıldırım Beyazıt University, Yenimahalle Training and Research Hospital Hospital Ankara, Türkiye
[4]Department of Pediatrics, Ankara Bilkent City Hospital Ankara, Türkiye
[5]Department of Biostatistics and Medical Informatics, Faculty of Medicine, Adıyaman University, Adıyaman, Türkiye
[6]Department of Pediatrics, Gülhane Training and Research Hospital, Ankara, Türkiye
[7]Department of Pediatric Cardiology, Ankara Bilkent City Hospital, Ankara, Türkiye
[8]Department of Pediatric Cardiology, Gülhane Training and Research Hospital, Ankara, Türkiye
[9]Department of Pediatric Neurology, Gülhane Training and Research Hospital, Ankara, Türkiye

ABSTRACT

Objective: The index of cardio-electrophysiological balance (iCEB) is a new non-invasive marker that can be used to predict malignant ventricular arrhythmias. Pediatric studies on iCEB are limited in number. Our study aimed to determine the range of its values in different age groups among school-age children.

Material and Methods: The study included patients aged 5-17 admitted to Gülhane Training and Research Hospital Pediatric Cardiology Outpatient Clinic between March 2020 and March 2022 without a history of chronic disease, cardiac disease, arrhythmia, or cardiac surgery. Participants were categorised into ages 5-8, 9-12, and 13-17. The iCEB and iCEBc values were calculated and compared between groups.

0000-0001-7121-3810 : GÜNEŞ Ö
0000-0002-3446-7034 : GÜNEY AY
0000-0003-4631-4980 : HALİL H
0000-0001-5662-4021 : KAYALI AKYOL A
0000-0001-9352-074X : AKYOL Ö
0000-0003-0677-7606 : ÜÇKARDEŞ F
0000-0003-1243-8731 : ÖZTELCAN GÜNDÜZ B
0000-0003-2978-8738 : AYDOĞMUŞ YH
0000-0001-7046-8571 : PAMUK U
0000-0001-9042-1789 : KILIÇ A
0000-0001-5432-8624 : ÜNAY B

Conflict of Interest / *Çıkar Çatışması*: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethics Committee Approval / *Etik Kurul Onayı*: This study was conducted in accordance with the Helsinki Declaration Principles. the study was obtained from the Gülhane Training and Research Hospital Ethics Committee (2020-91).

Contribution of the Authors / Yazarların katkısı*: *GÜNEŞ Ö: Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking responsibility for the research/study, Taking responsibility in patient follow-up, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***GÜNEY AY:*** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking responsibility for the research/study, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***HALİL H:*** Organizing, supervising the course of progress and taking responsibility for the research/study, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***KAYALI AKYOL A:*** Taking responsibility in patient follow-up, data management and reporting, execution of the experiments, Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar. ***AKYOL Ö:*** Taking responsibility in patient follow-up, data management and reporting, execution of the experiments, Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar. ***ÜÇKARDEŞ F:*** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Taking responsibility in patient follow-up, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***ÖZTELCAN GÜNDÜZ B:*** Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar. ***AYDOĞMUŞ YH:*** Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar. ***PAMUK U:*** Constructing the hypothesis or idea of research and/or article, Taking responsibility in patient follow-up, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***KILIÇ A:*** Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***ÜNAY B:*** Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar.

How to cite / *Atıf yazım şekli* : Güneş Ö, Güney AY; Halil AY, Kayalı Akyol A, Akyol Ö, Üçkardeş F et al. Comparison Between Cardio-Electrophysiological Balance Index and Corrected Values in Different Age Groups Among School-Age Children. Turkish J Pediatr Dis 202X;18:323-328.

Correspondence Address / Yazışma Adresi:
Ömer GÜNEŞ
Department of Pediatric Infectious Disesases,
Ankara Etlik City Hospital, Ankara, Türkiye
E-posta: dromergunes@gmail.com

Received / Geliş tarihi : 15.03.2024
Accepted / Kabul tarihi : 16.05.2024
Online published : 10.05.2024
Elektronik yayın tarihi
DOI: 10.12956/tchd.1449621

Results: The total number of 1303 cases were categorised into the 5-8 (n=270), 9-12 (n=389), and 13-17 (n=644) age groups. The mean iCEB and iCEBc values for all age groups were 4.39±0.53 and 5.16±0.53, respectively. Any difference was not detected among age groups of 5-8, 9-12, and 13-17 years in terms of iCEB and iCEBc values (4.42±0.56, 4.39±0.53 and 4.39±0.52 vs. 5.19±0.56, 5.15±0.55 and 5.16±0.52, respectively). However, a significant difference was found between male (n=699) and female (n=604) patients in terms of mean iCEB (4.23±0.52 vs. 4.59±0.47) and iCEBc (4.98±0.53 vs. 5.38±0.46) values (p <0.001).

Conclusion: iCEB and iCEBc values in school-age children did not differ according to age groups. However, these values differed between boys and girls. This study is the first to reveal normal ranges of iCEB and iCEBc values in school-age children.

Key Words: Child, ECG, iCEB, iCEBc, School-age

ÖZ

Amaç: Kardiyo-elektrofizyolojik denge indeksi (iCEB), malign ventriküler aritmileri tahmin etmede kullanılabilecek yeni, invazif olmayan bir belirteçtir. iCEB ile ilgili pediatrik çalışmalar sayıca sınırlıdır. Çalışmamız okul çağındaki çocuklarda farklı yaş gruplarındaki iCEB değerlerinin aralığını belirlemeyi amaçladı.

Gereç ve Yöntemler: Gülhane Eğitim ve Araştırma Hastanesi Çocuk Kardiyoloji Polikliniğine Mart 2020-Mart 2022 tarihleri arasında başvuran, kronik hastalık, kalp hastalığı, aritmi ve kalp cerrahisi öyküsü olmayan 5-17 yaş arası hastalar çalışmaya dahil edildi. Katılımcılar 5-8, 9-12 ve 13-17 yaş gruplarına ayrıldı. iCEB ve iCEBc değerleri hesaplandı ve gruplar arasında karşılaştırıldı.

Bulgular: Toplam 1303 vaka 5-8 (n=270), 9-12 (n=389) ve 13-17 (n=644) yaş gruplarına ayrıldı. Tüm yaş grupları için ortalama iCEB ve iCEBc değerleri sırasıyla 4.39±0.53 ve 5.16±0.53'di. iCEB ve iCEBc değerleri açısından 5-8, 9-12 ve 13-17 yaş grupları arasında farklılık saptanmadı (4.42±0.56, 4,.39±0.53 ve 4.39±0.52 vs. 5.19±0.56, 5.15±0.55 ve 5.16±0.52). Ancak erkek (n=699) ve kadın (n=604) hastalar arasında ortalama iCEB (4.23±0.52 vs. 4.59±0.47) ve iCEBc (4.98±0.53 vs. 5.38±0.46) değerleri açısından anlamlı fark bulundu (p <0.001).

Sonuç: Okul çağındaki çocuklarda iCEB ve iCEBc değerleri yaş gruplarına göre farklılık göstermedi. Ancak bu değerler kız ve erkek çocuklar arasında farklılık göstermektedir. Bu çalışma, okul çağındaki çocuklarda iCEB ve iCEBc değerlerinin normal aralıklarını ortaya koyan ilk çalışmadır.

Anahtar Sözcükler: Çocuk, EKG, iCEB, iCEBc, Okul çağı

INTRODUCTION

A new, simple, effective, easily calculable and non-invasive marker called the cardio-electrophysiological balance index (iCEB), which can be obtained by dividing the QT duration by the QRS duration (QT/QRS) and used in predicting malignant ventricular arrhythmias was first introduced to the literature by Lu et al. (1). The iCEB balances ventricular depolarization (QRS) and repolarisation (QT). It has been considered equivalent to the wavelength of the cardiac impulse, namely the cardiac wavelength. This cardiac wavelength increases significantly in predicting polymorphic ventricular tachycardia (torsades de pointes). At the same time, a decrease in it is crucial in predicting non-polymorphic ventricular tachycardia and fibrillation. In addition, it is a non-invasive marker and can be measured simply on surface ECG. Adult studies have been conducted on using iCEB and iCEBc values in various diseases. Among these diseases, COVID-19, end-stage renal disease, sarcoidosis, type 1 diabetes mellitus, tinnitus, subarachnoid haemorrhage, type myotonic dystrophy can be enumerated (2-9). However, studies revealing the ranges of average iCEB values in the pediatric age group are limited. Our study aimed to determine the typical ranges of iCEB and iCEBc values in school-age children using ECG. Records will be made according to the age groups and gender of the study participants.

MATERIALS and METHODS

Patients aged 5-17 years who applied to the pediatric outpatient clinics of Gülhane Training and Research Hospital between March 2020 and March 2022 for nonspecific chest pain, cardiac murmurs and health control were referred to the Pediatric Cardiology Outpatient Clinic for ECG. Monitoring was included in this prospective cross-sectional study. Patients who did not have congenital or acquired heart disease, any chronic disease, arrhythmia or cardiovascular surgery history, whose parents gave informed consent and whose echocardiographic examinations were performed were included in the study. Anthropometric (weight and height) measurements and arterial blood pressure measurements of the cases were performed. Those with height and weight values below the 3rd percentile and above the 97th percentile and those with body mass index and arterial blood pressure measurements below the 5th percentile and above the 95th percentile were excluded from the study (10,11). Cases of obesity, malnutrition, systemic hypertension and other systemic diseases were excluded from the study. Those with congenital or acquired heart disease after echocardiographic evaluation and those with arrhythmia after 24-hour Holter ECG evaluation were excluded from the study. Participants were categorised into ages 5-8, 9-12 and 13-17 years (12).

Electrocardiography recordings (25 mm/sec, 10 mV) were obtained with a 12-lead ECG device (G.E. Healthcare M.A.C.

2000, Milwaukee, U.S.A.) and analysed manually by two experienced paediatricians. Intra-reader variability was <2 ms for all intervals and <0.10 mV for all amplitudes. Inter-reader variability was a maximum of +/–5 ms for intervals including the QT and a maximum of 0.15 mV for the amplitudes, including the R waves. Heart rate, PR interval, QRS axis, QRS duration, and QT interval values were obtained from ECGs obtained independently from the derivations. On the lead DII, arithmetic means of three consecutive beats were taken to obtain PR interval duration and heart rate per minute. QRS, QT and QTc measurements used in these ratios were obtained from precordial leads using arithmetic means of three consecutive beats. The time from the beginning of the QRS complex to the end of the T wave was considered the QT interval. Bazzett formula was used for QTc calculations, and iCEB and iCEBc ratios were determined as follows: QTc = QT/√RR) QT/QRS (iCEB) and QTc/ QRS (corrected iCEB; iCEBc). In addition, the QRS, QT and QTc measurements used in calculating these ratios were obtained by taking the arithmetic average of three consecutive beats in precordial leads. The iCEB and iCEBc values were compared between age groups and genders.

Statistical analysis

Statistical analyses were performed using the IBM Statistical Package for the Social Sciences, version 25.0 (SPSS Inc., Armonk, NY, IBM Corp., USA). The conformity of quantitative variables with normal distribution was evaluated with the single-sample Kolmogorov- Smirnov test. Independent two-sample t-test was used to determine the difference between genders. ANOVA test was used to check the difference (if any) between age groups. The results were given as mean±standard deviation (mean±SD) and also minimuma and maximum values. Pearson correlation analysis was performed to determine the correlation of iCEB and iCEBc measurements (if any) with age groups. Simple linear regression analysis was used to investigate whether iCEB and iCEBc measurements were age-independent. The level of statistical significance was accepted as p<0.050.

Written informed consent was obtained from the parents of all children, as well as from the children aged 12-17 years. Approval for the study was obtained from the Gülhane Training and Research Hospital Ethics Committee (2020-91).

RESULTS

The study population consisted of 699 male and 604 female patients. Male and female study participants were included in the age groups of 5-8 (n= 270; 140 boys and 130 girls), 9-12 (n= 389; 194 boys, 195 girls) and 13-17 (n= 644; 365 boys, and 279 girls) years. The average weight was 23.82±3.53 kg for ages 5-8, 35.25±5.89 kg for ages 9-12, and 55.98±7.65 kg for ages 13-18. The average height was 120.56±4.76 cm for ages 5-8, 140.42±5.86 cm for ages 9-12, and 163.77±5.56 cm for ages 13-18. The average body mass index was 15.74±2.44 for ages 5-8, 17.62±2.37 for ages 9-12, and 20.78±2.47 for ages 13-18. Mean arterial blood pressure values were 98.95±6.74/60.25±7.45 mmHg for ages 5-8, 107.07±5.28/68.27±6.35 mmHg for ages 9-12, 114.35±6.38/73.78±6 for ages 13-18. Heart rates, QRS, QT, QTc and PR interval values are given according to age groups in Table I and the age groups and gender of the cases in Table II. The QRS intervals were shorter in the same age group, while QT and QTc intervals were more extended in female subjects.

The mean iCEB and iCEBc values for all age groups were 4.39±0.53 and 5.16±0.54, respectively. There was no difference between age groups regarding iCEB p=0.567) and iCEBc values (p=0.199). The iCEB and iCEBc values by age groups are summarised in Table III.

However, a significant difference was found between iCEB and iCEBc values between male and female genders in the same age group (p <0.001). The mean iCEB and iCEBc values of the male (n= 699) and female (n= 604) participants were 4.23±0.52 vs. 4.59±0.47 and 4.98±0.53 vs. 5.38±0.46, respectively (Table IV). As a result of the correlation analysis, no significant correlation was found between the iCEB and iCEBc values and the age of the participants (r=-0.003, p=0.908; r=-0.006, p=0.818, respectively). Increasing or decreasing age did not increase or decrease iCEB and iCEBc values. As a result of the regression analysis, both iCEB and iCEBc values were independent of age (β=-0.0005, p=0.908, β=-0.001, p=0.818). Increasing or decreasing age did not affect iCEB and iCEBc values. Percentiles of iCEB and iCEBc values of the study participants according to age groups and gender are given in Table V.

DISCUSSION

The studies conducted since the first definitions of iCEB/iCEBc values have focused on adult cases with pathological increases and decreases of these values because of diseases and drugs carrying an increased risk of arrhythmia (1). Limited relevant studies have been conducted on pediatric age groups and healthy subjects. Therefore, the findings in our study had to be compared with the reference ranges of iCEB and iCEBc values reported in studies performed in the healthy control groups.

First, in the literature, Sap et al. (13) aimed to examine ICEB and other risk markers regarding cardiac arrhythmia in children with acute rheumatic carditis. In their study, the mean ages of the patient and control groups, each consisting of 16 female and 24 male participants, had been 11.40±3.48 and 11.41±3.31 years, respectively. The iCEBc values were significantly higher in the group with acute rheumatic carditis. In contrast, relative increases in iCEB values in the patient group were not

Table I: ECG parameters by age groups

Age groups	Heart rate (bpm)*	QRS interval (msec*)	QT interval (msec)*	QTc interval (msec)*	PR interval (msec)*
5-8 years (n=270)	85.5±14.6	80.2±7.7	351.1±26.4	412.4±18.5	122.1±15.0
9-12 years (n=389)	86.3±13.2	81.1±8.0	352.6±23.8	414.1±16.5	125.2±14.4
13-18 years (n=644)	84.4±13.7	80.8±7.3	351.8±23.8	413.5±16.8	125.6±14.7

**mean±SD: mean±standard deviation*

Table II: ECG parameters by age groups and genders of the study participants

Age groups Gender	Heart rate (bpm)*	QRS interval (msec)*	QT interval (msec)*	QTc interval (msec)*	PR interval (msec)*
5-8 years					
Male (n=140)	82.2±12.8	83.0±8.1	344.8±26.7	407.6±19.5	122.4±15.1
Female (n=130)	88.9±15.7	77.2±5.9	357.8±24.5	417.6±16.0	121.9±15.0
9-12 years					
Male (n=194)	85.4±12.6	83.9±8.1	350.4±25.8	411.9±18.0	125.4±15.1
Female (n=195)	87.1±13.8	78.3±6.8	354.9±21.5	416.2±14.5	125.1±13.7
13-17 years					
Male (n=365)	83.4±13.4	83.0±7.6	349.4±24.3	411.6±17.6	125.6±14.8
Female (n=279)	85.6±14.0	77.9±5.8	355.0±22.7	416.0±15.4	125.5±14.7

** mean±SD: mean±Standard Deviation*

Table III: iCEB and iCEBc values by age groups

	Age groups			Difference between age groups
	5-8 years (n=270)	9-12 years (n=389)	13-17 years (n=644)	p
iCEB values *	4.42±0.56	4.39±0.53	4.39±0.52	0.567
iCEBc values*	5.19±0.56	5.15±0.55	5.16±0.52	0.199

**mean ±SD:mean±Standard Deviation, One-way analysis of variance was used*

statistically significant compared to the healthy controls. Their study stated that using iCEBc may be beneficial in addition to other electrocardiographic risk parameters for arrhythmia. In their study, the mean iCEB and iCEBc values in the patient and healthy control groups were 5.04±0.80 vs. 4.94±0.58 and 6.18±0.89 vs. 5.69±0.67, respectively. In our study, the mean iCEB and iCEBc values for all age groups within the 5-17 years range were 4.39±0.53 and 5.16±0.53, respectively. In our study of 1303 cases, iCEB and iCEBc values were lower than those of the above-mentioned healthy control group of 40 cases. In addition, our study detected a significant difference between male and female cases regarding both iCEB and iCEBc values. This issue was not addressed in their research.

In their study on 65 adult healthy control subjects and 40 adult patients, Robyns et al. (14) investigated the effects of drugs with arrhythmogenic potentials, such as sotalol and flecainide, on iCEB and iCEBc values. They suggested using a mean cut-off iCEB value of 4.24±0.5 and a reference range of 3.24–5 for healthy adults. Their study also found higher iCEB values in women than men ($p < 0.001$), which might stem from reduced QRS duration associated with the higher QT interval and smaller heart size under the impact of sex hormones. However, their study showed a lack of any significant difference among age groups concerning this issue. In addition, they emphasised that iCEB is not a heart rate-independent factor and may be beneficial in a specific heart rate range and stressed that in tachycardic patients, the use of corrected iCEB (iCEBc) instead of iCEB may be required (14). Our study's mean iCEB value was 4.39±0.53 for the 5-17 age group. Our mean (±SD) iCEB values were slightly higher than those indicated in the study. In addition, consistent with this study's findings, we observed lower QRS. However, QT and QTc interval values were higher in female than male subjects. The smaller cardiac muscle mass and size in female and male patients may explain this condition. Since our study group consisted of both prepubertal and postpubertal cases, it does not seem possible to say whether this phenomenon is associated with the impact of sex hormones. This issue may be clarified in a separate study. Considering that it may be more appropriate to use iCEBc in cases of increased heart rates, we conceive that the mean iCEBc measurement of 5.16±0.53 can be used as a cut-off value for the 5-17 age group.

The Third National Health and Nutrition Examination Survey (NHANES-III) examined the relationship between iCEBc, all-cause, and cardiac mortality rates in the hitherto most significant number of adult cases (n=5010) (mean age= 51.10±7.67 years; female cases=52.5%) whose electrocardiograms were in sinus rhythm, and was stated that elevated iCEBc (male ≥4.57 and

Table IV: Comparison of iCEB and iCEBc values by age groups and gender of the study participants

	Male (n=699)	Female (n=604)	p
iCEB values*			
5-8 years (n=270)	4.20±0.53 (n=140)	4.66±0.49 (n=130)	<0.001
9-12 years (n=389)	4.22± 0.52 (n=194)	4.56±0.48 (n=195)	<0.001
13-17 years (n=644)	4.25± 0.51 (n=365)	4.58±0.46 (n=279)	<0.001
All age groups 5-17 years (n=1303)	4.23±0.52	4.59±0.47	<0.001
iCEBc values*			
5-8 years (n=270)	4.96±0.54 (n=140)	5.44±0.46 (n=130)	<0.001
9-12 years (n=389)	4.96±0.54 (n=194)	5.35±0.49 (n=195)	<0.001
13-17 years (n=644)	5.0±0.53 (n=365)	5.37±0.44 (n=279)	<0.001
All age groups 5-17 years (n=1303)	4.98±0.53	5.38±0.46	<0.001

***** *mean±SD: mean±Standard Deviation, An independent two-sample t-test was used*

Table V: Percentiles of iCEB and iCEBc values according to the age groups and gender of the study participants

	Male (n=699)		Female (n=604)	
	2p	98p	2p	98p
iCEB values*				
5-8 years (n=270)	3.69	4.71	4.18	5.14
9-12 years (n=389)	3.72	4.72	4.09	5.03
13-17 years (n=644)	3.76	4.74	4.14	5.02
iCEBc values*				
5-8 years (n=270)	4.44	5.48	5.00	5.88
9-12 years (n=389)	4.44	5.48	4.87	5.83
13-17 years (n=644)	4.49	5.51	4.95	5.79

*****mean±SD: mean±Standard Deviation

female ≥4.98) may be an independent risk factor for cardiac or all-cause mortality among middle-aged adults (13-15). In our study, the mean iCEBc value (5.16±0.53) for the 5-17 age group was slightly higher with a similar standard deviation compared to the iCEB value indicated in the study mentioned above. In our research, the 5-17 age group was not evaluated regarding mortality rates. However, consistent with the study's findings, the mean iCEBc value of our female subjects (5.38±0.46) was higher than that of our male subjects (4.98±0.53).

In a retrospective study on smoking habits, Özdemir et al. (16) compared a total of 80 smokers with a mean age of 39.4±8.1 years with a control group of 82 non-smokers age-matched healthy cases. They found that smokers had higher iCEBc values than controls (5.10±0.49 and 4.68±0.39, respectively, p < 0.001), while iCEB values did not differ significantly between groups (4.37±0.46 and 4.32±0.42, respectively; p=0.456). The total number of healthy control subjects in our study (n= 1303) was significantly higher when compared with those (n= 82) included in the study mentioned above. While the mean iCEB value in our research (4.39±0.53) was close to the value indicated in the study mentioned above (4.32±0.42), our iCEBc value (5.16±0.54) was higher than that estimated (4.68± 0.39 in this study). However, both studies' standard deviations calculated for iCEB and iCEBc (0.42 vs. 0.53 and 0.39 vs. 0.54, respectively) were close.

In the study conducted by Afsin et al. (17) with a total of 108 adult atrial fibrillation patients using amiodarone (n=68) or propafenone (n=40) and 50 healthy adult control individuals, respective iCEB and iCEBc values were determined to be 4.2 ±0.4 and 4.6±0.4 in the healthy control group. In our study, the mean iCEB and iCEBc values of the 5-17 age group were 4.39±0.53 and 5.16±0.54, respectively. The mean iCEB and iCEBc values of our male (n= 699) and female (n= 604) participants were 4.23±0.52 vs. 4.59±0.47, and 4.98±0.53 vs 5.38±0.46, respectively. However, the total number of healthy control subjects (n= 50) in the above study was very scarce compared to our study population (n= 1303). While the mean iCEB value in our research (4.39±0.53) was close to the value mentioned in the study mentioned above (4.2±0.4), our mean iCEBc value (5.16±0.54) was higher than the value indicated in their study (4.6±0.4). However, the standard deviations of the mean iCEB (0.4 vs. 0.53) and iCEBc (0.4 vs. 0.54) values were comparable between both studies.

Our study's limitations include the small number of cases, its cross-sectional design, the possibility of missing data due to incomplete family reporting, and the failure to include data on the subsequent cardiological evaluations of the cases due to cross-sectional design.

In conclusion, we have determined that iCEB and iCEBc values in school-age children did not differ according to age groups. Still, these values were significantly different between boys and girls. Among school-age children aged 5-17, 4.23±0.52 and 4.59±0.47 can be used as the mean average cut-off values for iCEB. We think 4.98±0.53 and 5.38±0.46 can be cut-off values

for iCEBc in male and female cases, respectively. Differences in iCEB and iCEBc values between male and female cases may be due to the differences in cardiac muscle mass between genders. Ours is the first comprehensive study that attempts to reveal the typical ranges of iCEB and iCEBc values in school-age children and proposes using separate ranges for boys and girls. More extensive studies are needed on this subject.

REFERENCES

1. Lu HR, Yan GX, Gallacher DJ. A new biomarker--index of cardiac electrophysiological balance (iCEB)-plays an important role in drug-induced cardiac arrhythmias beyond QT-prolongation and Torsades de Pointes (TdPs). J Pharmacol Toxicol Methods 2013;68:250-9.
2. Asoglu R, Tibilli H, Asoglu E, Aladag N, Ozdemir M, Suner A. Evaluation of index of cardiac electrophysiological balance in COVID-19 patients. Bratisl Lek Listy 2021;122:598-604.
3. Alareedh M, Nafakhi H, Shaghee F, Nafakhi A. Electrocardiographic markers of increased risk of sudden cardiac death in patients with COVID-19 pneumonia. Ann Non-invasive Electrocardiol 2021;26:e12824.
4. Sivri S, Çelik M. Evaluation of index of cardiac-electrophysiological balance before and after hemodialysis in patients with end-stage renal disease. J Electrocardiol 2019;54:72-5.
5. Alsancak Y, Korkmaz C. Evaluation of Index of Cardiac-Electrophysiological Balance and Electrocardiographic Alternations in Patients with Sarcoidosis. Sakarya Med J 2021;11: 193-200.
6. Zorlu Ç, Ömür S. E. Evaluation of Index of Cardiac Electrophysiological Balance in Type 1 Diabetes Mellitus. Journal of Harran University Medical Faculty 2021;18: 441-5.
7. Kaya H, Suner A, Koparal M, Yucetas SC, Kafadar S. Evaluation of Tp-e interval, Tp-e/QT ratio and index of cardiac-electrophysiological balance in patients with tinnitus. BMC Cardiovasc Disord 2021;21:415.
8. Yücetas SC, Kaya H, Kafadar S, Kafadar H, Tibilli H, Akcay A. Evaluation of index of cardiac-electrophysiological balance in patients with subarachnoid hemorrhage. BMC Cardiovasc Disord 2022;22:477.
9. Okşul M, Bilge Ö, Türken A, Işık F, Akyüz A, Çap M, et al. Evaluation of Index of Cardiac Electrophysiological Balance in Patients With Myotonic Dystrophy Type 1. Cureus 2023;15:e34600.
10. Neyzi O, Bundak R, Gökçay G, Günöz H, Furman A, Darendeliler F, et al. Reference Values for Weight, Height, Head Circumference, and Body Mass Index in Turkish Children. J Clin Res Pediatr Endocrinol 2015;7:280-93.
11. Keskinoglu A, Keskinoglu B, Ozgur S, Kose T. Blood Pressure Percentiles in Turkish Children and Adolescents. J Pediatr Res 2020;7:279-85.
12. Rijnbeek PR, Witsenburg M, Schrama E, Hess J, Kors JA. New normal limits for the paediatric electrocardiogram. Eur Heart J 2001;22:702-11.
13. Sap F, Guney AY, Oflaz MB, Baysal T. Index of Cardiac Electrophysiological Balance in Electrocardiography of Children with Acute Rheumatic Carditis. Selcuk Med J 2022;38: 64-70.
14. Robyns T, Lu HR, Gallacher DJ, Garweg C, Ector J, Willems R, et al. Evaluation of Index of Cardio-Electrophysiological Balance (iCEB) as a New Biomarker for the Identification of Patients at Increased Arrhythmic Risk. Ann Non-invasive Electrocardiol 2016;21:294-304.
15. Chen X, Wang Z, Liu L, Zhang W, Tang Z, Liu B, et al. Prognostic value of index of cardiac electrophysiological balance among U.S. middle-aged adults. Front Cardiovasc Med 2023;10:1139967.
16. Özdemir L, Sökmen E. Effect of habitual cigarette smoking on the index of cardiac electrophysiological balance in apparently healthy individuals. J Electrocardiol 2020;59:41-4.
17. Afsin A, Asoglu R, Kobat MA, Asoglu E, Suner A. Evaluation of Index of Cardio-Electrophysiological Balance in Patients With Atrial Fibrillation on Antiarrhythmic-Drug Therapy. Cardiol Res 2021;12:37-46.