RESEARCH ARTICLE / *Araştırma Makalesi*

Evaluation of Index of Cardiac-Electrophysiological Balance and Electrocardiographic Alternations in Patients with Sarcoidosis

Sarkoidozlu Hastalarda Kardiyak-Elektrofizyolojik Denge İndeksinin ve Elektrokardiyografik Değişimlerin Değerlendirilmesi

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Abstract

Objective	Cardiac sarcoidosis (CS) can manifest with different clinical signs and has a poor prognosis, but the heart is rarely affected alone. We aim to evaluate the arrhythmogenic effects of sarcoidosis by using electrocardiography (ECG) in patients with or without cardiac involvement.
Materials and Methods	A total of 61 patients under follow-up for pulmonary sarcoidosis were retrospectively reviewed and 50 healthy volunteers were enrolled in the study. Sarcoidosis patients were also grouped as with or without cardiac involvement (n=11/ n=35). QRS, QT, Tp-e (T peak to end) intervals, P wave morphology were measured manually on ECG. Then, Tp-e/QT, Tp-e/QTc, QT/QRS (index of cardiac electrophysiological balance, (iCEB)), and QTc/QRS (iCEBc) ratios were calculated and compared between groups.
Results	Heart rate on ECG, QT/QTc interval, Tp-e intervals and Tp-e/QT ratio and PWD were significantly higher (p values < 0.018) and iCEB or iCEBc values were lower in the sarcoidosis group than controls (p = 0.001). And we could not find a relationship between non-cardiac and CS and ECG parameters including QTc, Tp-e/QT ratio and iCEB (p= 0.501, p= 0.753 and p=0.490, respectively).
Conclusion	The present study demonstrated a lower iCEB value and higher repolarization findings in sarcoidosis patient. However, there are no differences between with or without cardiac involvement due to sarcoidosis.
Keywords	Arrhythmia; electrocardiography; iCEB; sarcoidosis

Öz

Amaç	*Kardiyak sarkoidoz (KS) farklı klinik bulgularla ortaya çıkabilir ve kötü bir prognoza sahiptir, ancak kalp nadiren tek başına etkilenir. Bu çalışmamızda, kalp tutulumu olan veya olmayan hastalarda elektrokardiyografi (EKG) kullanarak sarkoidozun aritmojenik etkilerini değerlendirmeyi amaçladık.*
Gereç ve Yöntemler	*Pulmoner sarkoidoz nedeniyle takip edilen toplam 61 hasta retrospektif olarak incelendi ve 50 sağlıklı gönüllü çalışmaya alındı. Sarkoidoz hastaları da kalp tutulumu olan veya olmayan olarak gruplandırıldı (n = 11 / n = 35). EKG üzerinde; QRS, QT, Tp-e (T peak to end) intervali, P dalga morfolojisi manuel olarak ölçüldü. Daha sonra Tp-e / QT, Tp-e / QTc, QT / QRS (kardiyak elektrofizyolojik denge indeksi, (iCEB)) ve QTc / QRS (iCEBc) oranları hesaplandı ve gruplar arası karşılaştırıldı.*
Bulgular	*Sarkoidoz grubunda, kontrol grubuna göre kalp hızı, QT / QTc aralığı, Tp-e aralıkları ve Tp-e / QT oranı ve PWD anlamlı olarak yüksek (p değerleri <0,018), iCEB ve iCEBc değerleri daha düşüktü (p = 0,001). Kardiyak sarkoidozu olan ve olmayan grupta ise QTc, Tp-e / QT oranı ve iCEB dahil EKG parametreleri arasında bir ilişki bulunmadı (sırasıyla p = 0,501, p = 0,753 ve p = 0,490).*
Sonuç	*Bu çalışma, sarkoidoz hastalarının repolarizasyon değerlerinin daha yüksek, iCEB değerinin ise daha düşük olduğunu göstermiştir. Bununla birlikte, sarkodioza bağlı kalp tutulumu olan hastalarla, olmayan hastalar arasında ECG parametrelerine göre anlamlı bir fark görülmemiştir.*
Anahtar Kelimeler	*Aritmi; elektrokardiyografi; iCEB; sarkoidoz*

INTRODUCTION

Sarcoidosis is known as a multisystemic granulomatous disease with unexplained etiology which affect many organs in the body. But also, current reports argue that sarcoidosis has occurred as a result of increased immunological response for any reason in individuals with genetic predisposition.[1] Asymptomatic pulmonary involvement is the most common form in daily practice, but the disease may also affect heart, liver, peripheral lymph nodes, spleen, skin, eyes, and parotid glands.[2] Unfortunately, cardiac exposure in sarcoidosis has a poor prognosis, and the heart is rarely affected alone.[3] Involvement of heart and the emergence of related cardiac symptoms constitute 2-5% of patients with sarcoidosis.[4] And, 20-25% patients with sarcoidosis have an asymptomatic cardiac involvement according to autopsy reports.[5]

Cardiac sarcoidosis (CS) can manifest itself with different clinical signs. The affected anatomically area of the heart, the active period and extent of the disease are decisive for this condition.[6] Mainly, the clinical implications of CS are primarily due to arrhythmias, conduction disorders and heart failure.[7] Pericardial disease, sudden cardiac death, coronary artery or cardiac valves involvement are less frequently demonstrated.[8,9] In this context, some studies have been conducted on surface electrocardiography to predict arrhythmia in patients with sarcoidosis. QT interval prolongation, which is the most known ECG finding that is a marker for electrical instability and sudden cardiac death, was shown in patients with sarcoidosis.[10] T peak to end (Tp-e) interval on ECG is considered as an index of transmural dispersion of left ventricular repolarization and Tp-e/QT ratio is also used as a novel electrocardiographic index of ventricular arrhythmogenesis. Previously published studies demonstrated that a prolonged Tp-e and higher Tp-e/QT ratio has been associated with an increased risk of ventricular arrhythmias.[11,12] It has been suggested that Tp-e and Tp-e/QT ratios were higher in sarcoidosis patients.[13] Index of cardiac electrophysiological balance (iCEB), estimated as QT interval divided by QRS duration, is a novel risk indicator for predicting malignant ventricular arrhythmias.[14] An elevated iCEB level is accepted as a predictor of torsades de pointes (TdP) ventricular arrhyhtmias wheares decreased iCEB level is linked with non-torsades de pointes ventricular arrhyhtmias.[15]

In this study, we aimed to investigate the iCEB and it's association between Tp-e and Tp-e/QT ratio in patients with or without cardiac involvement of sarcoidosis to evaluate proarrhythmogenic effect.

MATERIAL and METHODS

2.1. Study population and patient selection

A total of 61 patients (30 males; mean age 43.4±10.6 years) under follow-up for pulmonary sarcoidosis and had cardiac magnetic resonance imaging for investigating for cardiac involvement were retrospectively reviewed and 50 healthy volunteers (32 males; mean age 42.4±8.6 years) were enrolled in the study. The study population was categorized as sarcoidosis group, control group and compared the parameters between groups. After that, we compared the parameters between in patients with cardiac (n= 11) and non-CS (n= 35). In sarcoidosis group, patients was diagnosed means of transbronchial ultrasound-guided lymph node or peripheric biopsy and biopsy-proven sarcoidosis was diagnosed in all patients. Patients with a history of myocardial infarction or coronary revascularization (via coronary artery bypass graft operation or percutaneous coronary intervention), those who documented atrial fibrillation, cardiac pacemaker implantation, sick sinus syndrome, any kind of bundle branch blocks, pre-excitation syndromes, atrioventricular block, left ventricular hypertrophy and valvular heart disease (moderate-to-severe), renal insuffiency (creatinin levels > 1.5 or glomeruler filtration rate below 50) electrolyte hemoastatis disorders, heart failure who need medical treatment, depressed left ventricular ejection fraction (EF < 55%) due to coronary artery disease were excluded from study. For this reason, a total of 14 patients (heart failure: 3, coronary artery disease: 3, documented atrial fibrillation: 3 insufficient

or inappropriate ECG data: 5, left bunddle block: 1) were excluded from this study, finally 46 patients data was analysed. A study flow chart has been illustrated in Figure 1.

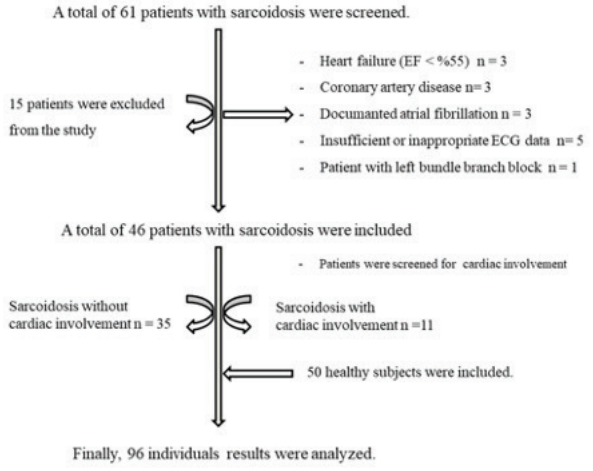

Figure 1. Flowcharts of the study

2.2. Definition of cardiac sarcoidosis

The electrocardiographic and echocardiographic features of the patients were evaluated. On electrocardiography, conduction abnormalities, branch blocks, atrial fibrillation, AV block presence were recorded. We could not investigate 24-hour Holter ECG monitoring records of patients because of retrospective design and lack of the records. In echocardiography, end-diastolic/end-systolic left ventricular diameter, interventricular septum and posterior wall end-diastolic thickness, regional or globally wall motion abnormalities, pressure of LV filling, mitral and tricuspid valves regurgitation, pericardial effusion, pulmonary artery pressure and ejection fraction were recorded. Myocardial wall motion abnormalities in patients with a history of obstructive coronary artery disease were excluded from study. The results of cardiac magnetic resonance (MR) imaging were evaluated of all patients with a diagnosis of sarcoidosis. Nevertheless, patients with late gadolinium enhacement (LGE) in cardiac MR imaging were examined with a definitive diagnosis of CS. Therefore, 11 patients were grouped as CS due to MR imaging findings.[16]

2.3. Electrocardiographical examinations

Heart rate, P-wave morphology, PR interval, QRS duration, QT distance and T-wave morphology were analyzed. All ECG samples were examined on a digital platform and measurements were then taken using special software (Adobe Photoshop) to provide the necessary magnification.

The beginning point of the P-wave was described as the first upward positive or downward negative deflection between the isoelectric line and the end of the P-wave was characterized as the point where the last deflection of the P-wave met the isoelectric line. Maximum (Pmax) and minimum P (Pmin) wave durations were recorded. P-wave dispersion (PWD) was defined as the difference between the maximum and minimum P-wave durations.[17] The QT interval was conventionally obtained by manually measuring from the onset of the QRS complex to the crossing point of the T wave and isoelectric line. The heart rate-corrected QT interval was calculated using Bazett's formula ($cQT = QT\sqrt{(R - R \text{ interval})}$). QT dispersion (QTd) was obtained by measuring the longest QT interval (QTmax) and the shortest QT interval (QTmin) in any lead.[18] QT interval measurements were taken by examining recordings from leads D2 and precordial V5, and the longer lead was recorded for statistical analysis. The distance from the peak of the T-wave (Tpeak) to the endpoint of the T-wave (T end) (Tpeak-end or Tp-e) was obtained from the chest leads. The Tp-e/QT ratio was obtained by dividing the Tp-e duration by the QT interval in the precordial V5 lead.[19] The index of cardiac electrophysiological balance (iCEB) was obtained by dividing the QT interval by the QRS duration in the same lead (D2 or V5).[14,15]

Statistical Analysis

SPSS® version 16.0 statistical package software (SPSS Inc., Chicago, IL, United States) was used for statistical analyses. We presented normally distributed quantitative variables as mean ± standard deviation or median value while we presented categorical variables in numbers and percentages. Normality of distribution was evaluated us-

ing the Kolmogorov–Smirnov test. Mean values of continuous variables were compared between independent groups using the Student's T-test, one-way ANOVA test, or Kruskal-Wallis test as appropriate. The chi-square test was performed to compare the study groups in terms of categorical variables. A p-value below 0.05 was considered statistically significant.

RESULTS

A total of 96 patients with a mean age of 59.46±11.12 years, 74 (77.1%) of whom were women, formed the study population. There was no statistically significant difference between the sarcoidosis group and control group in terms of gender, age and laboratory parameters except high density lipoprotein cholesterol, trigliseride and CRP (C-reactive protein). CRP levels were higher in sarcoidosis group as expected (p= 0.001). The study groups were comparable in terms of echocardiographic and electrocardiographical parameters. Accordingly, in patients with sarcoidosis, pulmonary artery pressure was higher and pericardial effusion rate was higher than control group (p= 0.002 and p= 0.045, respectively). Although QT maximum, QT minimum, P minimum were not different between groups, heart rate on ECG, QT/QTc interval, Tp-e intervals and Tp-e/QT ratio and PWD were significantly higher in sarcoidosis group (p values < 0.018). And also, iCEB or iCEBc values were lower in sarcoidosis group (p= 0.001). The demographic features, laboratory parameters, electrocardiographic and echocardiographic characteristics and comparison between groups are summarized in Table 1 and 2.

In the subgroup analysis, according to echocardiographic evaluation, we detected only that the left ventricular posterior wall thickness was increased in patients with CS (p = 0.001). And we found any relationship between non-cardiac and CS and ECG parameters including QTc, Tp-e/QT ratio and iCEB (p= 0.501, p= 0.753 and p= 0.490, respectively). Table 3 demonstrates the electrocardiographic parameters, echocardiographic characteristics and comparison between subgroups.

Table 1. Demographic and laboratory characteristics of patients and comparing parameters between Sarcoidosis group and Control group

Variables	Sarcoidosis group (n =46)	Control group (n= 50)	p value
Age (median, IQR)	57.54 (29-77)	61.24 (33-80)	0.528
Gender (female, n / %)	35 / 76,8	39 / 78	0.825
Smoking (n / %)	4 / 8.7	10 / 20	0.470
Hypertension (n / %)	19 / 41.34	25 / 50	0.395
Diabetes mellitus (n / %)	10 / 21.7	15 / 30	0.359
Hemoglobulin (mg/dl / mean±std)	13.24±1.33	13.65±1.57	0.186
Potasium (meq/L, mean±std)	4.34±0.32	4.27±0.71	0.121
Glomerular filtration rate (mL/min/ mean±std)	87.14±21.55	92.96±15.82	0.133
Total cholesterol (mg/ dl, mean±std)	203.11±52.99	203,64±44.41	0.961
LDL (mg/dl, mean±std)	122.59±39.73	123.13±37.11	0.949
HDL (mg/dl, mean±std)	42.5±12.45	48.30±12.48	**0.039**
Uric ascid (mg/dl, mean±std)	5.48±1.32	5.23±1.83	0.469
Glucose (mg/dl, median, IQR)	108.7 (89-112)	99.5 (89-129)	0.393
Creatinine (mg/dl, median, IQR)	0.78 (0.69-0.91)	0.71 (67-82)	0.063
Sedimantation (sn, median, IQR)	15 (13-20)	13.5 (6.7-24)	0.201
ALT (mg/dl, median, IQR)	19.25 (15.5-23.5)	20 (12.7-25)	0.638
AST (mg/dl, median, IQR)	19.5 (16.6-26)	20 (18-25)	0.336
Trigliseride (mg/dl, median, IQR)	162 (128-237)	135 (92-194)	**0.014**
CRP (mg/dl, median, IQR)	5.63 (3.6-9)	1.1 (0.1-3)	**0.001**

*ALT; alanine aminotransferase; AST; aspartate aminotransferase, CRP; C-reactive protein, HDL; high density lipoprotein cholesterol, IQR; interquartile range, LDL; low density lipoprotein cholesterol

Table 2. Comparing of echocardiographical and electrocardiographical parameters of groups

Variables		Sarcoidosis group (n =46)	Control group (n= 50)	p value
LVDD, (mm, mean±std)		44.16±4.6	47.02±4.9	**0.004**
LVSD, (mm, mean±std)		27.10±3.5	28.26±6.5	0.292
IVSD, (mm, mean±std)		10.55±1.4	9.84±0.97	0.006
PWT, (mm, mean±std)		10±1.67	9.48±1.7	0.084
LVEF (%, median, IQR)		61 (59-63)	60 (50-60)	0.122
Mitral inflow E velocity		71.32±16.3	71.32±19.7	0.919
Mitral inflow A velocity		79.34±20.8	76.3±18.5	0.453
Left atrial diameter, (mm, mean±std)		34.5 (31-39)	36.5 (33-38)	0.066
Mitral regurgitation (n/%)				
	- mild	45 (99)	47 (94)	0.268
	- moderate	1 (1)	3 (6)	
Tricuspid regurgitation (n/%)				
	-mild	44 (95.6)	47 (94)	
	-moderate	2 (4.4)	3 (6)	0.495
Pulmonary artery systolic pressure (mmHg, mean±std)		36.02±5.53	31.34±7.79	**0.002**
Pericardial effusion (n/%)		9 (19.5)	3 (6)	**0.045**
Electrocardiographical parameters				
Heart rate (pulse/min, mean±std)		80.19±16.97	72.74±12.38	**0.015**
P maximum (msn, mean±std)		91.5±17.78	78.4±26.6	**0.006**
P minimum (msn, mean±std)		47.39±12.6	49.20±19.7	0.597
PWD (mns, mean±std)		43.84±12.68	29.2±13.61	**0.001**
QT maximum (msn, mean±std)		389.13±38.35	380.24±32.82	0.224
QT minimum (msn, mean±std)		362±37.72	358.5±28.32	0.604
QT dispersion (msn, mean±std)		27.5±11.35	20.95±9.91	**0.004**
QRS (msn, mean±std)		91±17.33	71.64±24.68	**0.001**
Tpe interval (msn, mean±std)		79.13±18.83	67.20±20.77	**0.004**
QTc maximum (msn, mean±std)		412±27.33	413±32.77	0.763
QTc minimum (msn, mean±std)		385±28.8	392±31.1	0.244
QTc dispersion (msn, mean±std)		27±11.25	21.74±10.35	**0.018**
QT/QRS (iCEB) (mean±std)		4.37±0.65	5.92±1.97	**0.001**
cQT/QRS (iCEBc) (mean±std)		4.63±0.66	6.46±2.2	**0.001**
Tpe/QT ratio (mean±std)		0.20±0.04	0.17±0.05	**0.009**
Tpe/QTc (mean±std)		0.19±0.04	0.16±0.04	**0.002**

* IVSD; inter-ventricular septum, LVDD; left ventricular diastolic diameter, LVEF; left ventricular ejection fraction; LVSD ; left ventricular systolic diameter, PWD; P wave dispersion, PWT: posterior wall thickness, QTc; corrected QT interval, Tp-e; T peak to T end interval

Table 3. Comparing parameters of patients with and without cardiac sarcoidosis

Variables	Sarcoidosis without cardiac involvement (n =35)	Sarcoidosis with cardiac involvement (n = 11)	p value
CRP (mg/dl, mean±std)	7.7±6.6	7.8±7.2	0.960
Sedimantation (sn, mean±std)	19.55±11.2	16.45±9.09	0.411
Potasium (meq/L, mean±std)	4.6±0.28	4.35±0.36	0.052
IVSD, (mm, mean±std)	10.41±1.58	11±1.09	0.261
PWT, (mm, mean±std)	9.4±1.09	12.45±1.03	**0.001**
LVEF (%, median, IQR)	60.71±2.99	61.27±2.32	0.575
Pulmonary artery systolic pressure (mmHg, mean±std)	35.62±5.78	37.27±4.67	0.396
Pericardial effusion (n/%)	6 (17)	3 (27)	0.465
Electrocardiographical parameters			
Heart rate (pulse/min, mean±std)	79.97±18.13	80.9±13.30	0.875
P maximum (msn, mean±std)	93.71±18.68	84.72±12.98	0.146
P minimum (msn, mean±std)	51.57±11.61	34.09±2.02	**0.001**
PWD (mns, mean±std)	42±12.13	49.72±13.17	0.078
QT maximum (msn, mean±std)	388±34.72	392±50	0.726
QT minimum (msn, mean±std)	361.57±32.14	363.64±53.71	0.876
QT dispersion (msn, mean±std)	26.42±9.6	30.9±15.78	0.258
QRS (msn, mean±std)	91.82±18.18	88.36±14.77	0.569
Tp-e interval (msn, mean±std)	79.42±19.69	78.18±16.62	0.851
QTc maximum (msn, mean±std)	411.5±24.25	413.89±36.84	0.804
QTc minimum (msn, mean±std)	385±23	384.8±43.9	0.978
QTc dispersion (msn, mean±std)	26.42±9.62	29±15.78	0.501
QT/QRS (iCEB) (mean±std)	4.33±0.68	4.49±0.55	0.490
cQT/QRS (iCEBc) (mean±std)	4.6±0.7	4.74±0.54	0.535
Tp-e/QT ratio (mean±std)	0.20±0.05	0.20±0.04	0.753
Tp-e/QTc (mean±std)	0.19±0.04	0.18±0.03	0.802

* CRP; C reactive protein , IVSD; inter-ventricular septum, iCEB: index of cardioelectrophyslogical balance, LVEF; left ventricular ejection fraction, PWD; P wave dispersion, PWT: posterior wall thickness, QTc; corrected QT interval, Tp-e; T peak to T end

DISCUSSION

In the current study, our results indicate that Tp-e interval, Tp-e / QT ratio, PWD or index of cardiac electrophysiological balance value, knowns as predictors of the development of arrhythmia which can simply measured on standard 12-lead surface ECG, were higher in sarcoidosis patients than healthy subjects. However, the fact that these findings, were not supported in a small group of sarcoidosis with cardiac involvement, could not reveal that these markers were predictive of cardiac involvement.

The incidence of sarcoidosis in population is 10-20/100.000. Although CS is very rare, it has a poor prognosis and it is an indepented predictor for mortality and morbidity. And left ventricular systolic dysfunction is the most important marker for this situation.[20] CS is the main causes of 0.5% patients who who underwent to cardiac transplantation due to cardiomyopathy.[21] However, cardiac arrhythmias are still the first clinical presentation of symptomatic CS. A significant number of patients with CS (30%) can manifest themselves with complete AV block. Since the conduction system can be infiltrated with sarcoid granuloma, it is possible to see any degree of heart blocks.[22] Previously, it was speculated that atrial arrrhytmias may occur after atrial dilatation due to generalized cardiac involvement in sarcoidosis, instead of just atrial involvement.[23] However, supraventricular tachycardies has been detected 32% of patients with CS nearly in 6 years follow up period. It has been shown that atrial fibrillation is the most frequently supraventricular arrhythmia and left atrial enlargement is the main predictive factor.[24] In addition, sudden death due to malignant ventricular arrhythmias may be the first and only symptoms of cardiac involvement. Macroreentrany, re-entry, triggered activity and abnormal automaticity, due to granulomatous infiltration, inflammation and scaring of myocardium, are accepted as major reasons of ventricular arryhtmias.[25] The prevalence of CS in patients with unexplained ventricular tachycardia is 16-29% according to two studies with small sample size.[26,27] In this context, evaluation of cardiac involvement in patients with sarcoidosis is extremely important. Altough cardiac MR imaging, fluorodeoxyglucose positron emission tomography imaging or tissue biopsy are recommanded for diagnose cardiac involvement in patients with sarcoidosis, these advanced cardiac imaging tecniques is not recommended for patients without abnormalities on initial screening by symptoms/electrocardiogram/echocardiogram.[16] It has been demonstrated that the cardiac history (syncope, palpitation etc), ECG, 24 hours rhytm Holter monitoring and echocardiography have a specificity of 87% and a sensitivity of 100% for the diagnosis of CS.[28] From this point of view, ECG still maintains its place as the first diagnostic and screening test and, several parameters and intervals have been described on surface ECG to determine the arrhythmogenic risks.

The change of ECG parameters described above in sarcoidosis patients has been evaluated in several studies. Uyarel et al. demonstrated an increased QTd in patients with sarcoidosis and cardiac involvement. They also detected it was higher in sarcoidosis patients with cardiac involvement than those without.[10] Kasapkara and colleagues findings support increasing QT dispersion in patients with sarcoidosis and an elevated Tp-e and Tp-e/QT ratio were shown in the same study.[13] However, they did not grouped patients with cardiac or nonCS. In our study, we also found a higher QTd, Tp-e and Tp-e/QT ratio in sarcoidosis like these trials. But our study failed to demonstrate the significant difference between cardiac and non-cardiac sarcoidosis according to these parameters. Maybe the limited number of cardiac sarcoidos patient revealed of this result. The presence of patchy involvement away from the conduction system in MR imaging may also affect the results. In an another study which performed by Buyukoglan H. et al. have been shown a higher PWD in sarcoidosis patient that known as a predictor to the development of atrial fibrillation.[17,29] Herein, we also found a higher PWD value in patients with sarcoidosis than healthy subjects, but there was no statistically differences between cardiac and non-CS. The similarity of the left atrial diameter in both groups

may have caused such a result. And these results may have been seen due to early-stage CS of our study group. Finally, iCEB, which has been defined as a new risk predictor for malignant ventricular arrhythmias, was higher in patients with sarcoidosis. However, we also demonstrated that iCEB value was not different in patients with and without cardiac involvement.

In MR imaging, cardiac infiltration has a typically patchy and multifocal characteristics. The basal segments of the left ventricle are the most affected regions by granulomatosis involvement.[30] For this reason, small localized involvements away from the conduction system may not produce any signs on surface ECG. Perhaps, a large ventricular area should be involved to see surface ECG changes.

Study limitations

The most significant limitation in this trial was the insufficient number of patients with cardiac involvement and retrospective design of the study. In addition, the lack of patient history for previous arrhythmias is another limitation. Moreover, the lack of 24-hour electrocardiographic Holter monitoring to detect arrhythmic conditions in these patients may be considered as a limitation. Moreover, unknown using of drugs that affect the conduction system (beta-blockers, non-dihydropyridine calcium channel blockers or digital), and use of antibiotics with known efficacy on electrocardiography (erythromycin, azithromycin, etc.) may also be considered as a limitation.

CONCLUSION

To our knowledge, the present study is the first to use iCEB analysis in sarcoidosis patients to determine arrhythmogenic risk and we demonstrated a lower iCEB value in patients with sarcoidosis, but we failed to show statistically difference between cardiac and non-CS. Many of the patients with sarcoidosis may have a clinically silent cardiac involvement. Electrocardiography is still an easy-to-use and accessible diagnostic tool in daily practice. According to the literature, the predictors of arrhythmia in electrocardiography appear to be positive in patients with systemic sarcoidosis, but it is not possible to defend the same situation in patients with or without cardiac involvement. Further large scale, randomized, prospective, long-term follow-up studies are needed to clarify the role of iCEB and other electrocardiographical parameters in predicting ventricular arrhythmias and/or sudden cardiac death in patients with sarcoidosis.

Acknowledgment

None

Ethics Committee Approval

Before the beginning of the study, the necessary approval was received from Necmettin Erbakan University Meram School of Medicine's local ethics committee with 2020/2046 numbered decision in date 17.05.2020 and the study was conducted according to the Declaration of Helsinki.

Informed Consent

Patients included in the study were informed about the objective of the study and given written and verbal consents.

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

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