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**ORIGINAL PAPER**
*Diseases of the heart*

# Electrocardiographic abnormalities in patients with pulmonary sarcoidosis (RCD code: III)

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## Abstract

Sarcoidosis is a systemic inflammatory disease characterized by the presence of noncaseating granulomas. Etiology of the disease remains unknown. From 3.7% to 54.9% patients with extra-cardiac sarcoidosis have asymptomatic heart involvement. Conduction abnormalities, arrhythmias and congestive heart failure are the most common clinical manifestations of cardiac sarcoidosis (CS). The aim of the study was to evaluate the type and frequency of electrocardiographic abnormalities in patients with pulmonary sarcoidosis and to compare differences in the occurrence of electrocardiographic changes between patients diagnosed with CS and patients without confirmation of CS. **Materials and methods:** 49 patients (18 women, 31 men), mean age 45.6 ±12.2 years with biopsy-proven pulmonary sarcoidosis were enrolled in the study. The patients were divided into two groups. Group 1 consisted of 12 patients diagnosed with CS, and Group 2 of 37 patients without diagnosis of CS. 12-lead baseline electrocardiogram (ECG) was recorded for all participants. **Results:** 89.8% patients with pulmonary sarcoidosis had abnormal ECG. The most common ECG abnormalities were ST-T changes observed in 79.6%. Conduction abnormalities were present in 26.5% of patients. 22.45% patients had left axis deviation. Rhythm abnormalities were recorded in 20.4% of all analyzed ECGs. ECGs of 8.16% of patients met criteria of hypertrophy. There was a trend towards more frequent prevalence of some ECG changes in patients with CS than patients without CS. However, these differences were not statistically significant. **Conclusions:** We observed a trend towards more frequent prevalence of some ECG abnormalities in a group of patients with CS than in patients without CS. However, these differences were not statistically significant. ECG abnormalities in patients with pulmonary sarcoidosis require further diagnostics. JRCD 2017; 3 (3): 81–85

**Key words:** rare disease, electrocardiogram, conduction abnormalities, rhythm abnormalities, pulmonary sarcoidosis, cardiac sarcoidosis

## Background

Sarcoidosis is a systemic, inflammatory disease characterized by the presence of noncaseating granulomas. Etiology of the disease remains unknown. Organs commonly involved in the course of sarcoidosis include lungs, lymph nodes, skin, central nervous system and eyes [1]. Data from the literature show that 3.7%–54.9% patients with extra-cardiac sarcoidosis have asymptomatic heart involvement [2]. The most common clinical manifestations of cardiac sarcoidosis (CS) are conduction abnormalities, arrhythmias and congestive heart failure. Pericardial effusion, pulmonary hypertension, ventricular aneurysms and valvular disease may also occur [3].

Diagnostic tests used in screening for cardiac involvement in patients with pulmonary sarcoidosis are 12-lead electrocardiogram (ECG), Holter ECG monitoring, transthoracic echocardiography, cardiac magnetic resonance, myocardial perfusion scintigraphy and positron emission tomography. Currently, myocardial biopsy is not necessary for diagnosis of CS [2].

Specific treatment for CS is currently not available. Corticosteroids and other immunosuppressive agents are the first-line therapy. Other treatment options include cardiac ablation or device therapy such as implantation of a pacemaker, implantable cardioverter-defibrillator or cardiac resynchronization therapy. In some patients, heart transplantation remains the only option [2,4].

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**Table 1. Characteristics of the study group**

| Characteristics | mean/number | range/percent (%) |
|---|---|---|
| **Age (years)** | 45.63 | 22–72 |
| **Sex** | | |
| females | 18 | 36.73 |
| males | 31 | 63.26 |
| **Concomitant disease:** | | |
| None | 14 | 28.57 |
| Arterial hypertension | 18 | 36.73 |
| Coronary artery disease | 2 | 4.08 |
| Hyperlipidemia | 30 | 61.22 |
| Diabetes mellitus | 3 | 6.12 |
| **Heart Rhythm Society Criteria Positive for Cardiac Sarcoidosis** | 12 | 24.48 |

# Material and methods

## Study group

49 adult patients with pulmonary sarcoidosis: 18 females and 31 males were enrolled in the study. All patients were hospitalized in the Department of Cardiac and Vascular Diseases, Institute of Cardiology, Jagiellonian University Medical College in Krakow in years 2014–2017. The mean age of the patients was 45.6 ±12.2 years (range 22–72). All patients had histopathologically confirmed diagnosis of pulmonary sarcoidosis. Characteristics of the study group are shown in Table 1.

Patients were divided into two groups. Group 1 consisted of 12 patients (3 women, 9 men) diagnosed with CS. Group 2 consisted of 37 patients (15 women, 22 men) without confirmation of CS. Diagnosis of CS was based on criteria proposed by Heart Rhythm Society (HRS) Expert Consensus Statement on Arrhythmias Associated with Cardiac Sarcoidosis from 2014 [2]. Criteria adopted for the diagnosis of sarcoidosis are shown in Table 2. Analyzed ECG abnormalities were rated by age, sex, heart rate and the presence of concomitant diseases.

## Electrocardiographic Data

All patients had a 12-lead ECG recorded in the resting, supine position. All ECGs were evaluated by the authors according to the recommendations proposed by the Polish Cardiac Society [5].

Observed ECG abnormalities were divided into four groups. The first group contained conduction abnormalities such as: atrioventricular (AV) blocks, complete left or right bundle branch block (LBBB, RBBB), left anterior or posterior hemiblock (LAH, LPH) and nonspecific intraventricular conduction delay. The second group included rhythm abnormalities such as sinus bradycardia or tachycardia, atrial fibrillation or flutter, supraventricular or ventricular extrasystoles. The third group comprised of hypertrophic changes of left and/or right ventricle and enlargement of left and/or right atrium. Abnormalities of QRS axis, ST-T interval abnormalities, pathologic Q waves, small progression of R-waves and low QRS complexes are defined as other ECG changes and form the fourth group. ECGs without abnormalities were classified as normal.

# Statistical analysis

All analyses were conducted using STATISTICA software version 12. Mean values and standard deviation were determined by continuous variables. Categorical variables were presented as numbers and percentages. All analyzed variables were verified for the existence of normal distribution. Group differences between CS and non-CS patients were analyzed using chi-squared test. Spearman's rank test was used for analyses the correlations between variables. Statistical significance was set at $\alpha \leq 0.05$.

# Results

44 patients (89.8%) with pulmonary sarcoidosis had ECG changes classified as other ECG abnormalities. Among them, the most commonly observed were ST-T changes, which were present in 39 subjects (79.6%). Pathologic Q waves were observed in 12 subjects (24.5%) and left axis deviation in 11 patients (22.45%). The second most common group of changes were conduction abnormalities, which were observed in 13 patients (26.5%). The most

**Table 2. Adopted criteria for the diagnosis of cardiac sarcoidosis based on Heart Rhythm Society (HRS) Expert Consensus Statement on Arrhythmias Associated with Cardiac Sarcoidosis from 2014 [2]**

**Cardiac sarcoidosis was diagnosed in patients with biopsy proven extra-cardiac sarcoidosis if ≥1 of below criteria was present:**

- Steroid and/or immunosuppressant responsive cardiomyopathy or heart block
- Unexplained reduced of left ventricular ejection fraction (<40%)
- Unexplained sustained (spontaneous or induced) ventricular tachycardia
- Type 2 second-degree atrioventricular block (Mobitz II) or third-degree atrioventricular block
- Patchy uptake on cardiac positron emission tomography (PET)
- Late Gadolinium enhancement on cardiac magnetic resonance (CMR)
- Positive gallium uptake on myocardial scintigraphy

AND:
other causes of these changes have been excluded

**Table 3. Prevalence of electrocardiographic (ECG) changes in the study group**

| Type of ECG changes | number of patients | percentage (%) |
|---|---|---|
| CONDUCTION ABNORMALITIES | 13 | 26.53 |
| I-degree AV block | 6 | 12.24 |
| Right bundle branch block (RBBB) | 4 | 8.16 |
| Left anterior hemiblock (LAH) | 4 | 8.16 |
| Nonspecific intraventricular conduction defects | 2 | 4.08 |
| RHYTHM ABNORMALITIES | 10 | 20.4 |
| Sinus bradycardia | 8 | 16.33 |
| Ventricular extrasystoles | 1 | 2.04 |
| Atrial fibrillation | 1 | 2.04 |
| HYPERTROPHIC CHANGES | 4 | 8.16 |
| Left atrial enlargement | 2 | 4.08 |
| Left ventricular hypertrophy | 2 | 4.08 |
| OTHER ECG CHANGES | 44 | 89.79 |
| Pathologic Q wave | 12 | 24.49 |
| Low QRS complex voltage | 4 | 8.16 |
| QRS AXIS ABNORMALITIES | 11 | 22.45 |
| Left axis deviation | 11 | 22.45 |
| ST-T INTERVAL ABNORMALITIES | 39 | 79.59 |
| Inverted T wave | 3 | 6.12 |
| Peaked T wave | 2 | 4.08 |
| Flattened T wave | 20 | 40.81 |
| Biphasic T waves | 1 | 2.04 |
| Secondary ST-T changes | 6 | 12.24 |
| Nonspecific ST-T changes | 26 | 53.06 |

prevalent conduction abnormalities was 1st degree AV block observed in 6 subjects (12.2%), right bundle branch block (RBBB) and left anterior hemiblock block (LAH), each present in 4 patients (8.2%). Nonspecific intraventricular conduction delays was present in 2 patient (4.1%). Rhythm abnormalities were detected in 10 patients (20.4%). The most frequent rhythm abnormality was sinus bradycardia observed in 8 patients (16.3%), followed by ventricular extrasystoles and atrial fibrillation, each observed in 1 patient (2.1%). Hypertrophic changes were observed in 4 patients (8.2%): 2 patients (4.1%) had atrial enlargement and 2 subjects (4.1%) had left ventricular hypertrophy. 5 of all ECGs (10.2%) were classified as normal. Prevalence of ECG abnormalities in the study group are shown in Table 3.

Additionally, we observed statistically significant positive correlation between age and number of ECG changes (p=0.02). No correlation was observed between the presence of concomitant diseases and number of ECG abnormalities (p=0.38). Also, we did not observed correlation between heart rate and number of ECG abnormalities (p = 0.47).

Moreover, we compared changes in ECG between Group 1 (patients diagnosed with CS) and Group 2 (patients without CS). Differences in the incidence of ECG abnormalities between both groups are shown in Table 4. There was a trend towards more frequent prevalence of conduction and rhythm abnormalities and some other ECG changes in Group 1 than in Group 2. However, there were no statistically significant differences in prevalence of ECG abnormalities between Group 1 and 2. Normal ECG was recorded in 1 patient of Group 1 (8.3%) and 4 subjects of Group 2 (10.8%).

## Discussion

Data from the literature show, that ECG abnormalities are observed in 50% of patients with clinically manifested CS. Converesly, 3.2% to 8.6% of patients with asymptomatic CS have abnormal ECG [6]. These changes include various degrees of atrioventricular blocks, bundle branch blocks (right more common than left) and fascicular blocks. Other observed abnormalities include ST–T changes, pathologic Q waves and epsilon waves [2,7,8].

Heart Rhythm Society (HRS) Expert Consensus Statement on Arrhythmias Associated with Cardiac Sarcoidosis recommend performing 12-lead electrocardiogram in all patients with biopsy-proven extra-cardiac sarcoidosis (Class I). The sensitivity of ECG is estimated at 8% and specificity at 97%. Abnormal ECG is defined by HRS Experts as complete left or right bundle branch block and/or presence of unexplained pathologic Q waves in 2 or more leads and/or sustained 2nd- or 3rd-degree AV block, and/or sustained or non-sustained ventricular tachycardia (VT). Patients with biopsy-proven extra-cardiac sarcoidosis and thus defined abnormal ECG should undergo screening for CS, using advanced imaging techniques such as cardiac magnetic resonance and/or positron emission tomography [2].

Scholler et al. showed that the presence of abnormal ECG in a patient with pulmonary sarcoidosis should suggest cardiac sarcoidosis and requires additional testing for sarcoid heart involvement. Other reasons for ECG abnormalities has to be excluded [9]. Study performed in Japan on 227 patients with pulmonary sarcoidosis proved that electrocardiographic abnormalities such as: increased heart rate, prolonged PR interval, RBBB and ST-T abnormalities were associated with increased risk of cardiac events defined as: occurrence of advanced AV block, VT and systolic dysfunction. Authors suspected, that prolonged PR interval may reflect the early involvement of the basal part of interventricular septum where cells of conduction system are located, whereas ST segment abnormalities may result from early stage of myocardial damage [7].

Other large study from Sweden showed that the risk of CS development is significantly higher in sarcoidosis patients with abnormal ECG than in patients with a normal ECG (13.2% vs 0.1%). Moreover, coexistence of pathologic ECG and cardiac symptoms increased the risk of CS to 27.5%, compared to patients with abnormal ECG changes but no cardiac related symptoms 8.7% [10]. Similarly, Martusewicz-Boros and others proved that changes detected in 12-lead ECG were important risk factor for developing CS [11].

**Table 4. Prevalence of electrocardiographic abnormalities in Group 1 and Group 2**

| Type of ECG changes | PATIENTS WITH CS | | PATIENTS WITHOUT CS | | p value |
|---|---|---|---|---|---|
| | number of patients | percentage (%) | number of patients | percentage (%) | |
| CONDUCTION ABNORMALITIES | 4 | 33.33 | 9 | 24.32 | 0.53 |
| I-degree AV block | 1 | 8.33 | 5 | 13.51 | 0.63 |
| Right bundle branch block (RBBB) | 0 | 0 | 4 | 10.81 | - |
| Left anterior hemiblock (LAH) | 2 | 16.67 | 2 | 5.4 | 0.21 |
| Nonspecific intraventricular conduction defects | 2 | 16.67 | 0 | 0 | – |
| RHYTHM ABNORMALITIES | 3 | 25 | 7 | 18.91 | 0.65 |
| Sinus bradycardia | 2 | 16.67 | 6 | 16.22 | 0.97 |
| Ventricular extrasystoles | 0 | 0 | 1 | 2.7 | – |
| Atrial fibrillation | 1 | 8.33 | 0 | 0 | – |
| HYPERTROPHIC CHANGES | 2 | 16.67 | 2 | 5.4 | 0.21 |
| Left atrial enlargement | 0 | 0 | 2 | 5.4 | – |
| Left ventricular hypertrophy | 2 | 16.67 | 0 | 0 | – |
| OTHER ECG CHANGES | 10 | 83.33 | 34 | 91.89 | 0.39 |
| Pathological Q wave | 5 | 41.67 | 7 | 18.92 | 0.11 |
| Low QRS complex voltage | 1 | 8.33 | 3 | 8.1 | 0.98 |
| QRS AXIS ABNORMALITIES | 4 | 33.33 | 7 | 18.92 | 0.29 |
| Left axis deviation | 4 | 33.33 | 7 | 18.92 | 0.29 |
| ST-T ABNORMALITIES | 9 | 75 | 30 | 81.08 | 0.64 |
| Inverted T wave | 1 | 8.33 | 2 | 5.41 | 0.71 |
| Peaked T wave | 0 | 0 | 2 | 5.41 | – |
| Flattened T wave | 7 | 58.33 | 13 | 35.13 | 0.15 |
| Biphasic T waves | 0 | 0 | 1 | 2.7 | – |
| Secondary ST-T changes | 2 | 16.67 | 4 | 10.81 | 0.59 |
| Nonspecific ST-T changes | 6 | 50 | 20 | 54.05 | 0.80 |

In our study the prevalence and type of ECG abnormalities in patients with sarcoidosis are comparable to data from the literature. We suggest that 12-lead ECG may be a simple diagnostic tool for initial screening for CS.

We suspect that ECG changes in patients with pulmonary sarcoidosis can indicate early stage of heart involvement in witch lesions can not be detected by cardiac magnetic resonance. Follow-up is necessary to assess the impact of new ECG changes in patients with pulmonary sarcoidosis.

## Limitations of the study

Small number of enrolled patients is the main limitation of this study. Certainly, a larger number of participants would increase value of the research. However, our results regarding the prevalence of ECG abnormalities in patients with CS are comparable to data from the literature.

## Conclusions

There was a trend towards more frequent prevalence of some ECG abnormalities in the group of patients with CS than in patients without CS. However, these differences were not statistically significant. ECG abnormalities detected in patients with pulmonary sarcoidosis require further diagnostics because they may indicate cardiac involvement in the course of the disease.

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