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Cardiogniometry in psoriatic patients and its comparison with a control group

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ABSTRACT

Background: Cardiogniometry (CGM), a spatiotemporal electrocardiologic method may be useful as a cardiovascular diagnostic tool. Increased incidence of coronary artery or myocardial involvement and defects in automatic setting of heart activity have been reported in psoriasis which could be related to the presence of systemic inflammation. Cardiogniometry and the related parameters have been used in this study as a diagnostic technique in psoriasis patients.

Methods: Thirty patients with psoriasis and 30 healthy, age and sex-matched individuals with no history of cardiovascular diseases or traditional coronary risk factors were enrolled. Duration and severity of the disease, using psoriasis severity and area index (PASI) score were recorded. Electrocardiography and cardiogniometry were performed. Heart rate, QT interval and QT dispersion (QTD) were measured. SDNN (standard deviation of normal R-R interval) and myocardial ischemia score were determined by cardiogniometry.

Results: There was significant difference between the psoriasis patients and the controls in terms of heart rate (76.37 ± 14.41 vs 72.53 ± 9.684 , $p = 0.02$), myocardial ischemia score (-1.53 ± 2.63 vs -0.46 ± 0.73 , $p = 0.037$), corrected QT interval (392.64 ± 26.00 vs 377.26 ± 22.34 , $p = 0.017$) and QTD (32.00 ± 17.88 vs 6.67 ± 15.16 , $p < 0.001$). No statistically significant difference was found in SDNN (36.37 ± 21.01 vs 26.90 ± 14.88 , $p = .29$). There were moderate correlation between PASI and SDNN ($r = 0.427$, $p = 0.009$), heart rate ($r = 0.427$, $p = .009$) and score ($r = 0.481$, $p = .004$).

Conclusion: Abnormalities in resting ECG and CGM and their correlation with disease severity raises concerns about the need for cardiovascular follow-ups of psoriatic patients, especially those with severe disease.

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What is already known?

- Increased incidence of coronary artery or myocardial involvement and defects in automatic setting of heart activity have been reported in psoriasis which could be related to the presence of systemic inflammation.

What this study adds

- Cardiologic examination is an important work up in psoriatic patients especially cases with severe skin involvement. There are no data regarding cardiogniometry in psoriasis patients. CGM is a method, which could provide additive data using SDNN (as a marker for heart rate variability) and also myocardial ischemia score.

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It is characterized by hyper proliferation and loss of normal differentiation in the epidermis, vascular changes, and lymphocytic infiltration.

Although best known for its dermatologic manifestations, psoriasis may also accompany several other important morbidities, including: arthritis, cancer, Crohn's disease, ulcerative colitis, non-alcoholic steatohepatitis, diabetes, depression, and cardiovascular abnormalities.^{2,3}

Systemic inflammation in psoriasis is associated with many cardiovascular unfavorable changes including: endothelial dysfunction, hypertension, platelet adhesion, and heart rate variability.^{4,5} In a study by Ludwig et al. on psoriatic patients, increased risk of myocardial infarction was found even after controlling for coronary risk factors. This was more evident in those with severe diseases.⁶

Patients with psoriasis have a shorter life expectancy, ascribed to be due to cardiovascular abnormalities in most cases.⁷ Considering these data, it seems to be prudent to diagnose earlier such cardiovascular abnormalities and manage them properly for improving the survival in Psoriasis.

Cardiogoniometry (CGM) is a spatio-temporal orthogonal-lead method using multiple electrodes and an automated diagnostic algorithm to analyze a 12 s vectorcardiographic recording in the resting patient. It detects variables that are helpful in identifying ischemic heart disease or predicting heart rate variability, being performed under resting conditions.⁸

There are no data regarding cardiogoniometry in psoriasis patients. The aim of this study was to use ECG and CGM parameters as indicators of cardiovascular abnormalities in psoriatic patients and compare them with normal population.

2. Methods

Thirty patients, clinically diagnosed as psoriasis vulgaris by an academic dermatologist, were involved in this cross-sectional study from 2014 to 2015. They were selected consecutively from the patients visiting the dermatologic clinic (Imam Reza Hospital). The included patients did not have any clinical signs or symptoms of cardiac problems, history of heart diseases, neurologic events or conventional risk factors for atherosclerosis (hypertension, hyperlipidaemia, diabetes mellitus or cigarette smoking) or medications including beta blocker, systemic steroids or anticoagulants. Thirty healthy volunteer subjects were also enrolled. They were the colleagues or family members of the study author or psoriasis patients and did not have the clinical evidence of cardiac or systemic disorders. Having similar age range and sex ratio to the psoriatic group was considered while selecting the controls.

Psoriasis area and severity index (PASI) was used to assess psoriasis severity.⁹

This study was carried out in accordance with the code of ethics of the world medical association (declaration of Helsinki) for experiments involving humans and obtained the approval of research ethics committee of the Mashhad University of Medical Sciences. The informed written consent was obtained from each participant.

Both psoriasis and control groups underwent electrocardiography and cardiogoniometry.

2.1. Cardiogoniometry (CGM)

The study data were collected by a commercial CGM device (Cardiologic Explorer, Enverdis GmbH Medical Solutions, Germany; Model E12K34). Four electrodes are placed at four points on the patient's thorax as follows (Fig. 1): Electrode 1, at point V4 of Wilson (5th intercostal space in the mid-clavicular line); 2, at point V8 of Wilson (5th intercostal space in the scapular

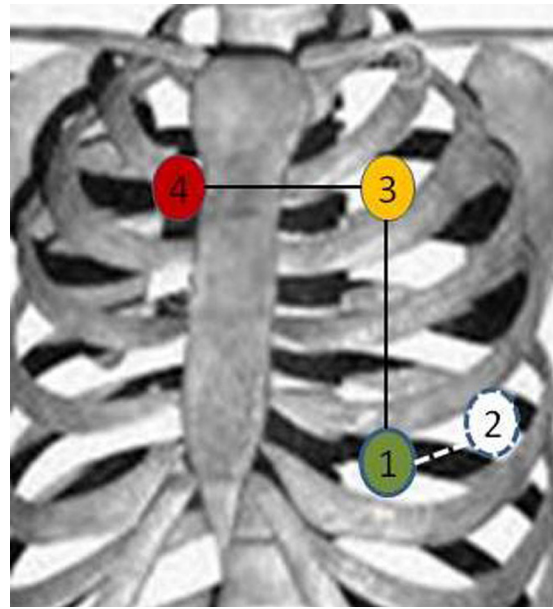


Fig. 1. Position of electrodes. For data recording only four thoracic electrodes are required and additional ground electrode also need. Green electrode is located in 5th intercostal space. Anterior–posterior (AP) chest diameter is determined and white electrode located just opposite side of green lead on posterior side. The distance of yellow and red electrodes is as the same of AP chest diameter.

line); 3, located perpendicularly above electrode 1 at 0.7 times the distance between electrode 1 and 2; Electrode 4, to the right of electrode 3 at the same distance as between points 1 and 3. Vectorial addition of the three potentials between pairs of these electrodes results in a vector that describes the electric field in each plane (X, Y, Z).

During the recording, the patients lay in a supine position and were asked to hold their breath for 12–15 s after normal expiration. If this was not possible, they were asked to perform shallow breathing and keep their thoracic excursions to a minimum.

Cardiogoniometry uses different parameters compiled into specific sets based on gender and conduction characteristics. Analysis of all parameters is fully automated. Myocardial ischemia score is expressed as values ≤ 0 (Figs. 2 and 3). Another parameter, defined as standard deviation of normal R-R interval (SDNN), is used analogs to the extent of heart rate variability.

The CGM results were collected by an independent investigator blinded to all patient data.

2.2. Twelve-lead electrocardiography

The resting 12-lead ECG (Cardisuny C120, Fukuda, Japan) was recorded after the CGM. All ECGs were analyzed by one independent investigator blinded to all patient data. The QT interval was measured from the onset of the QRS complex to the end of the T wave.

Due to the differences in QT interval in the different leads, the maximum QT interval, measured manually, was used in each case.

Corrected QT interval was measured using this formula¹⁰:

$$QTc = QT + 1.75(HR - 60)$$

QT dispersion was defined as maximum difference in QT interval considering all leads.

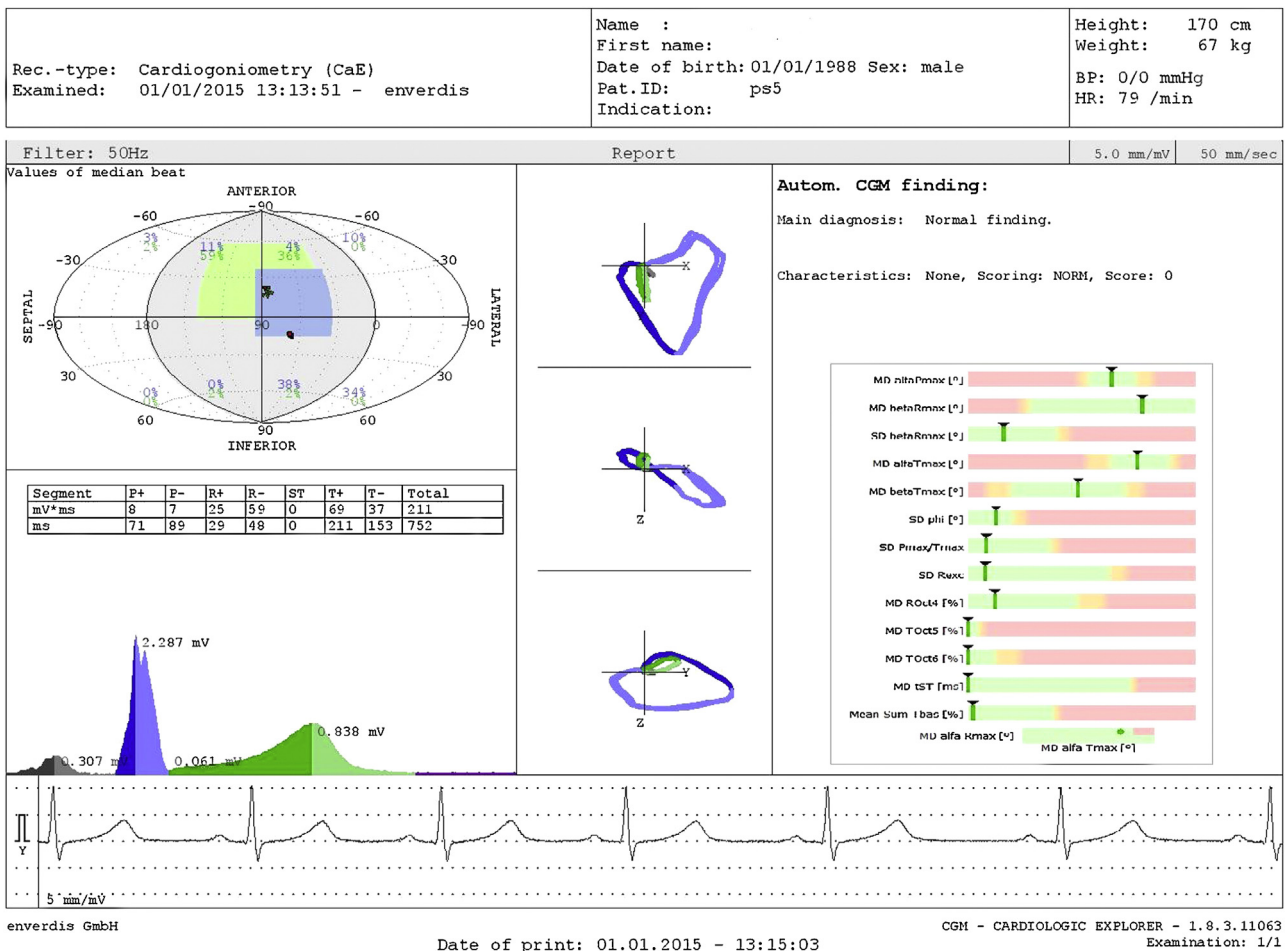


Fig. 2. Overall CGM findings. Left upper: octant configuration in the maximum vector display; left lower: potential of ECG waves. Center: show three-dimensional loop display: blue loop showing depolarization (R loop) with the green one, related to repolarization (T loop). Right: automatic interpretation and parameters. The analysis is done automatically. If parameters are in green range they are normal but yellow and red areas are compatible with abnormal finding.

Presence or absence of pathologic ST-T changes was evaluated in all electrocardiograms (e.g., ECG changes for myocardial ischemia or prior myocardial infarction). These criteria were defined as horizontal or down-sloping ST depression ≥ 0.05 mV in two contiguous leads; and/or T inversion ≥ 0.1 mV.

Serum level of magnesium, potassium and calcium were determined at the day of ECG analysis in all psoriatic patients.

2.3. Statistical analysis

All the statistical analyses were performed using the SPSS statistical software (Statistical Package for Social Sciences, version 16.0). Continuous variables were presented as means \pm standard deviation (SD). Normality tests (Kolmogorov-Smirnov and Shapiro-Wilk) were used to assess the distribution pattern of variables. T-test and chi-square test were used for analysis of quantitative and qualitative variables, respectively. In case the data were not normally distributed, non-parametric tests were used for comparison. Pearson correlation analysis was used to assess the correlation between variables. Level of significance was set at 0.05.

3. Results

Thirty psoriatic patients (40% (n : 12) female, the mean age of 45.43 ± 12.42 years) and 30 healthy persons as control group (40% (n : 12) female, the mean age of 43.90 ± 12.79 years) participated. Both groups were matched by the age ($p = 0.64$) and the sex. Neither psoriatic patients nor control group had risk factors for cardiovascular diseases (including hypertension, hyperlipidaemia, diabetes mellitus, cigarette smoking or family history of cardiovascular disease). All psoriatic patients had normal sinus rhythm without ST-T changes. ECG parameters (QT interval and dispersion) and CGM variables (myocardial ischemia score and SDNN) were gathered in both groups

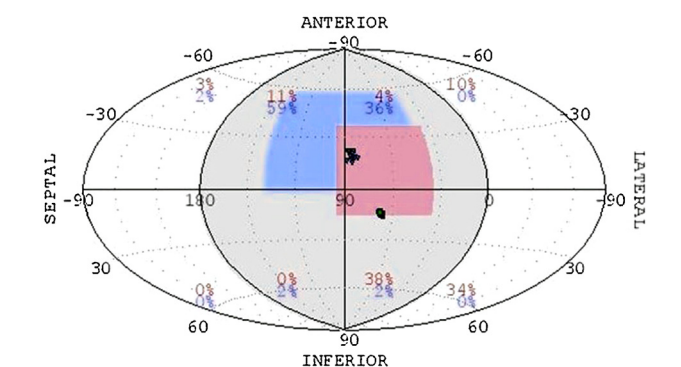


Fig. 3. CGM maximum vectors. Hemisphere topography: 8 octants are displayed. Apex located at the center, mid segments is around it and basal segments are outside the hemisphere. Normally, the vectors of depolarization and repolarization are at the standard area (green and blue area). Location and heterogeneity of R and T vector (depolarization and repolarization) determine ischemia.

Table 1
ECG and CGM related variables in normal and patient group.

Variable	Patient group N= 30	Control group N= 30	p value
QT interval	364.00 ± 18.495	355.33 ± 17.167	p=0.065
QT corrected	392.64 ± 26.00	377.26 ± 22.34	p=0.017
QT dispersion	32.00 ± 17.88	6.67 ± 15.162	p<0.001
Heart rate	76.37 ± 14.41	72.53 ± 9.684	p=0.02
SDNN	36.37 ± 21.01	29.60 ± 14.88	p=0.29
Myocardial ischemia score	-1.53 ± 2.63	-0.46 ± 0.73	p=0.037

All variables are given as mean ± SD; SDNN: standard deviation of normal R-R interval.

(Table 1). The mean value of these parameters was shown as comparative bar charts (Figs. 4–6).

There was significant difference between the psoriasis patients and the controls in term of myocardial ischemia score (-1.53 ± 2.63 vs -0.46 ± 0.73, p = 0.037). Thirty three percent of the controls had score <0 compared with 43% in the patient groups but the ranges were -2.0 in the controls compared to -8.0 in the patients (Figs. 6 and 7).

There was not significant correlation between QT interval and QT dispersion with PASI (r = 0.31, p = 0.873 and r = 0.213, p = 0.259), or between QT interval and disease duration (r = 0.051, p = 0.359). Moderate correlation was found between QT dispersion and the disease duration (r = 0.369, p = 0.022).

Heart rate showed positive correlation with PASI (r = 0.427; p = 0.009) but not with disease duration (p = 0.170; r = 0.180).

SDNN and myocardial ischemia score had positive correlation with PASI (r = 0.427; p = 0.009, r = 0.481; p = 0.004) but not with the disease duration (r = 0.124; p = 0.257; r = 0.233; p = 0.108).

4. Discussion

Cardiogniometry is a non-invasive cardiovascular diagnostic method, easy to use and inexpensive, providing automated interpretation. It was assumed to be useful for early diagnosis of ischemic heart disease especially in those patients who do not tolerate exercise testing. Support vector machines have been

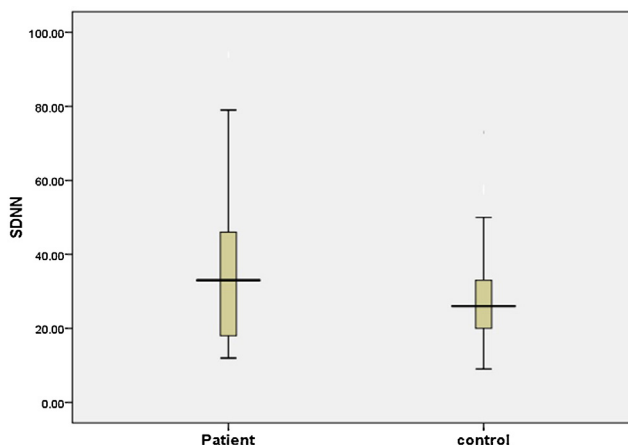


Fig. 5. Box-plots comparing the mean value of SDNN in the psoriatic patients and the controls, the error bars have been superimposed.

applied in this technique to increase the diagnostic accuracy (compared to the previous discriminant function analysis).

Resting ECG is not a precise screening method for detecting myocardial ischemia in the primary setting. On the other hand, exercise ECG often cannot be performed in all patients.¹¹

Vector cardiography (VCG) has been proposed as an alternative to the standard 12-lead ECG since the late 1930s.¹²

In VCG, spatial and temporal heterogeneity of the repolarization phase (named as T-wave variability and T-wave alternance) have been used for predicting ventricular tachyarrhythmia or sudden cardiac death.

But it never became widely used in routine clinical practice due to difficulty to interpret. On the other hand, coronary angiography and nuclear imaging methods caused the classic VCG being disappeared.

Cardiogniometry had been presented by Sanz et al. as an alternative to classic VCG in ischemic heart disease diagnosis (IHD).¹³ CGM is a vectorcardiographic method that is easier to record than the conventional ECG (4 leads instead of 12), clearly displays accurate three-dimensional surface electrophysiological

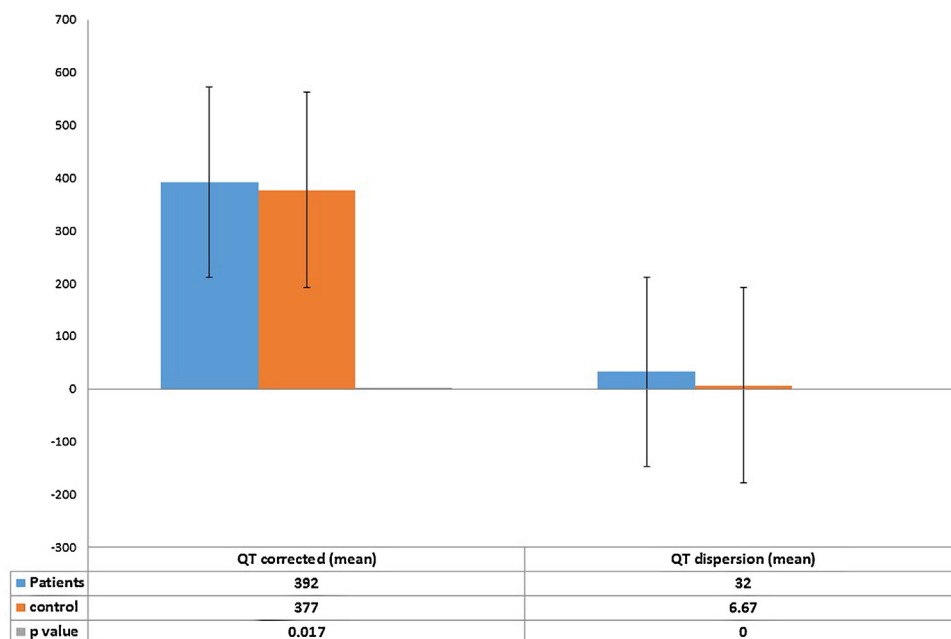


Fig. 4. Bar charts comparing the mean value of corrected QT interval and QT dispersion in the patients and controls. The error bars have been superimposed.

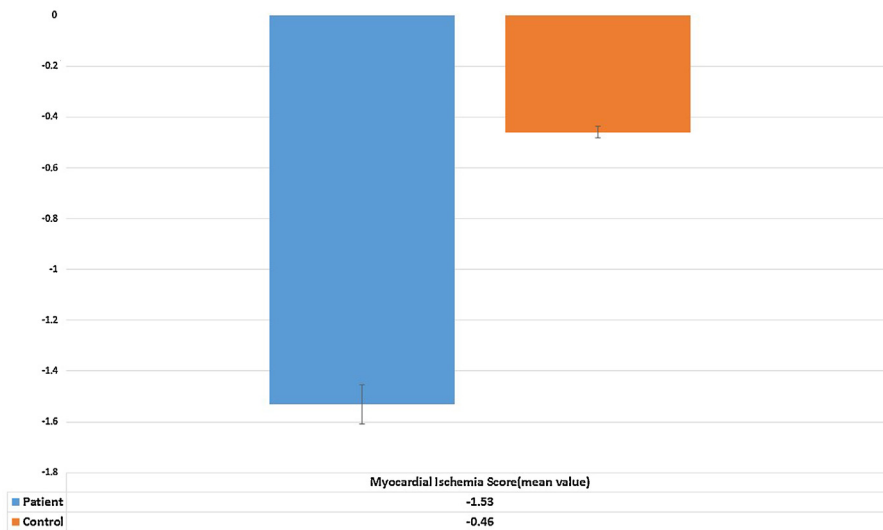


Fig. 6. Bar charts comparing the mean value of myocardial ischemia score in the patients and controls, the error bars have been superimposed.

information and provides automated diagnostic evaluation of digitalized measurements. The variables used in the CGM score serve to identify the abnormal spatial localization of cardiac potentials and abnormal beat-to-beat variability. The use of these variables is plausible since alterations of repolarization and depolarization potentials are commonly used in the ECG diagnosis of IHD.^{14,15}

In a study on psoriatic patient without history of heart disease, heart rate was significantly higher (day and night) than the control group using Holter monitoring. We did not use ECG Holter monitoring in our study. The heart rate in ECG was higher compared with the controls, showing positive correlation with PASI but not with the disease duration.¹⁶

QT dispersion (QTD) can be used to assess the homogeneity of cardiac repolarization and autonomic function denoting the increased heterogeneity of repolarization could be associated with increased risk of ventricular tachyarrhythmias.^{17,18}

QT interval and QTD was higher in psoriatic patients, which could be suggestive for increased risk of arrhythmia in such group (like the study by Simsek et al). There was also positive correlation between disease duration and QTD, which was moderate in our study ($r = 0.369$; $p = 0.022$), compared with Simsek et al. study who

found significant relation ($r = 0.693$, $p < 0.001$). There were not significant correlations between PASI and QT dispersion.¹⁹

The data on rhythm disturbances or conduction abnormalities are scarce. Increased sympathetic activity or systemic inflammation has been proposed as the mechanism of increased QT.²⁰

We did not include the inflammatory markers in this study. PASI score reflects the disease severity, thus it could also be regarded as a useful measure of systemic inflammatory processes intensity. Positive correlation was found between SDNN and PASI but not with QT dispersion in our study. This might suggest the inflammatory mechanism for increased heart rate variability in such patients.

The association of psoriasis with comorbidities increasing the risk of cardiovascular diseases was highlighted in many studies and psoriasis was also found to be independently related with myocardial infarction.²¹⁻²³ Psoriasis has been associated with an increased risk of atherosclerosis (e.g., ischemic heart disease and stroke). The prevalence of such risk factors seems to increase from mild to severe cases.²⁴

In a meta-analysis, CGM was accurate in detecting $\geq 50\%$ coronary artery stenosis at rest with a sensitivity of 73% and a specificity of 84%, respectively.²⁵

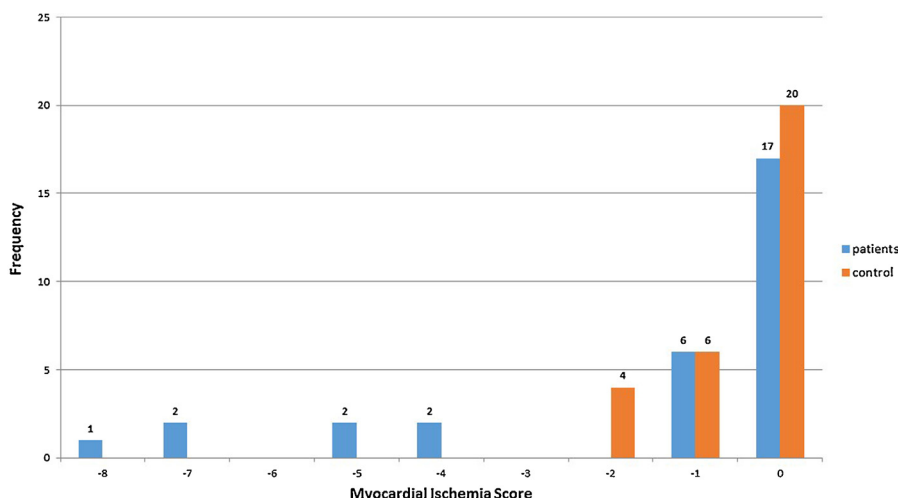


Fig. 7. Distribution of myocardial ischemia score in frequency in the patients and controls.

In study by Schupbacha et al., CGM showed a higher sensitivity but similar specificity of for detecting CAD compared with ECG.²⁶

In this study, there were no ST T changes in resting electrocardiogram but more negative values for myocardial ischemic score were noted in CGM in psoriatic patients. The main concern was that a confirmatory test for coronary artery disease (CAD) was not done, so the extent of atherosclerotic burden could not be evaluated and the differences found in ischemia score could not be simply ascribed to CAD. On the other hand, scores <0 was also detected in the controls which raised the suspicion for generalized applicability of CGM for myocardial ischemia detection in psoriasis.

After all, the abnormalities detected by CGM would raise concerns about further cardiovascular follow-up in psoriatic patients at least in those with severe disease. In other words, it is prudent to define the risk of cardiovascular disease in psoriasis and understand its determinants to propose the effective prevention strategies.

5. Conclusion

Cardiognoniometry is a new, noninvasive, quantitative electro diagnostic technique, which is helpful in identifying patients with cardiovascular abnormalities and also predicting heart rate variability. It can easily be performed at rest and provides an accurate, automated diagnostic score. Abnormalities in resting ECG and CGM and their positive relation with disease severity could raise concerns about further cardiovascular follow-up in psoriatic patients at least in those with severe disease. Whether increased QTcD and abnormalities in CGM parameters in patients with psoriasis predicts poorer clinical outcomes or mandates any special treatments warrants further study.

5.1. Limitations

Small number of study patients and lack of long-term clinical follow-up are the major limitations of our study. CT coronary angiography or conventional angiography was not done. The extent of atherosclerotic burden and the clinical importance of the differences found in CGM data could not be defined. Serum markers of inflammation were not measured, so the exact pathophysiologic mechanism of cardiovascular abnormalities could not be evaluated. Automated ECG measurements were not available and manual calculation QT measurements may be criticized.

Conflicts of interest

The authors have none to declare.

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