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Assessment of cardiac arrhythmias, P wave and QT dispersion in systemic sclerosis

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Abstract

Cardiac involvement in systemic sclerosis (SSc) is significant cause of SSc-related mortality. The objective of the study was to assess cardiac arrhythmias, P wave and QT dispersion in SSc patients. 40 SSc patients and 40 healthy participants who had similar sociodemographic characteristics with the patients were enrolled in the study. P wave dispersion (Pd), QT dispersion (QTd), and corrected QT (QTc) dispersion (QTcd) were calculated by measuring maximum (max) and minimum (min) of P wave, QT interval, QTc in 12-leads electrocardiography (ECG). Cardiac arrhythmias and conduction disorders were assessed by ECG and Holter-ECG. The mean age of SSc patients (92.5% of females) was 50.9±13.9 years similar with the healthy group (51.4±8.9). Abnormal ECG findings were found in 27.5% of SSc patients and remarkably higher in comparison to the healthy participants (p=0.019). The most frequently reported abnormal ECG findings were left anterior fascicular block (15%), ventricular premature beat (10%) and first-degree atrioventricular heart block (5%). The comparison of dispersion showed no statistically important difference in Pd between two groups (p=0.69) while QTd, QTc, QTcd, QTc min, and QTc max were markedly prolonged in patients with SSc (p=0.039; p<0.001; p=0.021; p<0.001; p<0.001, respectively). The assessment of Holter-ECG demonstrated that supraventricular tachycardia was frequently detected in patients with SSc (22.5% vs 2.5%; p=0.007). This study indicated a significantly elevated incidence of abnormal ECG results and SVT, an arrhythmia not typically identifiable through standard ECG but detectable via Holter monitoring, in patients with SSc. In the study, QTd, QTc, and QTcd intervals were significantly longer in SSc patients, which may indicate a susceptibility to arrhythmias.

Keywords: Arrhythmia, abnormal electrocardiography findings, dispersion, P wave, QT interval, systemic sclerosis

Introduction

Systemic sclerosis (SSc) is a chronic connective tissue disease that can progress with multiple organ involvement, resulting in vasculopathy, exaggerated inflammation, and fibrosis. One of the major organ involvements in SSc is the heart. Cardiac manifestations of SSc includes fibrosis of myocardium, inflammation of pericardium, disturbance of conduction system defects, and arrhythmias. It is considered that ischaemic, fibrotic, and inflammatory lesions form with microvascular changes, excessive and uncontrolled collagen deposition and ultimately fibrosis, and all of these lesions might affect all cardiac structures [1,2]. Cardiac involvement occurs in both subtypes of SSc while diffuse cutaneous SSc (dcSSc) is a risk factor for cardiac involvement. Although cardiac involvement progresses subclinical without any symptoms in most patients with SSc, mortality is high, and prognosis is poor [3].

One of the most common causes of SSc-related death is cardiac involvement, with a rate of 26%, and half of these causes are due to arrhythmias [4]. Fibrosis is considered as a major contributor of arrhythmias and conduction system disorders. In addition, the development of an obstructive vasculopathy is thought to cause myocardial hypoperfusion, leading to electrical inhomogeneities [5,6]. Although conduction system abnormalities in SSc are commonly observed, they may not result in clinical symptoms. In a study investigating cardiac conduction abnormalities in patients with SSc, arrhythmias were found in approximately 50% of Holter electrocardiogram (ECG) in patients with normal ECG [7]. Abnormal ECG changes are observed in 25-75% of patients with SSc [8].

The QT interval and P-wave dispersion (Pd) assessed by ECG

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indicate regional heterogeneity and repolarisation abnormalities of the ventricle and atrium. Prolongation of the QT dispersion (QTd) interval might lead to arrhythmias and sudden cardiac death by causing inhomogeneous conduction velocity and repolarisation re-entry mechanisms in different regions [9,10]. Clinical studies have shown that the QTd interval increases in chronic inflammatory rheumatological diseases [11,12]. The development of Pd results from prolongation of the intra- and inter-atrial conduction times and heterogeneous prolongation of the sinus impulses. This phenomenon increases the tendency of the atrial fibrillation [10].

This study aimed to assess dispersion of P wave and QT interval, arrhythmias, and conduction disturbances in SSc patients without known cardiac involvement compared to healthy participants. Besides, another aim of the study was to investigate the association between SSc-specific features, including organ involvements and disease subsets, and ECG/Holter findings.

Material and Methods

Patient selection and clinical features

Forty patients who fulfilled the 2013 ACR/EULAR SSc diagnostic criteria and were followed up at the Rheumatology Department of Ankara University Faculty of Medicine were included. Patients were excluded if they did not meet the diagnostic criteria, had known congenital heart disease, pacemaker implantation, known arrhythmia, heart failure or coronary artery disease. 40 healthy individuals with similar socio-demographic characteristics to the patient group, no known disease, and who accepted the study were included as the control group. The cross-sectional study was approved by the Ethics Committee of Ankara University Faculty of Medicine (Ethics No: 20-847-15) and supported by the Ankara Medical Faculty Foundation. Written informed consent was obtained from all participants who agreed to enroll in the study.

Disease subtypes were determined according to the extent of skin involvement [13]. Age at disease onset was considered as the time of the first symptom, including Raynaud's phenomenon. Interstitial lung disease (ILD), presence/history of digital ulcer, gastroesophageal involvement, pulmonary arterial hypertension (PAH), renal crisis, positivity for antinuclear antibodies (ANA) and SSc-specific antibodies (anti-centromer and anti-Scl70) were assessed.

The assessment of electrocardiography and 24-hour holter rhythm

After 20 minutes of rest, a 12-lead ECG at a rate of 50 mm/sec and 20 mm/mV was performed in the control and patient groups. Right and left bundle branch block, hemiblock, atrioventricular block, ST depression, T-negativity, and arrhythmias were accepted as abnormal ECG findings. Heart rate was calculated by dividing 3000 by the number of small squares between two consecutive R-R. If the heart rate was slower than 60 beats/min, it was considered sinus bradycardia; if it was faster than 100 beats/min, it was considered sinus tachycardia. In the analysis of 12 leads, the duration of P-wave was measured; duration of maximum P-wave (P max) and minimum P-wave (P min) were detected, and Pd was calculated as the disparity between P max and P min (Pd=P max-P min) [10]. The QT interval was measured in 12 leads and maximum QT (QT max) and minimum QT (QT min) were determined, and QTd was calculated as the disparity between QT max and QT min (QTd=QT max-QT min) [9].

The corrected QT interval (QTc) was computed using the Bazett formula ($QTc=QT/\sqrt{RR}$) [14]. QTc was calculated in 12 leads, maximum QTc (QTc max) and minimum QTc (QTc min) were determined, and QTc dispersion (QTcd) was calculated as the difference between QTc max and QTc min values.

All participants underwent a 24-hour Holter ECG. The Holter ECG was interpreted by the investigating cardiologist. The heart rate (minimum, maximum and mean), the presence of arrhythmia, and the type of arrhythmia were evaluated with Holter ECG for all participants.

Statistical analysis

Statistical analyses were performed with SPSS software. Descriptive statistics were reported with mean±standard deviation for continuous variables, median (min-max) for non-normally distributed parameters, and frequency and percentage for categorical variables. Pearson chi-square and Fisher's exact tests were performed to evaluate categorical variables. The Student's t-test for statistical significance between two independent groups was used for variables that conformed to the normal distribution, and the Mann-Whitney U test was performed to compare the variables not normally distributed between groups. The statistical significance was accepted as $p < 0.05$.

Results

The mean age of the SSc patients (92.5% female) was 50.9±13.9 years, and 72.5% of patients had limited cutaneous SSc (lcSSc) disease subtype. The mean age at disease onset was 42.7±13.7 years, and the median duration of disease was 5 (min:2-max:41) years. The distribution of clinical features of SSc patients based on disease subtype is shown in Table 1. Abnormalities in ECG findings were reported in 27.5% of patients, and the most common abnormal ECG findings were left anterior fascicular block (15%), ventricular premature beat (VPB; 10%), first-degree atrioventricular block (5%) and right bundle branch block (5%). Abnormalities in ECG findings were observed in 7.5% of the control group; abnormal ECG findings were significantly more common in patients with SSc compared to healthy individuals (p=0.019), and left anterior fascicular block was significantly more common in SSc patients (p=0.026). The mean heart rate on ECG was significantly higher in patients with SSc (p=0.004) (Table 2).

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Table 1. Clinical features according to SSc disease subtypes

	SSc (n=40)	lcSSc (n=29)	dcSSc (n=11)	p
Age (years), mean±SD	50.90±13.91	49.86±13.63	53.64±14.94	0.451
Gender, female, n (%)	37 (92.5)	26 (89.7)	11 (100)	0.548
Age at disease onset (years), mean±SD	42.70±13.69	42.21±12.68	44.00±16.67	0.717
Duration of disease (years), median (min-max)	5 (2-41)	4 (2-41)	5 (2-26)	0.402
Digital ulcer, n (%)	12 (30)	7 (24.1)	5 (45.5)	0.254
Interstitial lung disease, n (%)	17 (42.5)	10 (34.5)	7 (63.6)	0.153
Gastro-oesophageal involvement, n (%)	33 (82.5)	24 (82.8)	9 (81.8)	1.000
Pulmonary arterial hypertension, n (%)	9 (22.5)	6 (20.7)	3 (27.3)	0.670
Renal crisis, n (%)	3 (7.5)	2 (6.9)	1 (9.1)	1.000
ANA positivity, n (%)	38 (95)	27 (93.1)	11 (100)	1.000
Anti-centromere	14 (35.0)	9 (31)	5 (45.5)	0.469
Anti-Scl-70	9 (22.5)	5 (17.2)	4 (36.4)	0.227

ANA: anti-nuclear antibody, SSc: systemic sclerosis

Table 2. Comparative evaluation of ECG and Holter ECG findings of SSc and healthy control group

	SSc (n=40)	Control (n=40)	P
Heart rate (beats/min), mean±SD	81.20±17.49	71.75±9.91	0.004
Sinus tachycardia, n (%)	4 (10)	0	0.116
Sinus bradycardia, n (%)	4 (10)	2 (5)	0.675
QRS (ms), median (min-max)	82 (55-166)	83 (40-120)	0.481
P (ms), median (min-max)	50 (18-128)	60 (20-80)	0.138
RR (ms), median (min-max)	780 (520-1480)	852 (660-1140)	0.007
PR (ms), mean±SD	149.4±26.1	143.4±27.6	0.321
QT (ms), median (min-max)	368.5 (291-450)	363 (340-428)	0.973
QTc (ms), mean±SD	418.4±25.1	396.1±25.9	<0.001
Abnormal ECG findings, n (%)	11 (27.5)	3 (7.5)	0.019
Right bundle branch block, n (%)	2 (5)	0	0.494
Left anterior fascicular block, n (%)	6 (15)	0	0.026
Atrioventricular block, n (%)	2 (5)	1 (2.5)	1.000
Ventricular premature beats, n (%)	4 (10)	0	0.116
ST depression, n (%)	0	2 (5)	0.494
T negativity, n (%)	1 (2.5)	0	1.000
P max (ms), median (min-max)	80 (60-120)	80 (25-120)	0.133
P min (ms), median (min-max)	30 (10-60)	30 (15-45)	0.250
Pd (ms), median (min-max)	50 (30-80)	52.50 (10-80)	0.697
QT max (ms), median (min-max)	400 (320-480)	388 (350-428)	0.078
QT min (ms), median (min-max)	320 (260-400)	320(280-360)	0.949
QTd (ms), mean±SD	75.98±28.28	64.08±22.17	0.039
QTc max (ms), mean±SD	460.6±31.1	423.6±26.9	<0.001
QTc min (ms), mean±SD	373.0±29.8	350.8±20.9	<0.001
QTcd (ms), mean±SD	87.65±29.62	72.73±26.91	0.021
Holter ECG findings			
Ventricular premature beats, n (%)	7 (17.5)	14 (35)	0.075
Atrial fibrillation, n (%)	3 (7.5)	0	0.241
Atrial premature beat, n (%)	9 (22.5)	23 (57.5)	0.001
Supraventricular tachycardia, n (%)	9 (22.5)	1 (2.5)	0.007
Max heart rate (beats/min)	125 (100-183)	128 (91-162)	0.519
Median (min-max)	52.05±8.38	51.98±6.56	0.965
Minimum heart rate (beats/min), mean±SD	78.10±11.50	77.48±7.78	0.777

ECG: electrocardiogram, SSc: systemic sclerosis, Pd: p wave dispersion, QTc: corrected QT interval, QTd: QT dispersion, QTcd: corrected QT dispersion

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The assessment of ECG findings in terms of clinical features in SSc patients demonstrated that no remarkable relationship was detected between the presence of organ involvement and abnormal ECG findings except SSc-renal crisis. All three patients with renal crisis had abnormal ECG findings; two patients had left anterior fascicular block, and one had PVC. ECG abnormalities were observed in only 21.6% of patients without renal crisis and statistically lower than in patients with renal crisis (p=0.017).

The examination of Holter ECG in SSc patients revealed supraventricular tachycardia (SVT) in 9 (22.5%), atrial premature beats (APB) in 9 (22.5%), VPB in 7 (17.5%) and atrial fibrillation (AF) in 3 (7.5%). In the control group, APB was detected in 23 (57.5%), VPB in 14 (35%) and SVT in 1 (2.5%) participant. The frequency of SVT was markedly increased in SSc patients, whereas the frequency of APB was significantly higher in the healthy participants (p=0.007 and p=0.001, respectively). In the Holter ECG evaluation, the mean heart rate was similar in both groups in contrast to the ECG finding (p=0.777). There was no important difference reported in Holter ECG findings of the patient group when scrutinized with respect to clinical features and organ involvement (p>0.05).

The values of Pd, P max, and P min were found to be similar in both groups (p>0.05). The assessment of QTcd and QTd showed that QTc, QTd, QTcd, QTc max, and QTc min intervals exhibited statistically significant prolonged in SSc patients compared to the control group (p<0.001; p=0.039; p=0.021; p<0.001; p<0.001, respectively). In the comparison of ECG and dispersion findings in disease subsets and the control groups, the heart rate was higher in the lcSSc and dcSSc patients (p=0.035; p=0.019) (Table 3). Abnormal ECG findings were observed in only one case (9%) in dcSSc patients, while they were detected in 34.5% of the lcSSc patients, and this frequency was markedly higher than the control group (p=0.012). In dispersion assessment, QTd and QTc intervals were significantly prolonged in lcSSc patients compared to the control group (p=0.009; p=0.005). In the Holter ECG evaluation, the frequency of SVT was significantly higher in the patients with lcSSc compared to the healthy participants (24.1% vs 2.5%; p=0.008). The frequency of APB was found to be increased in healthy participants in comparison to patients with lcSSc (57.5% vs 17.2%; p=0.002); however, no statistically significant difference was found when compared to dcSSc patients (57.5% vs 36.4%; p=0.36).

Table 3. Evaluation of ECG findings and dispersion between SSc subtypes and control group

	Control (n=40)	lcSSc (n=29)	dcSSc (n=11)	p1	p2	p3
Heart rate (beats/min), median (min-max)	72.50 (51-53)	78 (49-129)	80 (52-105)	0.035	0.019	0.396
QRS (ms), median (min-max)	83 (40-120)	84 (55-160)	80 (60-94)	0.318	0.836	0.316
P (ms), median (min-max)	60 (20-80)	50 (22-124)	54 (18-60)	0.436	0.038	0.447
RR (ms), median (min-max)	852.5 (660-1140)	800 (520-1480)	770 (575-1180)	0.043	0.008	0.347
QT (ms), median (min-max)	365 (340-428)	369 (291-450)	360 (316-440)	0.784	0.279	0.458
QTc (ms), median (min-max)	397.5 (343-451)	422 (358-465)	413 (388-461)	0.001	0.025	0.976
Abnormal ECG findings, n (%)	3 (7.5)	10 (34.5)	1 (9.1)	0.012	1.000	0.233
Right bundle branch block, n (%)	0	2 (6.9)	0	-	-	-
Left anterior fascicular block, n (%)	0	6 (20.7)	0	-	-	-
Atrioventricular block, n (%)	1 (2.5)	2 (6.9)	0	0.568	-	-
Ventricular premature beat, n (%)	0	3 (10.3)	1 (9.1)	-	-	1.000
ST depression, n (%)	2 (5)	0	0	-	-	-
T negativity, n (%)	0	1 (3.4)	0	-	-	-
P max (ms), median (min-max)	80 (25-120)	80 (60-120)	80 (60-80)	0.454	0.036	0.074
Pmin (ms), median (min-max)	30 (15-45)	30 (10-60)	30 (18-50)	0.502	0.138	0.393
Pd (ms), median (min-max)	52.5 (10-80)	50 (30-80)	50 (30-62)	0.985	0.340	0.362
QT max (ms), median (min-max)	388 (350-428)	400 (320-480)	400 (330-480)	0.144	0.147	0.736
QT min (ms), median (min-max)	320 (280-360)	320 (280-400)	340 (260-400)	0.366	0.113	0.121
QTd (ms),median (min-max)	62 (20-128)	80 (40-160)	60 (20-100)	0.009	0.908	0.082
QTc max (ms), median (min-max)	428.5 (371-429)	454 (413-519)	450 (405-537)	<0.001	0.002	0.976
QTc min (ms), median (min-max)	346 (316-396)	367 (292-413)	384 (353-447)	0.005	<0.001	0.095
QTcd (ms), median (min-max)	75 (20-154)	92 (45-146)	70 (32-118)	0.005	0.954	0.058

p1: control vs. lcSSc; p2: control vs. dcSSc; p3: lcSSc vs. dcSSc. ECG: electrocardiogram, dcSSc: diffuse cutaneous systemic sclerosis, lcSSc: limited cutaneous systemic sclerosis, SSc: systemic sclerosis, Pd: p wave dispersion, QTc: corrected QT interval, QTd: QT dispersion, QTcd: corrected QT dispersion

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Discussion

Cardiac involvement is one of the major-health threatening manifestations in SSc. The common findings of cardiac involvement involve myocarditis and diastolic dysfunction due to myocardial involvement, arrhythmias, and pericarditis in SSc. Although the exact prevalence of cardiac involvement in SSc remains uncertain due to its often clinically silent nature, studies indicate a prevalence ranging from 7% to 39%. Notably, arrhythmia associated with cardiac involvement stands out as one of the most leading causes of mortality in SSc [4,15]. In our study, 27.5% of SSc patients had abnormal ECG findings in contrast to 7.5% in the healthy control. The most common conduction abnormalities seen in SSc were left anterior fascicular block, VPB and 1st-degree AV block. In a study conducted in Sweden in which SSc and control group with a large patient population were evaluated, abnormality in ECG was reported in 28% of SSc patients in accordance with the results of our study. However, abnormality was found in 17% of the control group [16]. In an electrophysiological study involving 183 SSc patients, abnormal ECG findings were detected in 43% of the patients, and it was reported that conduction disorders constituted 20% of these. In the Holter ECG evaluation of the patients, APB was found in 61%, SVT in 21% and VT in 7% [17].

Supraventricular arrhythmias are observed more frequently than ventricular tachycardia in SSc patients [18]. In our study, SVT and APB were observed most frequently in SSc patients, whereas PVC was less frequently observed during the Holter ECG assessment. SVT was found to be more common in patients with SSc comparison to healthy participants. Surprisingly, APB was more frequently detected in the healthy control; however, when evaluated according to disease subtypes, it was shown that there was no important difference observed with regard to APB between dcSSc, which is considered a risk factor for cardiac involvement, and healthy individuals.

Prolongation of the QT interval and increased QT dispersion may confer a risk of ventricular arrhythmias and sudden cardiac death [19,20]. Two major physiopathological mechanisms are thought to be responsible for the impairment of ventricular repolarisation: impairment of cardiac innervation by autonomic nervous system dysfunction and prolongation of ventricular return time due to myocardial damage. The QT interval is thought to be prolonged in SSc as a consequence of autonomic neuropathy, myocardial fibrosis and conduction system fibrosis [21]. In a study by Sgreccia et al., QTc max, QTd and QTcd were significantly increased in SSc [22]. Similarly, in our study, QTc max, QTc min, and QTc intervals were significantly increased in SSc. Besides, QTd and QTcd interval were markedly raised in SSc patients.

Pd indicates prolongations in intraatrial and interatrial conduction time and regional changes in myocardial activation. Prolongation in interatrial and intraatrial conduction time is thought to increase the tendency for atrial fibrillation [10]. There are several studies showing that atrial arrhythmias and Pd are increased in SSc patients. Can et al. demonstrated that Pd and P max values were prominently higher in patients with SSc in contrast to healthy participants [23]. In another study, Pd was significantly increased in SSc than control, whereas no difference was found for QTcd, QTc max and QTc min [24]. In contrast, our study showed that Pd did not increase significantly in SSc patients.

There is no study in the literature evaluating the relationship between electrophysiological abnormalities and arrhythmias with clinical features and organ involvement in SSc. In our study, left anterior fascicular block and VPB were found in the ECG of 3 patients with a history of renal crisis, and abnormal ECG findings were significantly more common in patients with renal crisis than patients without renal involvement. In a study in which cardiac involvement was evaluated with clinical features, it was found that the presence of renal crisis was a risk factor for cardiac involvement [3]. Although the patient sample size was small, our findings suggest the need for caution about arrhythmias and conduction abnormalities in SSc patients with renal crisis. Nevertheless, it is important to conduct a study including a larger sample size of patients to validate this evidence.

In addition, there is no study comparing the electrophysiological aspects of different subtypes of systemic sclerosis (dcSSc and lcSSc) despite their distinct organ involvement, clinical presentations, and prognostic differences. Our investigation revealed that both disease subset groups displayed a significantly prolonged QTc interval, indicative of susceptibility to arrhythmias compared to the control group. Additionally, patients with lcSSc exhibited significantly prolonged QTd and QTcd values compared to healthy individuals.

The main limitation of our study was the inclusion of a small number of patients, with a predominant representation of lcSSc subtype, which might influence the ECG findings. Another limitation is that our study was cross-sectional, and it is more difficult to establish a cause-effect relationship between QT dispersion and abnormal ECG changes regarding disease progression and arrhythmia susceptibility in SSc compared to prospective cohort studies.

Conclusion

Abnormal ECG findings were significantly higher in SSc patients, and arrhythmias not detected on ECG could be detected on Holter ECG. Considering that P-wave and QT dispersion are precursors for the development of arrhythmia, the prolonged QTd and QTcd interval in SSc patients supports the susceptibility to arrhythmia due to disease pathophysiology.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
Ankara Medicine Faculty Foundation for ECG-Holter assessment.

Ethical Approval
The study was approved by the Ethics Committee of Ankara University Faculty of Medicine (Ethics No: 20-847-15).

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References

1. Ridolfi RL, Bulkley BH, Hutchins GM. The cardiac conduction system in progressive systemic sclerosis: clinical and pathologic features of 35 patients. Am J Med. 1976;61:361-6.
2. Lubitz SA, Goldbarg SH, Mehta D. Sudden cardiac death in infiltrative cardiomyopathies: sarcoidosis, scleroderma, amyloidosis, hemachromatosis. Prog Cardiovasc Dis. 2008;51:58-73.
3. Fernández-Codina A, Simeón-Aznar CP, Pinal-Fernandez I, et al. Cardiac involvement in systemic sclerosis: differences between clinical subsets and influence on survival. Rheumatol Int. 2017;37:75-84.
4. Tyndall AJ, Bannert B, Vonk M, et al. Causes and risk factors for death in systemic sclerosis: a study from the EULAR Scleroderma Trials and Research (EUSTAR) database. Ann Rheum Dis. 2010;69:1809-15.
5. Sebestyen V, Szucs G, Pall D, et al. Electrocardiographic markers for the prediction of ventricular arrhythmias in patients with systemic sclerosis. Rheumatology. 2020;59:478-86.
6. Schicchi N, Valeri G, Moroncini G, et al. Myocardial perfusion defects in scleroderma detected by contrast-enhanced cardiovascular magnetic resonance. Radiol Med. 2014;119:885-94. Erratum in: Radiol Med. 2014;119:958.
7. Ferri C, Bernini L, Bongiorni MG, et al. Noninvasive evaluation of cardiac dysrhythmias, and their relationship with multisystemic symptoms, in progressive systemic sclerosis patients. Arthritis Rheumatol. 1985;28:1259-66.
8. Bournia V-K, Tountas C, Protogerou AD, et al. Update on assessment and management of primary cardiac involvement in systemic sclerosis. J Scleroderma Relat Disord. 2018;3:53-65.
9. Higham PD, Campbell RW. QT dispersion. Br Heart J. 1994;71:508-10.
10. Dilaveris PE, Gialafos EJ, Sideris SK, et al. Simple electrocardiographic markers for the prediction of paroxysmal idiopathic atrial fibrillation. Am Heart J. 1998;135:733-8.
11. Cindas A, Gökçe-Kutsal Y, Tokgözoglu L, Karanfil A. QT dispersion and cardiac involvement in patients with rheumatoid arthritis. Scand J Rheumatol Suppl. 2002;31:22-6.
12. Yavuz B, Atalar E, Karadag O, et al. QT dispersion increases in patients with systemic lupus erythematosus. Clin Rheumatol. 2007;26:376-9.
13. LeRoy EC, Black C, Fleischmajer R, et al. Scleroderma (systemic sclerosis): classification, subsets and pathogenesis. J Rheumatol. 1988;15:202-5.
14. Moss AJ. Measurement of the QT interval and the risk associated with QTc interval prolongation: a review. Am J Cardiol. 1993;72:23B-5.
15. Bruni C, Buch MH, Furst DE, et al. Primary systemic sclerosis heart involvement: A systematic literature review and preliminary data-driven, consensus-based WSF/HFA definition. J Scleroderma Relat Disord. 2022;7:24-32.
16. Nordin A, Björnådal L, Larsson A, et al. Electrocardiography in 110 patients with systemic sclerosis: a cross-sectional comparison with population-based controls. Scand J Rheumatol. 2014;43:221-5.
17. Kostis JB, Seibold JR, Turkevich D, et al. Prognostic importance of cardiac arrhythmias in systemic sclerosis. Am J Med. 1988;84:1007-15.
18. Clements PJ, Furst DE, Cabeen W, et al. The relationship arrhythmias and conduction disturbances to other manifestations of cardiopulmonary disease in progressive systemic sclerosis (PSS). Am J Med. 1981;71:38-46.
19. Schwartz PJ, Wolf S. QT interval prolongation as predictor of sudden death in patients with myocardial infarction. Circulation. 1978;57:1074-7.
20. Glancy JM, Garratt CJ, Woods KL, de Bono DP. QT dispersion and mortality after myocardial infarction. Lancet. 1995;345:945-8.
21. Dessein PH, Joffe BI, Metz RM, et al. Autonomic dysfunction in systemic sclerosis: sympathetic overactivity and instability. Am J Med. 1992;93:143-50.
22. Sgreccia A, Morelli S, Ferrante L, et al. QT interval and QT dispersion in systemic sclerosis (scleroderma). J Intern Med. 1998;243:127-32.
23. Can I, Onat AM, Aytemir K, et al. Assessment of atrial conduction in patients with scleroderma by tissue Doppler echocardiography and P wave dispersion. Cardiology. 2007;108:317-21.
24. Karaahmet T, Tigen K, Gurel E, et al. Impact of systemic sclerosis on electromechanical characteristics of the heart. Heart Vessels. 2010;25:223-8.