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ORIGINAL ARTICLE

# Is the development of arrhythmia predictable in rheumatoid arthritis?

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***ABSTRACT***

**Objectives:** This study aimed to determine whether there is a difference in the electrocardiography (ECG) measurements of healthy controls and rheumatoid arthritis (RA) patients and to predict whether they can be used to determine the risk of arrhythmia in patients.

**Patients and methods:** The prospective study included 50 cardiac asymptomatic RA patients (38 males, 12 females; mean age: 46.8±9.1 years; range, 18 to 60 years) who met the 2010 American College of Rheumatology/European Alliance of Associations for Rheumatology RA criteria and 50 healthy volunteers (34 males, 16 females; mean age: 43.4±10.4 years; range, 18 to 60 years) as a control group between June 1, 2022, and August 31, 2022. Disease activity of the patients was calculated with the Disase Activity Score (DAS28). Heart rate, minimum and maximum QT intervals, QT dispersion, minimum and maximum P waves, P wave dispersion (Pd), minimum and maximum Tp-e intervals, Tp-e dispersion, minimum and maximum corrected QT (QTc) intervals, QTc dispersion, and the Tp-e/QTc ratio in ECGs were calculated.

**Results:** The mean disease duration of the RA group was 9.09±5.74 years. The mean C-reactive protein level was 9.83±8.29, the mean erythrocyte sedimentation rate was 26.12±16.28 mm/h, and the mean DAS28 was 3.03±0.37. There was a statistically significant increase in the maximum P wave, Pd, maximum QT, QT dispersion, maximum QTc, QTc dispersion, maximum Tp-e, Tp-e dispersion, and Tp-e/QTc dispersion parameters in the RA group compared to the control group, while there was a significant decrease in the minimum P wave, minimum QT, and minimum QTc parameters.

**Conclusion:** In our study, the Pd, QTc dispersion, Tp-e dispersion, and Tp-e/QTc dispersion values of our patients, which indicate the risk of atrial and ventricular arrhythmia, were found to be significantly higher. This finding suggests that our patients had an increased risk of cardiac morbidity and mortality. Arrhythmias are the likely source of the increase in sudden cardiac death in RA, and these new indicators measured on ECG can be used as standardized cardiovascular morbidity and mortality indicators in the future.

***Keywords:*** Arrhythmia, electrocardiography, rheumatoid arthritis.

Rheumatoid arthritis (RA) is a systemic inflammatory disease with articular and nonarticular involvements affecting the synovial joints. During the course of this disease, all cardiac structures (conducting system, myocardium, endocardium, coronary arteries, and valves) may be affected. Various clinical pictures, such as pericarditis, myocarditis, myocardial fibrosis, arrhythmias, coronary artery disease, valve disease, pulmonary hypertension, and heart failure, may occur.[1]

The most common arrhythmia in patients with RA is atrial fibrillation (AF).[2] Other common arrhythmias are premature ventricular complex and ventricular tachycardia.[3] The main cause of rhythm disturbance is coronary vasculitis and coronary atherosclerotic disease, which cause

inflammatory lesions and perfusion defects of the myocardium.[4] Increased sympathetic and decreased parasympathetic activity may play an important role in the development of ventricular tachycardia in RA patients.[5]

The longest P wave duration in electrocardiography (ECG) is called P maximum ($P_{max}$), whereas the shortest P wave duration is called P minimum ($P_{min}$). The difference between the maximum and minimum P wave durations is defined as the P wave dispersion (Pd).[6] An increase in Pd indicates the presence of variable and heterogeneous atrial electrical activity, a predisposition to atrial reentry formation and AF.[7]

The distance from the start of the QRS complex to the end of the T wave is called the QT interval. It shows the sum of the electrical depolarization and repolarization times of the ventricular muscle. The shortest QT duration is defined as QT minimum ($QT_{min}$), and the longest QT duration is defined as QT maximum ($QT_{max}$). The difference between the maximum and minimum QT times is defined as the QT dispersion (QTd). The heart rate and the duration of the QT interval vary. For this reason, it should be corrected for heart rate. The Bazett formula is most commonly used for this correction. According to this formula, the QT duration is divided by the square root of the duration of the preceding R-R interval, and the corrected QT (QTc) is calculated.[8] The difference between the QTc distances [minimum ($QTc_{min}$ and maximum ($QTc_{max}$)] is called the corrected QT dispersion (QTcd). QTd is a parameter that indicates regional heterogeneity in myocardial repolarization. High QTd indicates low ventricular repolarization homogeneity, which indicates ventricular instability.[9] It has been shown that an increase in QTd, which is accepted as a marker of regional heterogeneity in myocardial repolarization, causes severe ventricular arrhythmias and sudden cardiac death through the reentry mechanism.[10] It has been shown that QTd is associated with increased cardiovascular mortality and morbidity in ischemic heart disease, peripheral vascular disease, hypertension, dilated and hypertrophic cardiomyopathies, and chronic renal failure.[11]

The time between the point where the T wave reaches its maximum amplitude and the end point of the T wave is called the Tp-*e* interval. In the ECG, the longest Tp-*e* time is defined as Tp-*e* maximum (Tp-$e_{max}$), and the shortest Tp-*e* time is defined as Tp-*e* minimum (Tp-$e_{min}$). The difference between the maximum and minimum Tp-*e* times is called Tp-*e* dispersion (Tp-ed). The Tp-*e* interval is considered to be a reflection of ventricular transmural repolarization dispersion on the ECG.[12] An increase in ventricular repolarization dispersion is accepted as an important risk factor for ventricular arrhythmias. A prolonged Tp-*e* interval reflects the abnormal distribution of ventricular repolarization and is associated with an increased risk of ventricular arrhythmias. Therefore, the Tp-*e* interval is a noninvasive screening method for arrhythmogenesis.[13]

The Tp-*e*/QT ratio is one of the new markers that can predict cardiac arrhythmias. As the body weight increases, the Tp-*e* interval and QT increase linearly, while the Tp-*e*/QT ratio remains constant.[13,14] The Tpe/QT ratio is significantly increased in patients at risk for arrhythmic events, such as Brugada syndrome, short QT syndrome, and long QT syndrome, and in organic heart diseases, such as acute myocardial infarction.[14]

Although arrhythmia susceptibility is known in RA, there are limited studies on arrhythmia predictors. In our study, we evaluated $P_{min}$, $P_{max}$, Pd, Tp-$e_{min}$, Tp-$e_{max}$, Tp-ed, $QT_{min}$, $QT_{max}$, $QTc_{min}$, $QT_{max}$, QTcd, and Tp-*e*/QTc values in the patient and control groups. As far as we can research, there is no other study in the literature evaluating all of these parameters in RA. In this study, we aimed to determine whether there is a difference in the measurements of healthy controls and RA patients and to predict whether they can be used to determine the risk of arrhythmia in patients.

## PATIENTS AND METHODS

The prospective study included 50 RA patients (38 males, 12 females; mean age: 46.8±9.1 years; range, 18 to 60 years) who fulfilled the 2010 American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR) RA criteria[15] and 50 healthy controls (34 males, 16 females; mean age: 43.4±10.4 years;

range, 18 to 60 years) who applied to the Physical Medicine and Rehabilitation Outpatient clinic of the Medicine Faculty of Fırat University between June 1, 2022, and August 31, 2022. Patients with no known diabetes, hypertension, cardiovascular disease, renal failure, lung disease, hypercholesterolemia, no smoking history, and normal sinus rhythm on ECG were recruited. A 12-lead ECG was taken for the patient and control groups. Heart rate, $QT_{min}$, $QT_{max}$, QTd, $P_{min}$ $P_{max}$, Pd, Tp-$e_{min}$, Tp-$e_{max}$, Tp-ed, $QTc_{min}$, $QTc_{max}$, QTcd, and Tp-e/QTc were calculated from ECGs. Echocardiographic images were obtained from all individuals with a probe operating at 1.5 to 4.5 MHz on the GE Vivid brand T8 model echocardiography device (General Electric, New York, USA). Left atrium diameters and left ventricular ejection fractions were measured.

Medicines used by patients were recorded. Disease activity of the patients was calculated with the Disease Activity Score (DAS28). The number of tender and swollen joints, serum C-reactive protein (CRP) level, global evaluation of the patient, and Visual Analog Scale measurements were used in the calculation.[16]

### Statistical analysis

Data were analyzed using IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as percentages. The Mann-Whitney U test was used to compare continuous variables in both groups. The chi-square test was used to compare categorical values. A $p$ value $<0.05$ was considered statistically significant.

## RESULTS

There was no significant difference between the sex distribution, age, and body mass index of the patient and control groups (Table 1). Similarly, no significant difference was found between the ejection fraction and left atrium diameters in the echocardiographic examinations of the two groups (Table 2).

Although all patients had a history of corticosteroid and conventional synthetic disease modifying drug (DMARD) use in the past, 10 patients were using biologic DMARDs, 47 patients were using conventional synthetic DMARDs, eight patients were using corticosteroids, and seven patients were using nonsteroidal anti-inflammatory drugs at the last examination. The mean dose of steroids was 9.5±3.66 mg/day. The mean disease duration of the RA group was 9.09±5.74 years. The mean

**Table 1.** Demographic characteristics of the groups

| | Patient group | | Control group | | |
|---|---|---|---|---|---|
| | % | Mean±SD | % | Mean±SD | $p$ |
| Age (year) | | 46.8±9.1 | | 43.4±10.4 | 0.078 |
| Sex<br>Female | 76 | | 68 | | 0.373 |
| Body mass index (kg/m$^2$) | | 25.66±3.99 | | 25.60±3.23 | 0.145 |

SD: Standard deviation.

**Table 2.** Echocardiographic data of the patient and control groups

| | Patient group | Control group | |
|---|---|---|---|
| | Mean±SD | Mean±SD | $p$ |
| Ejection fraction (%) | 60.10±2.57 | 58.90±3.81 | 0.068 |
| Left atrium diameter (mm) | 30.08±3.56 | 31.24±4.15 | 0.137 |

SD: Standard deviation.

**Table 3.** Laboratory values and clinical characteristics of the patients

| | RA group | |
|---|---|---|
| | % | Mean±SD |
| C-reactive protein (mg/dL) | | 9.83±8.29 |
| Erythrocyte sedimentation rate (mm/h) | | 26.12±16.28 |
| Disease Activity Score-28 | | 3.03±0.37 |
| Disease duration (year) | | 9.09±5.74 |
| bDMARD use (%) | 20 | |
| csDMARD use (%) | 94 | |
| Steroid use (%) | 16 | |
| NSAID use (%) | 14 | |
| Steroids dose (mg/day) | | 9.5±3.66 |

SD: Standard deviation; bDMARD: Biologic disease-modifying anti-rheumatic drug; csDMARD: Convantionel sentetic disease-modifying anti-rheumatic drug; NSAID: Non-steroidal antiinflammatory drug.

CRP level was 9.83±8.29, the mean erythrocyte sedimentation rate was 26.12±16.28 mm/h, and the mean DAS28 was 3.03±0.37 (Table 3).

While there was a statistically significant increase in $P_{max}$, Pd, $QT_{max}$, QTd, $QTc_{max}$, QTcd, Tp-$e_{max}$, Tp-ed, and Tp-e/QTcd parameters in the RA group compared to the control group, there was a significant decrease in the $P_{min}$ $QT_{min}$, $QTc_{min}$ parameters. Heart rate and Tp-$e_{min}$ values were not significantly different (Table 4).

## DISCUSSION

In our study, there was a statistically significant difference between the $QT_{min}$, $QT_{max}$, QTd, $P_{min}$ $P_{max}$, Pd, Tp-$e_{max}$, Tp-ed, $QTc_{min}$, $QTc_{max}$, QTcd, Tp-e/QTc measurements of our RA patients and healthy controls. It was thought that our cardiac asymptomatic patients could have an increased risk of both atrial and ventricular arrhythmias.

The arrhythmia in RA is based on diffuse cardiac involvement with inflammatory lesions. In addition, it has been shown that coronary vasculitis and coronary atherosclerotic disease, which cause myocardial perfusion defects, have a

**Table 4.** Electrocardiographic data of the patient and control groups

| | Patient group | Control group | |
|---|---|---|---|
| | Mean±SD | Mean±SD | *p* |
| Heart rate (beats/min) | 79.38±14.99 | 79.98±10.21 | 0.352 |
| $P_{min}$ (ms) | 47.20±11.95 | 59.40±14.90 | **0.000** |
| $P_{max}$ (ms) | 118.60±19.58 | 103.40±14.22 | **0.000** |
| Pd (ms) | 71.40±22.03 | 44.00±10.69 | **0.000** |
| $QT_{min}$ (ms) | 298.70±34.41 | 312.40±32.29 | **0.043** |
| $QT_{max}$ (ms) | 379.60±30.58 | 365.88±32.89 | **0.033** |
| QTd (ms) | 80.90±26.92 | 55.48±19.30 | **0.000** |
| $QTc_{min}$ (ms) | 336.96±40.74 | 351.08±27.89 | **0.046** |
| $QTc_{max}$ (ms) | 431.24±44.32 | 414.72±3010 | **0.032** |
| QTcd (ms) | 93.68±35.37 | 64.42±23.60 | **0.000** |
| Tp-$e_{min}$ (ms) | 50.00±14.56 | 52.40±9.80 | 0.336 |
| Tp-$e_{max}$ (ms) | 103.60±19.56 | 92.30±12.15 | **0.001** |
| Tp-ed (ms) | 53.00±18.43 | 39.90±10.32 | **0.000** |
| Tp-e/QTc | 0.241±0.051 | 0.223±0.032 | **0.032** |

SD: Standard deviation; $P_{min}$: P minimum; $P_{max}$: P maximum; Pd: P dispersion; $QT_{min}$: QT minimum; $QT_{max}$: QT maximum; Qtd: QT dispersion; $QTc_{min}$: Corrected QT minimum; $QTc_{max}$: Corrected QT maximum; QTcd: Corrected QT dispersion; Tp-$e_{min}$: Tp-e minimum; Tp-$e_{max}$: Tp-e maximum; Tp-ed; Tp-e dispersion; Tp-e/QTc: Tp-e/corrected QT.

proarrhythmic effect, and antibodies against the cardiac conduction system play an important role in conduction abnormalities in RA patients.[4,17]

Local atrial complement activation in RA causes tissue injury. Injury, myocyte necrosis, and fibrosis of the atrial myocardium cause atrial remodeling. Structural changes within the atrial wall can lead to electrical inhomogeneity, different conduction rates, and inhomogeneous refractory periods throughout the atrial myocardium, which may be reflected in the ECG examination as prolonged P wave duration and increased Pd.[18]

P wave dispersion is a new electrocardiographic marker associated with heterogeneous and discontinuous propagation of sinus impulses. Increased Pd is a risk factor for the development of paroxysmal AF in patients. It has been shown that increased Pd can be used to predict the transition from paroxysmal AF to AF.[7] In our study, the increase in $P_{max}$ and Pd parameters in the RA group was found to be statistically significant compared to the control group, consistent with other studies in the literature.[19,20]

It has been reported that an increase in QTd is associated with ventricular arrhythmias, sudden deaths in hypertrophic cardiomyopathies, sudden deaths in ischemic heart diseases, and left ventricular failure.[21-23] The increased susceptibility to develop fatal ventricular arrhythmias is the most likely mechanism explaining the high risk of sudden cardiac death in RA. An increasing number of studies have investigated QT interval parameters (QT, QTc, QTd, and QTcd) in RA, and it has been consistently shown that QT variables significantly increase in these patients.[3,4,24,25] There has also been direct evidence of a link between QT interval abnormalities and the risk of ventricular arrhythmia or death.[3,26,27] It has been shown that QTc duration has a positive correlation with mortality in RA.[26] In our study, $QT_{max}$, QTd, $QTc_{max}$, and QTd values were observed to be increased in the RA group compared to the control group.

Relatively new ECG ventricular repolarization markers such as Tp-e interval and the Tp-e interval/QT ratio are can predict ventricular arrhythmias and sudden cardiac death in the recent period. The Tp-e interval reflects the degree of distribution of repolarization.[28] Recent studies have suggested that the Tp-e interval and Tp-ed are a transmural dispersion index pointing to the prognostic importance of arrhythmic risk in various conditions.[29] It has been shown that the Tp-e/QT ratio and the Tp-e/QTc ratio as a transmural dispersion index can also be used as noninvasive arrhythmia indicators. Since Tp-e/QT and Tp-e/QTc are independent of heart rate change, they are indicators that can reflect transmural repolarization dispersion more accurately compared to "Tp-e interval, QT dispersion and QTc dispersion".[30] In our study, $Tp\text{-}e_{max}$ and Tp-ed were significantly prolonged in the RA group compared to the control group. In the study of Acar et al.,[31] Tp-e was found to be increased, similar to our study. In addition, in our study, the Tp-e/QTc ratio was observed to be prolonged in the RA group compared to the control group, similar to the study of Aladağ et al.[32] In the literature review, we could not find any other study comparing Tp-ed in RA and healthy controls.

There are some limitations to this study. Although the patient group in our study was selected from cardiac asymptomatic patients, coronary angiography is the gold standard test for the diagnosis of ischemic heart disease, and there may be patients with ischemic heart disease. Ten of our patients had a history of biological agent use, and all of them had a history of DMARD and corticosteroid use. These drugs may have had effects on cardiac conduction systems. In addition, the relatively small number of patients is among the limitations of our study.

In conclusion, Pd, QTcd, Tp-ed, and Tp-e/QTcd values, which indicate atrial and ventricular arrhythmia risk, were found to be significantly higher in RA patients. This finding suggested that our patients had an increased risk of cardiac morbidity and mortality, although they were still asymptomatic from a cardiac point of view. Arrhythmias are the likely source of the increase in sudden cardiac death in RA, and it is important to distinguish patients at risk of arrhythmias. These new indicators collected from ECG, which is a simple, noninvasive, and inexpensive diagnostic method, can be

used as standardized markers of cardiovascular morbidity and mortality in the future. Larger prospective studies are needed to show the correlation between these parameters and cardiac involvement.

**Ethics Committee Approval:** The study protocol was approved by the Medicine Faculty of Fırat University Ethics Committee (date: 09.06.2022, no: 9001). The study was conducted in accordance with the principles of the Declaration of Helsinki.

**Patient Consent for Publication:** A written informed consent was obtained from each patient.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Author Contributions:** Idea/consept, data collection: M.A.G., E.Y.U., M.F.U.; Design: E.Y.U., G.A.; Control/supervision: A.G., M.A.K.; Analysis, critical review: G.A.; Literatüre review: A.G.; Writing the article: E.Y.U.; References and fundings: G.A., M.F.U.

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## REFERENCES

1. Caporali R, Pallavicini FB, Filippini M, Gorla R, Marchesoni A, Favalli EG, et al. Treatment of rheumatoid arthritis with anti-TNF-alpha agents: A reappraisal. Autoimmun Rev 2009;8:274-80. doi: 10.1016/j.autrev.2008.11.003.
2. Pizzuto K, Averns HL, Baranchuk A, Abdollah H, Michael KA, Simpson C, et al. Celecoxib-induced change in atrial electrophysiologic substrate in arthritis patients. Ann Noninvasive Electrocardiol 2014;19:50-6. doi: 10.1111/anec.12097.
3. Göldeli O, Dursun E, Komsuoglu B. Dispersion of ventricular repolarization: A new marker of ventricular arrhythmias in patients with rheumatoid arthritis. J Rheumatol 1998;25:447-50.
4. Alkaabi JK, Ho M, Levison R, Pullar T, Belch JJ. Rheumatoid arthritis and macrovascular disease. Rheumatology (Oxford) 2003;42:292-7. doi: 10.1093/rheumatology/keg083.
5. Schwemmer S, Beer P, Schölmerich J, Fleck M, Straub RH. Cardiovascular and pupillary autonomic nervous dysfunction in patients with rheumatoid arthritis - a cross-sectional and longitudinal study. Clin Exp Rheumatol 2006;24:683-9.
6. Okutucu S, Aytemir K, Oto A. P-wave dispersion: What we know till now? JRSM Cardiovasc Dis 2016;5:2048004016639443. doi: 10.1177/2048004016639443.
7. Dilaveris PE, Gialafos EJ, Sideris SK, Theopistou AM, Andrikopoulos GK, Kyriakidis M, et al. Simple electrocardiographic markers for the prediction of paroxysmal idiopathic atrial fibrillation. Am Heart J 1998;135:733-8. doi: 10.1016/s0002-8703(98)70030-4.
8. Park MK, Guntheroth G. Normal ECG values and deviations from normal. In: Park MK, Guntheroth G, editors. How to read pediatric ECGs. 3rd ed. St.Louis: Mosby Year Book; 1992. p. 42-54.
9. Day CP, McComb JM, Campbell RW. QT dispersion: An indication of arrhythmia risk in patients with long QT intervals. Br Heart J 1990;63:342-4. doi: 10.1136/hrt.63.6.342.
10. Pye MP, Cobbe SM. Mechanisms of ventricular arrhythmias in cardiac failure and hypertrophy. Cardiovasc Res 1992;26:740-50. doi: 10.1093/cvr/26.8.740.
11. Beaubien ER, Pylypchuk GB, Akhtar J, Biem HJ. Value of corrected QT interval dispersion in identifying patients initiating dialysis at increased risk of total and cardiovascular mortality. Am J Kidney Dis 2002;39:834-42. doi: 10.1053/ajkd.2002.32005.
12. Antzelevitch C. T peak-Tend interval as an index of transmural dispersion of repolarization. Eur J Clin Invest 2001;31:555-7. doi: 10.1046/j.1365-2362.2001.00849.x.
13. Castro-Torres Y, Carmona-Puerta R, Katholi RE. Ventricular repolarization markers for predicting malignant arrhythmias in clinical practice. World J Clin Cases 2015;3:705-20. doi: 10.12998/wjcc.v3.i8.705.
14. Gupta P, Patel C, Patel H, Narayanaswamy S, Malhotra B, Green JT, et al. T(p-e)/QT ratio as an index of arrhythmogenesis. J Electrocardiol 2008;41:567-74. doi: 10.1016/j.jelectrocard.2008.07.016.
15. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3rd, et al. 2010 Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum 2010;62:2569-81. doi: 10.1002/art.27584.
16. Prevoo ML, van 't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum 1995;38:44-8. doi: 10.1002/art.1780380107.
17. Eisen A, Arnson Y, Dovrish Z, Hadary R, Amital H. Arrhythmias and conduction defects in rheumatological diseases--a comprehensive review. Semin Arthritis Rheum 2009;39:145-56. doi: 10.1016/j.semarthrit.2008.05.001.
18. Klein RM, Vester EG, Brehm MU, Dees H, Picard F, Niederacher D, et al. Inflammation of the myocardium

as an arrhythmia trigger. Z Kardiol 2000;89 Suppl 3:24-35.
19. Yavuzkir M, Ozturk A, Dagli N, Koca S, Karaca I, Balin M, et al. Effect of ongoing inflammation in rheumatoid arthritis on P-wave dispersion. J Int Med Res 2007;35:796-802. doi: 10.1177/147323000703500608.
20. Guler H, Seyfeli E, Sahin G, Duru M, Akgul F, Saglam H, et al. P wave dispersion in patients with rheumatoid arthritis: Its relation with clinical and echocardiographic parameters. Rheumatol Int 2007;27:813-8. doi: 10.1007/s00296-007-0307-8.
21. Buja G, Miorelli M, Turrini P, Melacini P, Nava A. Comparison of QT dispersion in hypertrophic cardiomyopathy between patients with and without ventricular arrhythmias and sudden death. Am J Cardiol 1993;72:973-6. doi: 10.1016/0002-9149(93)91118-2.
22. Puddu PE, Bourassa MG. Prediction of sudden death from QTc interval prolongation in patients with chronic ischemic heart disease. J Electrocardiol 1986;19:203-11. doi: 10.1016/s0022-0736(86)80030-9.
23. Barr CS, Naas A, Freeman M, Lang CC, Struthers AD. QT dispersion and sudden unexpected death in chronic heart failure. Lancet 1994;343:327-9. doi: 10.1016/s0140-6736(94)91164-9.
24. Cindas A, Gökçe-Kutsal Y, Tokgözoglu L, Karanfil A. QT dispersion and cardiac involvement in patients with rheumatoid arthritis. Scand J Rheumatol 2002;31:22-6. doi: 10.1080/030097402317255327.
25. Lazzerini PE, Acampa M, Capecchi PL, Hammoud M, Maffei S, Bisogno S, et al. Association between high sensitivity C-reactive protein, heart rate variability and corrected QT interval in patients with chronic inflammatory arthritis. Eur J Intern Med 2013;24:368-74. doi: 10.1016/j.ejim.2013.02.009.
26. Panoulas VF, Toms TE, Douglas KM, Sandoo A, Metsios GS, Stavropoulos-Kalinoglou A, et al. Prolonged QTc interval predicts all-cause mortality in patients with rheumatoid arthritis: An association driven by high inflammatory burden. Rheumatology (Oxford) 2014;53:131-7. doi: 10.1093/rheumatology/ket338.
27. Chauhan K, Ackerman MJ, Crowson CS, Matteson EL, Gabriel SE. Population-based study of QT interval prolongation in patients with rheumatoid arthritis. Clin Exp Rheumatol 2015;33:84-9.
28. Yayla Ç, Özcan F, Aras D, Turak O, Özeke Ö, Çay S, et al. Tp-e interval and Tp-e/QT ratio before and after catheter ablation in patients with premature ventricular complexes. Biomark Med 2017;11:339-46. doi: 10.2217/bmm-2016-0263.
29. Yayla C, Yayla KG, Acar B, Unal S, Ertem AG, Akboga MK. Atherosclerosis in inflammatory bowel disease. Angiology 2017;68:462. doi: 10.1177/0003319716661068.
30. Yamaguchi M, Shimizu M, Ino H, Terai H, Uchiyama K, Oe K, et al. T wave peak-to-end interval and QT dispersion in acquired long QT syndrome: A new index for arrhythmogenicity. Clin Sci (Lond) 2003;105:671-6. doi: 10.1042/CS20030010.
31. Acar GR, Akkoyun M, Nacar AB, Dirnak I, Yıldırım Çetin G, Nur Yıldırım M, et al. Evaluation of Tp-e interval and Tp-e/QT ratio in patients with rheumatoid arthritis. Turk Kardiyol Dern Ars 2014;42:29-34. doi: 10.5543/tkda.2014.52959.
32. Aladag N, Guner A, Arslan C, Kalkan AK, Kahraman S, Agus HZ, et al Assessment of proarrhythmic ventricular electrophysiological remodeling in patients with rheumatoid arthritis. Herz 2022;47:465-70. doi: 10.1007/s00059-021-05072-9.