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Evaluation of Tp-e interval and Tp-e/QT ratio in Iraqi Patients with Rheumatoid Arthritis

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Abstract

Objectives: Several studies have suggested that the interval from the peak to the end of the electrocardiographic T wave (Tp-e) may correspond to the transmural dispersion of repolarization and that increased Tp-e interval and Tp-e/QT ratio are associated with malignant ventricular arrhythmias. The aim of this study was to evaluate ventricular repolarization by using the Tp-e interval and Tp-e/QT ratio in patients with rheumatoid arthritis (RA), and to assess the relation with inflammation.

Study design: A case-control study includes seventy patients (57 females, 13 male mean age 48.3±12.3years) with RA and 46 controls (39 females, 7 males; mean age, 46.8 ±13.1 years) were included. From the 12-lead electrocardiogram, Tp-e interval and Tp-e/QT ratio were measured. Blood samples were taken for erythrocyte sedimentation rate (ESR). These parameters were compared between groups. The relationship between ventricular repolarization and inflammation was assessed by Pearson correlation coefficients.

Results: Tp-e interval and Tp-e/QT ratio were increased in RA patients compared to the controls (72.47 ±6.6vs 66.17 ±3.4ms,0.19 ±0.01vs 0.17±0.01; $p<0.001$ and $p<0.001$, respectively).The Tp-e/QT ratio was also correlated with ESR($R=0.3$, $P=0.02$)

Conclusion: In RA patients, the increased frequency of ventricular arrhythmias may be explained by increased indexes of ventricular repolarization and their relationship with inflammation.

Keywords: NIL

Introduction

Rheumatoid arthritis (RA) a chronic systemic inflammatory disease that mainly targets the synovial joints as well as extra-articular structures.[(1)]It usually presents with pain, swelling and stiffness affecting the small joints of the hands, feet and wrists.[(2)]

The overall world prevalence of RA is approximately 0.5% to 1% [(3)] and is more common in female (female: male, 3:1). Although RA may present at any age, the typical age of onset in women is the late childbearing years; in men, RA develops more often in the sixth decade.[(4)] The prevalence can differ in different ethnic groups as it may drop to 0.3% in the Chinese [(5)]and increase to 5% in Pima Indians of Arizona.[(6)]Definite RA was observed in 1% of population samples in Iraq.[(7)]

Cardiac disease in RA can take many forms. It has become apparent that increased risk of premature death in RA is due largely to an increased incidence of cardiovascular disease, primarily myocardial infarction and congestive heart failure. In a detailed study of rheumatoid patients using echocardiography, Holter monitors, and electrocardiography, it was reported that 70% of patients with nodular disease and 40% of those with non-nodular RA have some

cardiac involvement, including valve thickening or incompetence.[8]

Inflammation, as an independent predictor of cardiovascular mortality and sudden death. Indicators of abnormal ventricular repolarization such as QTc prolongation, QT interval dispersion, and autonomic dysfunction have been implicated in the pathogenesis of sudden cardiac death. The QT interval represents the time from onset of ventricular depolarization (beginning of the Q wave) to completion of repolarization (end of T wave). The corrected QT interval (QTc) estimates the QT at a standardized heart rate of 60 bpm, while QT interval dispersion (QTd) is measure of the dispersion of ventricular repolarization (maximum QT interval - minimum QT interval). In the general population both prolongation of QTc and increased QTd are known risk factors for sudden cardiac death.

To evaluate ventricular repolarization by using the Tp-e interval and Tp-e/QT ratio in patients with rheumatoid arthritis (RA), and to assess the relation with inflammation.

Methods

Patients

This case-control study was conducted at the Baghdad Teaching Hospital in Baghdad from June 2016 to October 2017. The study included 70 consecutive patients (57 females, 13 male mean age 48.3±12.3years) who were diagnosed as having RA according to the revised classification of the American College of Rheumatology. The control group comprised46 age- and gender-matched healthy volunteers (39 females, 7 males; mean age, 46.8 ±13.1 years). This study was granted full ethical approval from the local ethics committee and all the patients have given us their consents prior to the commencement of our study. Exclusion criteria were the presence of history of the following:-Coronary artery disease, arterial hypertension, primary cardiomyopathy, valvular heart disease, and atrioventricular conduction abnormalities on the ECG, thyroid dysfunction, anemia, renal or pulmonarydisease, and poor electrocardiographic imaging. All the patients were in sinus rhythm, and none was taking medications such as antiarrhythmics, tricyclic antidepressants, antihistaminics,or antipsychotics.

All the patients were receiving one or more disease-modifying anti-rheumatic drugs (hydroxychloroquine, methotrexate, and sulfasalazine) and steroids. Blood samples were taken for erythrocyte sedimentation rate (ESR), and rheumatoid factor (RF). Disease activity was measured by using Clinical Disease Activity Index (CDAI)](appendix4).

Electrocardiography:

The 12-lead ECG was recorded at a paper speed of 25 mm/s. ECG measurements of QT and Tp-eintervals were performed. Subjects with U waves on their ECGs. The QT interval was measured from the beginning of the QRS complex to the end of the T wave, and was corrected for heart rate using the Bazett formula: cQT = QT/√ (R-R interval). The Tp-einterval was defined as the interval from the peak of T wave to the end of T wave, and was corrected for heart rate. Measurements of the Tp-e interval were performed from precordial leads. The Tp-e/QT ratio was calculated from these measurements.

Statistical analysis:

SPSS version 23 was used for data entry and analysis. Mean and slandered deviation was used to represent the numerical data. Independent student t-test, was used to confirm significance as well as pearson correlation was used to determine the power and direction of correlation between different parameters. P-value<0.05 was considered significant.

Results

Table 1 revealed that the mean age, BMI of patients group were 48.4±12.3sd,26.6±4.6sd respectively while of control group were 46.9±13.2sd,27.9±2.4sd respectively and this difference was statistically non-significant(p>0.05). With regards to sex distribution, no significant difference was reported between two groups where the results showed that the female represented 81.4% of patient group and 84.7% of control group while male patients represented 18.6% 15.3% respectively.

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Table.1. Demographic characteristics and BMI of studied groups

	Patients			Control			p-value
	No.	%	Mean±SD	No.	%	Mean±SD	
Age/year			48.4±12.3			46.9±13.2	0.5
Gender							
Female	57	81.4%		39	84.7%		0.4
Male	13	18.6%		7	15.3%		
BMI kg/m^2			28.6±4.9			27.9±2.4	0.3

BMI: body mass index. SD: standard deviation. P-value>0.05 was considered significant.(kg/m2): kilogram per square meter

Table 2 showed that the mean value of SBP and DBP of patients group was higher than that of control group (122.9 ±13.8,74.06±13.9) (118.8±9.6,72.6±7.4) respectively but this difference did not reach the significant level(p=0.08,0.5) while the mean value of ESR level of patients group was significantly higher than that of control group (28.2±5.1,15.5±8.1) .

Table.2. Mean value of studied parameters for studied groups

	Patients		Control		p-value
	Mean	SD	Mean	SD	
SBP(mmHg)	122.9	13.8	118.8	9.6	0.08
DBP(mmHg)	74.06	13.9	72.6	7.4	0.5
ESR(mm/hr)	28.2	5.1	15.5	8.1	0.001
CDAI	23.4	8.8			

SBP: Systolic blood pressure. DBP: Diastolic blood pressure. ESR: Erythrocyte sedimentation rate. CDAI: Clinical disease activity index. SD: Standard deviation. mmHg: millimeters of mercury.mm/hr: millimeters/hour. P-value>0.05 was considered significant

Table 3 demonstrates that the mean value of QT and c-QT of patients group (372.7±16.5,441.8±40.2) were higher than that of control group (369.2±10.6,432.1±36.3) but this difference was statistically non –significant (p=0.1 for both) while the mean value of Tp-e,cTp-e and Tp-e/QT ratio of patients group was significantly higher than control group(p=0.001 for all) .

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Table.3. Electrocardiographic findings of studied groups

	Patients		Control		
	Mean	SD	Mean	DS	p-value
QT(ms)	372.7	16.5	369.2	10.6	0.1
T p-e(ms)	72.47	6.6	66.17	3.41	0.001
c.QT(ms)	441.8	40.2	432.1	36.3	0.1
cTp-e(ms)	85.8	9.4	77.5	7.2	0.001
T p-e/QT	0.19	0.01	0.17	0.01	0.001

SD: standard deviation. QT, Tp-e are intervals measured in electrocardiography. c QT: corrected QT interval. c Tp-e:correctedTp-e interval. T p-e/QT : A ratio of T p-e to QT intervals.ms: millisecond. P-value<0.05 was considered significant.

Table 4 showed that there was direct significant correlation between the ESR level and CDAI (R=0.9, P=0.001) as well as between ESR and Tp-e/QT ratio (R=0.3, P=0.02) but no significant correlation was reported between Tp-QT and CDAI (P>0.05) as seen in table 4 and figures1,2,3.

Table.4.Correlation between studied parameters

		ESR	CDAI	T p-e/QT
ESR(mm/hr)	Pearson Correlation	1	0.5	0.3
	p-value		0.001	0.02
CDAI	Pearson Correlation	0.5	1	0.07
	p-value	0.001		0.5
T p-e/QT	Pearson Correlation	0.3	0.07	1
	p-value	0.02	0.5	

ESR: Erythrocyte sedimentation rate. CDAI: Clinical disease activity index. T p-e/QT : A ratio of T p-e to QT intervals. P-value>0.05 was considered significant.

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Figure.1.Correlation between TP-e/QT and CDAI

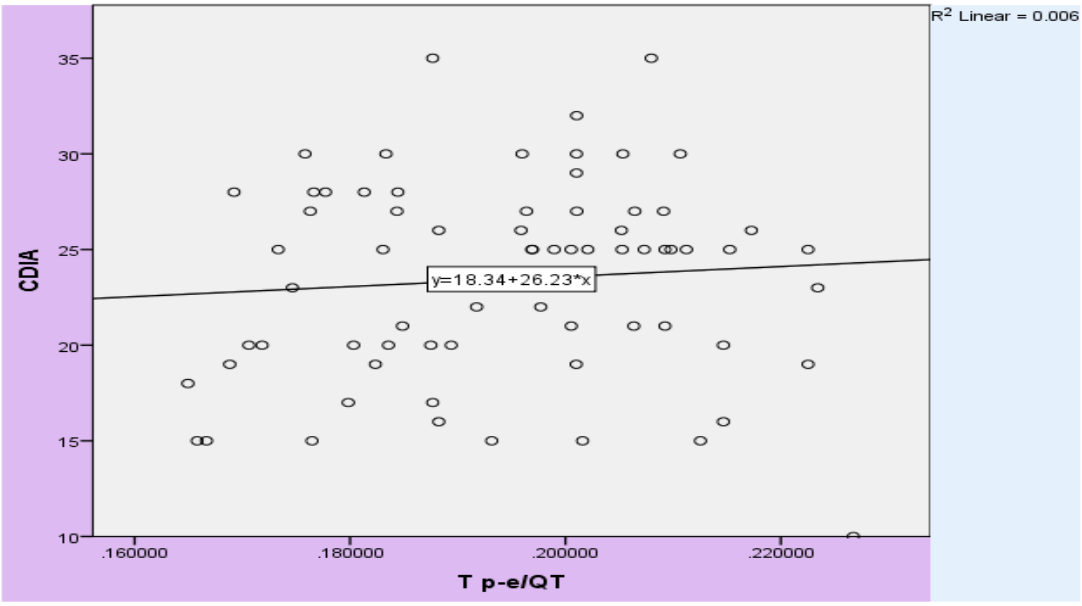

Figure.2.Correlation between TP-e/QT and ESR

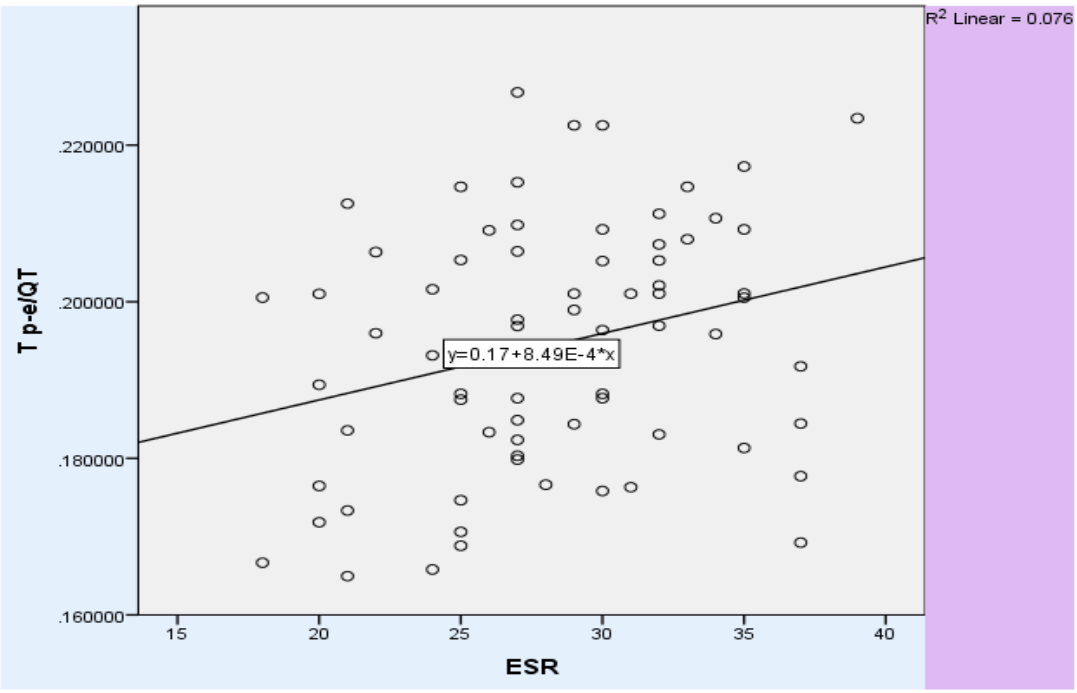

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Figure.3.Correlation between ESR and CDAI

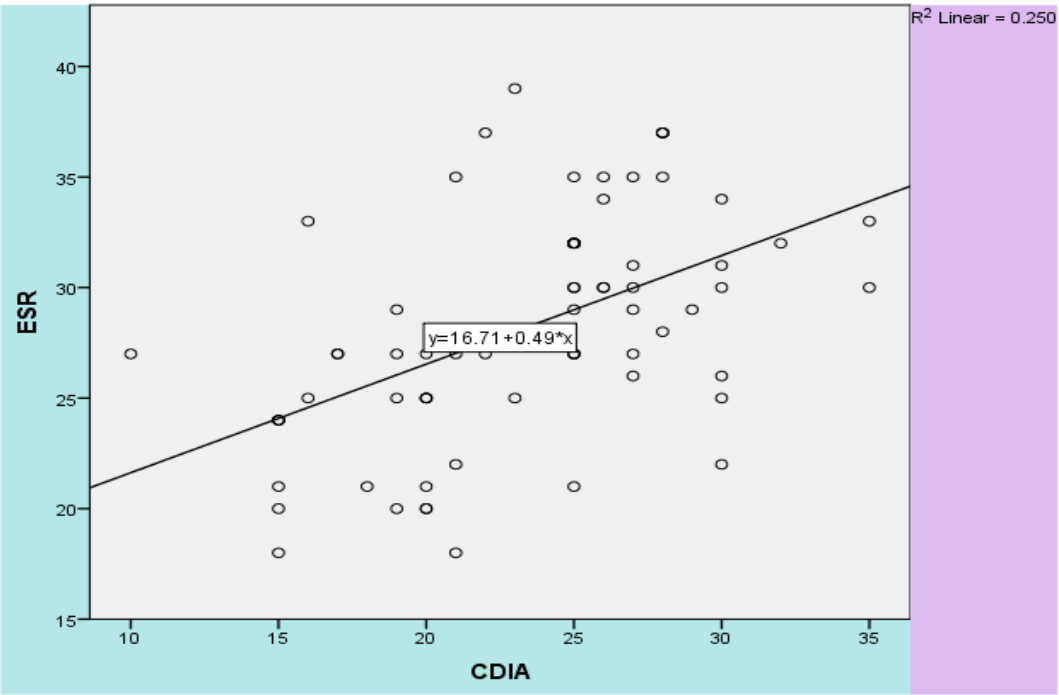

Table 5 showed that there was a significant direct correlation between the age of the patients and SBP (R=0.41, p=0.001), SBP and DBP (R=0.3, P=0.006). Significant direct correlation was also reported between Tp-e and Tp=e/QT ratio (0.87, p=0.001). The Tp-e interval and Tp-e/QT ratio were not correlated with age, systolic/diastolic blood pressure under study as seen also in figure 4.

Table.5.Correlation between studied parameters

		Age	SBP	DBP	T p-e	T p-e/QT
Age	Pearson correlation	1	0.41	0.2	-0.12	-0.15
	p-value		0.001	0.07	0.13	0.1
SBP	Pearsoncorrelation	0.4	1	0.3	-0.08	0.06
	p-value	0.001		0.006	0.4	0.6
DBP	Pearsoncorrelation	0.2	0.3	1	-0.14	-0.06
	p-value	0.07	0.006		0.3	0.6
T p-e	Pearsoncorrelation	-0.12	-0.08	-0.14	1	0.87
	p-value	0.13	0.4	0.3		0.001

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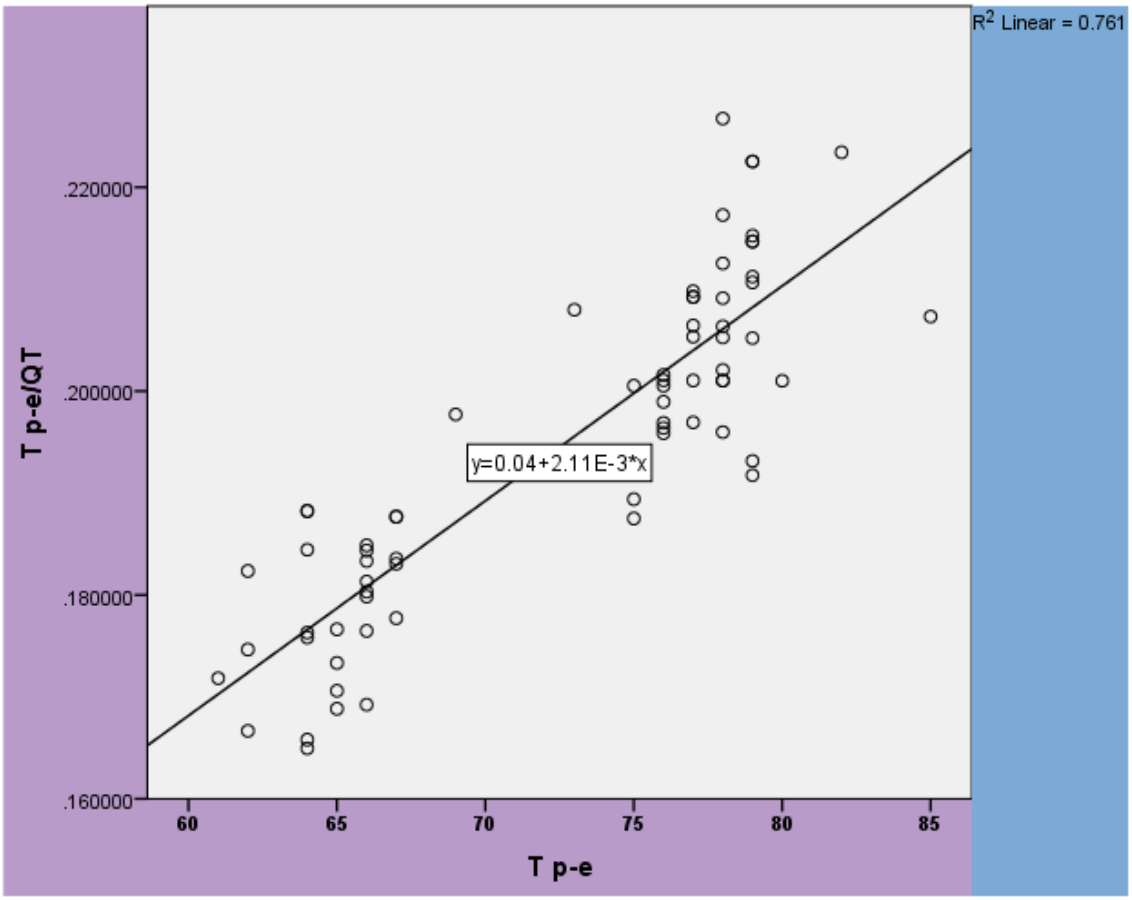
T p-e/QT	Pearson correlation	-0.15	0.06	-0.06	0.87	1
	p-value	0.1	0.6	0.6	0.001	

SBP: Systolic blood pressure. DBP: Diastolic blood pressure. QT, Tp-e are intervals measured in electro cardiography. T p-e/QT : A ratio of T p-e to QT intervals. P-value<0.05 was considered significant.

Figure.4.Correlation between TP-e/QT and Tp-



Discussion

Rheumatoid arthritis is a systemic disease characterized by increased inflammatory activity. Several forms of cardiac involvement have been described in RA .[9] This study showed that, the Tp-e interval and Tp-e/QT ratio were significantly increased in patients with RA when compared to control subjects. According to this; the increased cardiovascular morbidity and mortality in RA patient could be due to complex ventricular arrhythmias. The Tp-e interval and Tp-e/QT ratio could be electrocardiographic markers of increased dispersion of ventricular repolarization and might be used as an electrocardiographic index of ventricular arrhythmogenesis and sudden cardiac death .

A previous study made by Acar G. et al. (2014) [10] showed an agreement with this study regarding to prolongation of Tp-e interval and Tp-e/QT ratio in RA patient than controls. Another study by Nacar AB. et al.(2013)[11] demonstrated finding in agreement with this current study. They reported that the Tp-e interval and Tp-e/ QT ratio were increased in ankylosing spondylitis patients, and these ventricular repolarization indices were correlated with inflammation. These electrocardiographic parameters were significantly correlated with ESR and this agree with that reported by Acar G. et al.[10]. This correlation could be due to that, pro-inflammatory cytokines, particularly TNF-α, directly prolong cardiac cells action potential

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duration by regulating ion channels involved in ventricular repolarization.

This study showed there is no significant relationship between the prolongation of the Tp-e interval ,Tp-e/QT ratio and the disease activity and that was incomparable with the results of the Acar G. et al.[10]study ; in which they suggested that ,the increment in prevalence of ventricular arrhythmias and cardiovascular mortality risk might caused by increased ventricular repolarization heterogeneity and increased inflammation in RA patients[10]. Other study by Bathon JM. et al. (2010)[12] They reported that myocardial fibrosis is a well-known complication of RA, which is thought to develop due to chronic inflammation . Their result was based on the using of cardiac MRI tool in assessing myocardial abnormalities which were frequent in RA patients without known cardiac disease. Abnormal cMRI findings were associated with higher RA disease activity, suggesting a role for inflammation in the pathogenesis of myocardial involvement in RA.

Abnormalities of ventricular repolarization due to cardiac structural changes and increased inflammatory activity could result in increased sudden cardiac deaths and ventricular arrhythmias in RA patients.

The major limitation of this study is the lack of follow-up of the patients. It does not assess the association between ventricular arrhythmias with the Tp-e interval and Tp-e/QT ratio. It does not evaluate the potential prognosticrole of the electrocardiographic ventricular repolarizationindies with respect to future untoward events. Thus, long-term follow-up and large-scale prospective studies are needed to determine the predictive value of prolonged Tp-e interval and increased Tp-e/QT ratio in this population. Finally, manual measurement of QT and Tp-e intervals on ECG strip might have underpowered the results because these would be more reliable if measured on the higher solution screen of a digital system.

In conclusions; the study revealed that the Tp-e interval and Tp-e/QT ratio were increased in RA patients. The results also revealed that these electrocardiographic ventricular repolarization indexes were significantly correlated with inflammation. The Tp-e interval and Tp-e/QT ratio might be useful markers of cardiovascular morbidity and mortality due to complex ventricular arrhythmias in patients with RA.

References

1. Bennett GA, Cobb S, Jacox R et al. Proposed diagnostic criteria for rheumatoid arthritis. Bull Rheum Dis 1956; 7(4):121-4.
2. Christopher VT, Joan MB. Rheumatoid arthritis. In: Klippel JH StoneJH,Crofford LJ, White PH, eds., Primer on rheumatic diseases, 13th ed., New York, USA, Springer science and business media 2008; 114-21.
3. Silman AJ, Pearson JE. Epidemiology and genetics of rheumatoid arthritis. Arthritis Res 2002;4(suppl 3):S265-72.
4. Silman A., Klareskog L., Breedveld F. et al. Proposal to establish a register for the long term surveillance of adverse events in patients with rheumatic diseases exposed to biological agents: the EULAR Surveillance Register for Biological Compounds. Ann Rheum Dis 2000; 59(6): 419-20.
5. Firestein GS, Budd RC, Gabriel SE et al. RA, etiology and pathogenesis. In:Kelley's Textbook of Rheumatology.9thEd. China, Elsevier. 2013; p1059.
6. Doherty M, Ralstom SH. Walker BR et al. Musculoskeletal disorders. In:Davidson's Principles and Practice of Medicine. 21thEd. London, Elsevier's Health Sciences Rights Department. 2010; p1088.
7. Al-Rawi ZS, Alazzawi AJ, Al-Ajilli FM. et al Rheumatoid Arthritisin population samples in Iraq: Ann Rheum Dis 1978; 37(1): 73-5.
8. Firestein GS, Budd RC, Gabriel SE et al. RA, etiology and pathogenesis. In:Kelley's Textbook of Rheumatology.9thEd. China, Elsevier. 2013; p1125.
9. Mountantonakis S, Deo R. Biomarkers in atrial fibrillation,ventricular arrhythmias, and sudden cardiac death. CardiovascTher2012;30:74-80.
10. Acar G, Akkoyun M, Nacar A, et al.Evaluation of Tp-e interval and Tp-e/QT ratio in patients with rheumatoid arthritis.Turk KardiyolDernArs. 2014;42(1):29-34.

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11. Acar G, Yorgun H, Inci MF, Akkoyun M, Bakan B, Nacar AB, et al. Evaluation of Tp-e interval and Tp-e/QT ratio in patientswith ankylosing spondylitis. Mod Rheumatol 2013 Apr 12.

12. Kobayashi Y, Giles JT, Hirano M, Yokoe I, Nakajima Y,Bathon JM, et al. Assessment of myocardial abnormalitiesin rheumatoid arthritis using a comprehensive cardiac magneticresonance approach: a pilot study. Arthritis Res Ther 2010;12:R171.

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