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DIABETIC DISORDERS ASSOCIATION WITH ARRHYTHMIA & SUDDEN CARDIAC DEATH IN THE LIGHT OF ELECTROCARDIOGRAPHIC AND LABORATORY OUTCOMES

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Abstract:

Objectives: *Arrhythmia and unexpected cardiac death risk is increased in cardiac microvascular circulation and diabetic disorders. T p-e dispersion, T peak – T end (T p-e) interval & (T p-e / QT) & (T p-e / QTc) proportions which are measured through ECG (Electrocardiogram) are relatively new parameters for ventricular arrhythmogenesis evaluation. Our research was aimed on the comparison of QT dispersion (QTcd) corrected, QT (QTd) dispersion, T p-e interval, P dispersion (Pd), (T p-e / QT) & (T p-e / QTc) proportions and T p-e dispersion in T2DM (Type – II Diabetes Mellitus) cases in the healthy selected research population.*

Methods: *We retrospectively analyzed the electrocardiographic parameters of one hundred T2DM cases and also made a comparison with the ECG outcomes of one hundred healthy controls (matched age, body weight, sex and height).*

Results: *Higher proportions of QT dispersion (QTcd) corrected, QT (QTd) dispersion, T p-e interval, P dispersion (Pd), (T p-e / QT) & (T p-e / QTc) proportions and Tp-e dispersion were observed in the affected cases. There was a significant association in the hemoglobin (Hb) A1c & QTd, T p-e dispersion, Pd, QTcd, (T p-e / QTc) & (T p-e / QT) parameters as observed through "linear regression analysis". Significant positive association as observed among systolic blood pressure, low-density lipoprotein and T p-e dispersion values.*

Conclusion: *We can predict arrhythmia risk through the assessment of T p-e interval, T p-e / QT, T p-e dispersion and (T p-e / QTc) proportions, through the suggestion of ventricular repolarization heterogeneity, P-wave & Pd reflecting atrial repolarization heterogeneity in T2DM cases.*

Keywords: *Electrocardiography, Arrhythmia, Type II Diabetes Mellitus (T2DM) and HbA1c.*

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INTRODUCTION:

High CVD risk is found in the T2DM patients which causes mortality and morbidity associated with diabetes [1]. Prothrombotic state is created by T2DM, which also leads to an acute state of coronary syndrome by reducing antiaggregant factors and endothelial damage like prostacyclin and nitric oxide enhance thrombotic substance like factor VII, fibrinogen and suppressing fibrinolysis with the factors of plasminogen activation inhibition [2]. Glycosylation of LDL (low-density lipoprotein) is also an important factor among these patients including glycosylation as the particles of LDL become even atherogenic. Dyslipidemia has its own contribution in endothelial dysfunction. Additionally, proinflammatory cytokines expression like tumor necrosis alpha factor, interleukin serum – 6 and C – reactive (protein) is enhanced in T2DM cases which leads to proinflammatory state. Arrhythmias and coronary artery disease which is caused by rapid atherosclerosis development is common complication [2, 3].

Blood circulation in diabetic cases in cardiac microvascular bed is disturbed on the basis of autonomic neuropathy, proinflammatory state and prothrombotic which increases the arrhythmia, sudden cardiac death and silent infarction risk [4].

For the increased arrhythmia risk, we often use surface ECG (Electrocardiogram). Measurements including QTc, QTcd and QTd reveal cardiac repolarization heterogeneity through surface ECG. These parameters are also used for the identification of associated risks with enhanced ventricular arrhythmia risk [5, 6]. It has been observed through QT interval prolongation and QTd increase are associated with cardiac mortality [6]. It has been also observed that (Pd) was sovereign risk for atrial flutter & atrial fibrillation [7, 8]. T p-e interval, T p-e / QT, T p-e dispersion & T p- e / QTc measured through ECG have been currently observed through literary efforts as new features for the ventricular arrhythmogenity evaluation in numerous disease incidences. Few studies also compared aforementioned parameters (QTd, QTcd and QTc) for longer durations and produced reliable outcomes for the detection of an impaired ventricular repolarization [9]. Sudden cardiac death can be associated with such parameters like (QTd, QTcd and QTc) as they are affected through rate of heart [6]. T p-e interval, T p-e / QTc rates and T p-e / QT can also be utilized as a parameter for the assessment of ventricular repolarization which are also reliable for the ventricular repolarization assessment which is also affected by the rate of heart [9, 10].

METHODS:

Our research was carried out at Mayo Hospital, Lahore (June 2016 to May 2017). We assessed the ECG outcomes of 100 T2D cases (40 males and 60 females) with mean age as (46.5 ± 6.2 years) in the age bracket of (29 – 58 years). These cases were followed because of metabolism and endocrinology disease. We also compared the ECG outcomes of 100 T2D cases with healthy BMI, age and sex among (34 males and 66 females) with mean age as (45.6 ± 8.3 years) in the age bracket of (19 – 68 years). We did not include the cases with coronary artery disease history, peripheral arterial illness, cerebrovascular illness, ventricular & atrial arrhythmia, disease of valvular heart; cardiomyopathy, chronic pulmonary illness, hypertension, malignancies, chronic disease of liver, chronic and acute insufficiency of renal, electrolyte disturbance, anemia, thyroid dysfunction or related major illness cases. We included only cardiac check-up cases and all assessed for echocardiographic outcomes without an indication of normal ejection fractions and valvular heart pathology. Electrocardiography (pulse wave, Pd, QT interval, QTc, QTd, Tp-e etc.) and laboratory outcomes (Blood sugar fasting, HbA1c, TSH, LDL, TC, HDL etc.) were assessed after informed consent and ethical permission.

SPSS was used for statistical analysis. Mean and SD were used for the descriptive data presentation. Chi-Square and "Mann-Whitney U test" was also carried out with a P-value (< 0.05). Confidence level was taken as 95% with P-value as (<0.05).

RESULTS:

Higher proportions of QT dispersion (QTcd) corrected, QT (QTd) dispersion, T p-e interval, P dispersion (Pd), (T p-e / QT) & (T p-e / QTc) proportions and Tp-e dispersion were observed in the affected cases. There was a significant association in the hemoglobin (Hb) A1c & QTd, T p-e dispersion, Pd, QTcd, (T p-e / QTc) & (T p-e / QT) parameters as observed through "linear regression analysis". Significant positive association as observed among systolic blood pressure, low-density lipoprotein and T p-e dispersion values. Detailed outcomes analysis has been made in the given tables with corresponding figures.

Table – I: Demographic, clinical, and laboratory characteristics of patients and controls

Variables	Patients (n=100)	Controls (n=100)	P-Value
Age (years)[a]	46.5±6.2	45.6±8.3	0.37
Male/Female (n)	40/60	34/66	0.32
Height (cm)[a]	164.1±9.7	165.9±8.7	0.15
Weight (kg)[a]	82.5±15	80.8±17.5	0.47
Systolic blood pressure (mmHg)[a]	124±10.9	116.3±12	<0.001
Diastolic blood pressure (mmHg)[a]	73.7±9	69.7±8.7	0.002
Triglyceride (mg/dL)[b]	154(735-41)	122.5(398-36)	<0.001
Cholesterol (mg/dL)[a]	209.8±42.5	189.9±29.7	<0.001
LDL (mg/dL)[a]	128.7±34.5	116.4±25	0.01
HDL (mg/dL)[a]	43.7±8.1	47.1±10.1	0.01
Fasting glucose (mg/dL)[b]	164.5(103-456)	93.5(78-100)	<0.001
HbA1c (%)[b]	8.4(5.2-13.5)	5.35(4.5-6.1)	<0.001
TSH (uIU/mL)[a]	1.81±0.99	2.02±0.85	0.14
Free T4 (ng/dl)[a]	0.89±0.12	0.85±0.12	0.06
Hemoglobin (gr/dl)[a]	14.3±1.3	13.9±1.6	0.06
Hematocrit (%)[a]	43±3.1	42.1±3.4	0.08
Sodium (mmol/L)[a]	138.8±2.4	139.3±1.9	0.14
Potassium (mmol/L)[a]	4.46±0.33	4.44±0.30	0.53
Calcium (mg/dl)[a]	9.48±0.33	9.44±0.35	0.39
Smoker/non-smoker (n)	25/75	35/65	0.11

Table – II: Comparison of the electrocardiographic parameters of the groups

Variables	Patients		Controls		P-value
	Mean	± SD	Mean	± SD	
Heart rate, (bpm)	80.5	12.2	74.6	10.1	<0.001
P wave (ms)	127.6	19.8	98.8	19.2	<0.001
QT interval (ms)	395.4	23.8	387.4	21.1	0.01
QTc interval (ms)	449.1	24.9	430.7	25.3	<0.001
Tp-e interval (ms)	101	17.5	87.4	18.7	<0.001
P dispersion (ms)	74.9	17.2	50.9	16.8	<0.001
QT dispersion (ms)	72.4	19.5	47.8	15.8	<0.001
QTc dispersion (ms)	89.4	29.8	53.2	19.3	<0.001
Tp-e dispersion (ms)	48.8	18.1	32.7	16.3	<0.001
Tp-e/QT	0.25	0.04	0.22	0.04	<0.001
Tp-e/QTc	0.22	0.04	0.2	0.04	0.01

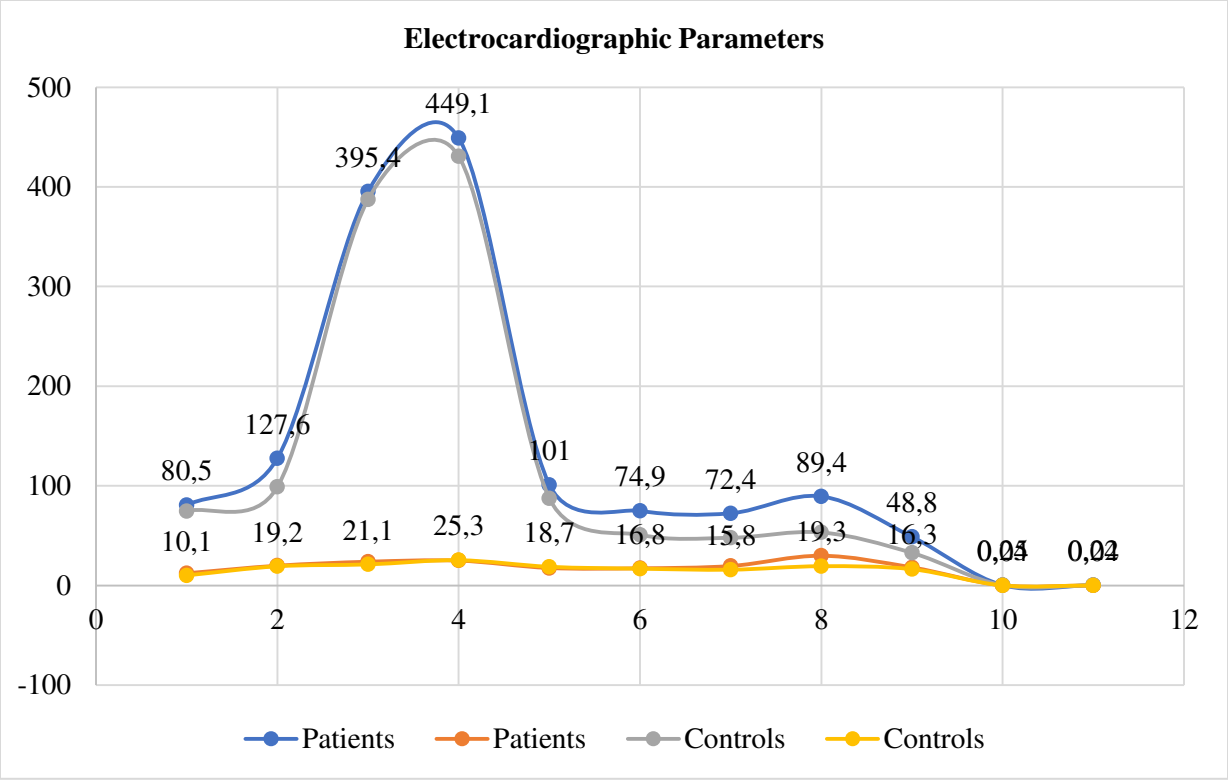
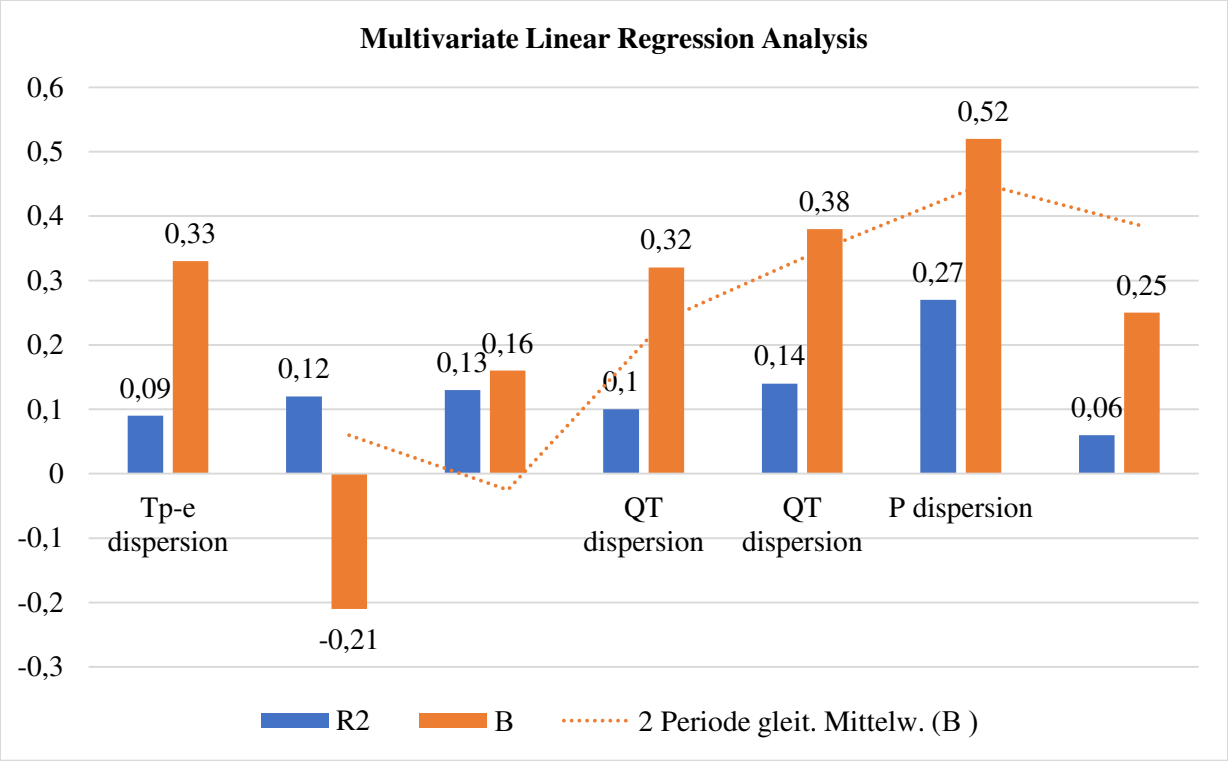


Table – III: Multivariate linear regression analysis of variable influencing electrocardiographic parameters in the patient and control groups

Multivariate Linear Regression Analysis		R^2	B	Confidence Interval (95%)	P-value
Tp-e dispersion	**HbA1c**	0.09	0.33	0.15-0.42	<0.001
	LDL	0.12	-0.21	-0.02 - 0.03	0.01
	Systolic blood pressure	0.13	0.16	0.001-0.05	0.04
QT dispersion	**HbA1c**	0.1	0.32	0.17-0.47	<0.001
QT dispersion	**HbA1c**	0.14	0.38	3.2-7.4	<0.001
P dispersion	**HbA1c Tp-e/QT**	0.27	0.52	0.36-0.62	<0.001
	HbA1c	0.06	0.25	0.002-0.009	0.001



DISCUSSION:

In numerous CVD & non – CVD illnesses, QTc, QTd & QT interval are increased in healthy patients [11]. About diabetic autonomic dysfunction it is known that it effects CVD system and research efforts have observed about QTc, QTd and QT interval were extended in such cases [5, 6 & 12]. Furthermore, the relation between QT prolongation and sudden cardiac deaths is associated to diabetic autonomic neuropathy [13].

Reliability of such parameters have been studies in the recent years which indicate ventricular arrhythmogenesis. Furthermore, T p-e dispersion, T p-e interval, T p-e/QTc and T p-e / QT proportions are novel markers of the trans-myocardial repolarization. However, the reliability is also affected by heart rate and body weight [9, 14]. Atherosclerosis increased is caused by endothelial dysfunction, hypercoagulability, diabetic dyslipidemia, enlarged platelet adhesion, impaired fibrinolysis, autonomic neuropathy, oxidative stress and hyperglycemia toxic effects in T2D cases [15]. Although pathophysiological mechanism in T2D cases is not completely established, risk of ventricular arrhythmia and atrial fibrillation is increased; that may be attributed to structural abnormalities due to increased fibrosis and prolonged hyper-glycemia in ventricular and atrial myocardium [16, 17].

Ventricular arrhythmias formation can be explained through reentry circuits, increased autonomy and triggered activity. Favorable environment about the micro-reentry circuits formation is caused by myocardial fibrosis (living myocardial tissue cell loss and myocardial conduction). Ventricular arrhythmias (simple ventricular extra systole to severe ventricular tachycardia) can be initiated by impaired electrical heart balance and because of an increased in the sympathetic system [18, 19]. We observed that Tp-e dispersion, Tp-e interval, Tp-e/QTc and Tp-e/QT ratios were prolonged in diabetic cases against control group. Positive association was observed through multivariate linear regression analysis between P dispersion and HbA1c, QTd, Tp-e dispersion, QTcd, Tp-e/QTc and Tp-e/QT ratios; whereas, systolic blood pressure and LDL level were linked with Tp-e dispersion.

Tokatli et al. included 43 T2D cases and showed higher Tp-e/QT, Tp-e interval and Tp-e/QTc in patients than controls [20]. Moreover, positive correlation between glucose, HbA1c and these parameters was observed through Pearson correlation analysis. We also included Tp-e dispersion that showed cardiac risk predictor as (HbA1c). We also observed a positive association among LDL, systolic blood pressure and Tp-e dispersion. Clemente et al. observed Tp-e dispersion as a novel investigative marker which was high in T2D cases that can be compared with our outcomes [21].

Atrial fibrillation can be caused by T2D incidence [22]. An important and noninvasive indicator is Pd for intra trial conduction heterogeneity which forms reentry substrate (atrial fibrillation pathophysiological mechanisms) [23, 24]. In Type I and II diabetes Pd was observed high in diabetic cases than controls [22, 25]. We observed increased Pd and PW duration in T2D cases than controls. Additionally, a positive association between Pd and HbA1c was also observed through "multivariate linear regression analysis". We may also say that with an increase in HbA1c, Pd also increases with an increase in the atrial fibrillation risk.

CONCLUSION:

We can predict arrhythmia risk through the assessment of T p-e interval, T p-e / QT, T p-e dispersion and (T p-e / QTc) proportions, through the suggestion of ventricular repolarization heterogeneity, P-wave & Pd reflecting atrial repolarization heterogeneity in T2DM cases.

REFERENCES:

1. Clemente D, Pereira T, Ribeiro S. Ventricular repolarization in diabetic patients: characterization and clinical implications. Arq Bras Cardiol. 2012;99(5):1015-1022. doi:10.1590/S0066-782X2012005000095.
2. Bissinger A, Grycewicz T, Grabowicz W, Lubinski A. The effect of diabetic autonomic neuropathy on P-wave duration, dispersion and atrial fibrillation. Arch Med Sci.2011;7(5):806-812. doi: 10.5114/aoms.2011.25555.
3. Dilaveris PE, Gialafos EJ, Andrikopoulos GK, Richter DJ, Papanikolaou V, Poralis K, et al. Clinical and electrocardiographic predictors of recurrent atrial fibrillation. Pacing Clin Electrophysiol. 2000;23(3):352-358, doi: 10.1111/j.1540-159. 2000.tb06761. x.
4. 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(5):733-738. doi: 10.1016/S0002-8703(98)70030-4.
5. Yazici M, Ozdemir K, Altunkeser BB, Kayrak M, Duzenli MA, Vatankulu MA, et al. The effect of diabetes mellitus on the P-wave dispersion. Circ J. 2007;71(6): 880-883.doi: 10.1253/circj.71.880.
6. Cox AJ, Azeem A, Yeboah J, Soliman EZ, Aggarwal SR, Bertoni AG, et al. Heart rate-corrected QT interval is an independent predictor of all-cause and cardiovascular mortality in individuals with type 2 diabetes: Diabetes Heart Study. Diabetes Care. 2014;37(5): 1454-1461.doi: 10.2337/dc13-1257.
7. Li Z, Hertervig E, Carlson J, Johansson C, Olsson SB, Yuan S. Dispersion of refractoriness in patients with paroxysmal atrial fibrillation: Evaluation with simultaneous endocardial recordings from both atria. J Electrocardiol. 2002;35(3):227-234. doi: 10.1054/jelc.2002.33973.
8. Ozdemir R, Guzel O, Kucuk M, Karadeniz C, Yılmaz U, Calik T, et al. The impact of 3:1 ketogenic diet on cardiac repolarization changes in children with refractory seizures: A prospective follow-up study. Neuropediatrics.2016;47(3):157-161. doi: 10.1055/s-0036-1582139.
9. 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(6): 567-574.doi: 10.1016/j.jelectrocard.2008.07.016.
10. Ozdemir R, Isguder R, Kucuk M, Karadeniz C, Ceylan G, Katipoglu N, et al. A valuable tool in predicting poor outcome due to sepsis in pediatric intensive care unit: Tp-e/QT ratio. J Trop Pediatr. 2016;62(5):377-384. doi: 10.1093/tropej/fmw021.
11. Okin PM, Devereux RB, Howard BV, Fabsitz RR, Lee ET, Welty TK. Assessment of QT interval and QT dispersion for prediction of all-cause and cardiovascular mortality in American Indians. Circulation. 2000;101(1):61-66. doi: 10.1161/01.CIR.101.1.61.
12. Veglio M, Chinaglia A, Cavallo PP. QT interval, cardiovascular risk factors and risk of death in diabetes. J Endocrinol Invest. 2004;27(2):175-181. doi: 10.1007/BF03346265.
13. Eranti A, Kerola T, Aro AL, Tikkanen JT, Rissanen HA, Anttonen O, et al. Diabetes, glucose tolerance, and the risk of sudden cardiac death. BMC Cardiovasc Disord.2016;24(16):51. doi: 10.1186/s12872-016-0231-5.
14. Shimizu M, Ino H, Okeie K, Yamaguchi M, Nagata M, Hayashi K, et al. T-peak to T-end interval may be a better predictor of high-risk patients with hypertrophic cardiomyopathy associated with a cardiac troponin Imputation than QT dispersion. Clin Cardiol. 2002;25(7):335-339. doi: 10.1002/clc.4950250706.
15. Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati FL, Powe NR, et al. Meta-Analysis: Glycosylated Hemoglobin and Cardiovascular Disease in Diabetes Mellitus. Ann Intern Med. 2004;141(6):421-431. doi: 10.7326/0003-4819-141-6-200409210-00007.
16. Mandala S, Di TC. ECG Parameters for

Malignant Ventricular Arrhythmias: A Comprehensive Review. J Med Biol Eng. 2017;37(4):441-453. doi: 10.1007/s40846-017-0281-x.

17. Kato T, Yamashita T, Sekiguchi A, Sagara K, Takamura M, Takata S, et al. What are arrhythmogenic substrates in diabetic rat atria? J Cardiovasc Electrophysiol.2006;17(8):890-894. doi: 10.1111/j.1540-8167.2006.00528. x.
18. Piers SR, Everaerts K, Van der GRJ, Hazebroek MR, Siebelink HM, Pison LA, et al. Myocardial scar predicts monomorphic ventricular tachycardia but not polymorphic ventricular tachycardia or ventricular fibrillation in non-ischemic dilated cardiomyopathy. Heart Rhythm. 2015;12(10):2106-2114. doi: 10.1016/j.hrthm.2015.05.026.
19. Qu Z, Weiss JN. Mechanisms of ventricular arrhythmias: from molecular fluctuations to electrical turbulence. Annu Rev Physiol. 2015;77(1):29-55. doi: 10.1146/annurevphysiol-021014-071622.
20. Tokatli A, Kilicaslan F, Alis M, Yiginer O, Uzun M. Prolonged Tp-e interval, Tp- e/QT ratio and Tp-e/QTc ratio in patients with type 2 diabetes mellitus. Endocrinol Metab.2016;31(1):105-112. doi: 10.3803/EnM.2016.31.1.105.
21. Svensson AK, Svensson T, Kitlinski M, Almgren P, Engstrom G, Nilsson PM, et al. Incident diabetes mellitus may explain the association between sleep duration and incident coronary heart disease. Diabetologia. 2018;61(2): 331-341.doi: 10.1007/s00125-017-4464-3.
22. Kluppelholz B, Thorand B, Koenig W, Gala TH, Meisinger C, Huth C, et al. Association of subclinical inflammation with deterioration of glycaemia before the diagnosis of type 2 diabetes: the KORA S4/F4 study. Diabetologia.2015;58(10):2269-2277. doi: 10.1007/s00125-015-3679-4.
23. Beckman AJ, Creager AM, Libby P. Diabetes and atherosclerosis: Epidemiology, pathophysiology and management. JAMA.2002;287(19):2570-2580. doi: 10.1001/jama.287.19.2570.
24. Suys BE, Katier N, Rooman RP, Matthys D, De Beeck LO, Du Caju MV, et al. Female Children and Adolescents with Type1 Diabetes Have More Pronounced Early Echocardiographic Signs of Diabetic Cardiomyopathy. Diabetes Care.2004;27(8):1947-1953. doi: 10.2337/diacare.27.8.1947.
25. Ninkovic VM, Ninkovic SM, Miloradovic V, Stanojevic D, Babic M, Giga V, et al. Prevalence and risk factors for prolonged QT interval and QT dispersion in patients with type 2 diabetes. Acta Diabetologica. 2016;53(5):737-744. doi:10.1007/s00592-016-0864-y.