Prevalence and risk factors of prolonged QTc interval in type 2 diabetic patients; impact of the type of treatment and quality of glycemic control

V. Ninkovic[1], M. Dobric[2], DJ. Jakovljevic[3], S. Ninkovic[4], G. Bubanja[1], V. Miloradovic[4], D. Zivojinovic[1], M. Babic[1], B. Milovanovic[1], V. Giga[2]

(1) Specialistic Hospital "Merkur", the National Educational Centre for Diabetes, Vrnjacka Banja, Serbia

(2) Clinic of Cardiology, Clinical Centre of Serbia, University of Belgrade, Belgrade, Serbia

(3) Newcastle University, Medical School, Institute for Ageing and Health, Newcastle upon Tyne, United Kingdom

(4) Clinical Centre Kragujevac, University of Kragujevac, Faculty of Medicine, Kragujevac, Serbia

Introduction: A prolonged heart rate-adjusted QT (QTc) interval is considered a risk factor for malignant arrhythmias and sudden cardiac death. The aim of this study was to assess the prevalence and predictors of prolonged QTc interval in patients with type 2 diabetes (T2D).
Methods: This study included 501 T2D patients treated in National Educational Centre for Diabetes, Specialistic Hospital (SH) "Merkur", Vrnjacka Banja, Serbia, from September 2011 to July 2012 (table 1). We analysed baseline clinical and laboratory data including: age, gender, duration of diabetes, body mass index, presence of coronary artery disease (CAD), presence of polyneuropathy, type of treatment, renal function, and the presence of traditional risk factors for CAD. In all patients 6-8 blood samples were taken within 24 h and following parameters of glycoregulation were analysed: fasting blood glucose (FBG), mean value of blood glucose (MBG), and mean amplitude of glucose excursion (MAGE), as well as HbA1c (table 2). In baseline ECG QT interval was measured using digital ruler. Heart rate corrected QT interval (QTc) was calculated using Bazett's formula, considering QTc> 440 msec as prolonged, and QTc> 500 msec as significantly prolonged.

Table 1. Basic clinical and demographic characteristics of diabetic type 2 population treated in SH „Merkur", Vrnjacka Banja

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Characteristics	All Patients
Number of Patients	501
Female	224
Age	60.4±8.1(years)
Mean diabetes duration	9.9±6.8 (years)
Hypertension	394
Coronary artery disease	114
Chronic kidney disease	43

Table 2. The observed variables and their definition

Varaible	Definition
Age	
Sex	
Diabetes duration	
Body mass index	
Hypertension	The values of SBP/DBP≥140/90 mmHg in two measurements or on antihypertensive treatment
Actual TA (systolic, diastolic)	
Coronary artery disease	Previous ACS, CABG, PCI, positive coronarography findings, positive exercise stress test, typical effort angina, or Minnesota code 1.1 and 1.2 in ECG tracings.
Chronic kidney disease	eGFR<60 ml/min/1.73 m^2 (MDRD)
CVA (ishaemic, haemorhagic, TIA)	
Smoking (actual, former)	
Distal symetric polyneuropathy	Positive EMNG findings or symptomps and signs compatible with polyneuropathy, including determination of vibratory perception threshhold
Retinopathy (nonproliferative, proliferative)	
Type of treatment (Sulfonilurea, metformin, insulin, and combination)	
HbA1c, Fasting blood glucosae, Mean blood glucosae	
MAGE	Arithmetic mean of absolute diferences of peak and subsequent nadir of glucosae values in daily profile of glycemia , while only diferneces >1SD of mean value of glycemia are taken into account

Results: Prolonged QTc (>440 msec) was present in 44% (221) of our patients, however, prolongation of QTc > 500 msec was observed in only 2% (10) of patients. QTc duration >440 ms was associated in univariable analysis with age, female gender, treatment with sulfonylurea, and different parametres of glycemic control (HbA1c, FBG, MBG, and MAGE), as well as with the history of CAD and presence of diabetic polyneuropathy (table 3). However, MBG (B=2.192, p<0.001), female gender (B=8.844, p<0.001), history of CAD (B=8.636, p=0.001), and treatment with sulfonylurea (B=5.198, p=0.027) remained independently associated with QTc > 440 ms in multivariable analysis (table 4). On the other hand, QTc **>** 500 msec was independently related only to the history of CAD and MBG (OR=12.145, 95% CI 1.818 – 81.146 and OR=1.457, 95% CI 1.154 – 1.840, respectively, p<0.001 for both) (table 5).

Table 3. Predictors of QTc>440 ms-univariable analysis

Varible	B	p
Age	0.427	0.002
Female sex	10.724	<0.001
Treatment with sulfonilurea	5.707	0.012
Coronary artery disease	10.508	<0.001
Polineuropathy	7.335	0.004
HbA1c	2.660	0.002
Fasting blood glucosae	1.763	<0.001
MAGE	1.463	0.009
Mean blood glucosae	2.168	<0.001

Table 4. Predictors of QTc>440 ms-multivariable analysis

Variable	B	p
Mean blood glucosae	2.192	<0.001
Female sex	8.844	<0.001
Coronary artery disease	8.636	0.001
Treatment with sulfonilurea	5.198	0.027

Table 5. Predictors of QTc>500 ms-multivariable analysis

Variable	OR (95% CI)	p
Coronary artery disease	12.145 (1.818-81.146)	<0.001
Mean blood glucosae	1.457 (1.154-1.840)	<0.001

Conclusions: Prolonged QTc was highly prevalent with 44% of our T2D patients demonstrating QTc>440 msec. However, significantly prolonged QTc of >500 msec, which is clearly associated with risk of malignant arrhythmias, was indentified in only 2% of our patients, and was independently related to the mean blood glucose and the history of CAD.