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The Effects of Metabolic Syndrome on TpTe Interval and TpTe/QT Ratio in Patients with Normal Coronary Arteries

Normal Koroner Artere Sahip Hastalarda Metabolik Sendromun TpTe Aralığına ve TpTe/QT Oranına Etkisi

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Abstract

Objective: T wave peak to T wave end (TpTe) interval and TpTe/QT have been accepted as predictors of ventricular arrythmia. In this study our aim is to investigate the effect of metabolic syndome on these parameters in patients with angiographically normal coronary arteries.

Materials and Methods: Thirty patients with metabolic syndrome (4 male, mean age 52±7.8 years) and twenty patients without metabolic syndrome as control group (8 male, mean age 54±9.3 years) were included. TpTe interval and TpTe/QT ratio were measured from the 12-lead electrocardiogram. These parameters were compared between the groups

Results: When compared with to the control group the systolic and diastolic blood pressure, pulse pressure, waist circumference, triglyceride and fasting plasma glucose levels were higher and HDL cholesterol level was lower in the metabolic syndrome group. In the analysis of electrocardiography, QT dispersion (QTd) and corrected QTd were significantly increased in metabolic syndrome group as compared to the controls group (44±14 versus 30±12 ms and 433±10 versus 405±4 ms, all p value p=0.01). TpTe interval and TpTe/QT ratio were also significantly higher in patient with metabolic syndrome (112±10 versus 91±10 ms and 0.25±0.02 versus 0.22±0.01, all p value p=0.01).

Conclusion: According to these results, we supposed that TpTe/QT ratio and TpTe interval is prolonged and those patients with metabolic syndrome may be at greater risk of ventricular arrhythmias.

Key Words: TpTe/QT ratio, arrhytmia, metabolic syndrome

Özet

Amaç: T dalgası sonu ile pik T dalga (TpTe) aralığı ventriküler aritmi belirleyicileri olarak kabul edilmiştir. Bu çalışmada amacımız anjiyografik olarak normal koroner arterleri olan hastalarda bu parametreler üzerine metabolik sendromun etkisini araştırmaktır.

Gereç ve Yöntem: Metabolik Sendromlu 30 hasta (4 erkek, ort. yaş 52±7,8 yıl) ve kontrol grubu olarak metabolik sendromu olmayan 20 hasta (8 erkek, ort. yaş 54±9,3 yıl)dahil edildi. TpTe aralığı ve TpTe/QT oranı 12 kablolu elektrokardiyogram ile ölçüldü. Bu parametreler gruplar arasında karşılaştırıldı.

Bulgular: Kontrol grubu ile kıyaslandığında metabolik sendrom grubunda sistolik ve diyastolik kan basıncı, nabız basıncı, bel çevresi, trigliserid ve açlık glukoz düzeyleri daha yüksek, HDL kolesterol düzeyleri düşüktü. Elektrokardiyogram analizlerinde QT dispersiyonu (QTd) ve düzeltilmiş QTd metabolik sendrom grubunda kontrol grubu ile kıyaslandığında anlamlı derecede artmış bulundu (44±14 ms karşı 30±12 ms ve 433±10 karşı 405±4 ms, tüm p değeri p=0,01). TpTe aralığı ve TpTe/QT oranı metabolik sendromlu hastalarda anlamlı derecede yüksekti (112±10 karşı 91±10 ms and 0,25±0,02 karşı 0,22±0,01, tüm p değeri p=0,01).

Sonuç: Bu sonuçlara göre, metabolik sendromu olan hastalarda TpTe/QT oranı ve TpTe aralığının uzadığını ve bu hastaların ventriküler aritmi bakımından daha fazla risk altında olabileceğini varsaymaktayız.

Anahtar Kelimeler: TpTe/QT oranı, aritmi, metabolik sendrom

Introduction

Metabolic syndrome (MetS) has been an increasing health problem worldwide for the last three decades [1]. It is a clustering of cardiovascular risk factors consisting of abdominal obesity, hypertension, atherogenic dyslipidemia, hyperglycemia, and prothrombotic and proinflammatory conditions [2].

Prolonged cardiac repolarization is associated with susceptibility to ventricular tachyarrhythmia, usually in the form of *torsades de pointes*, which can degenerate into life-threatening arrhythmias such as ventricular fibrillation [3].

Myocardial repolarization has been evaluated using various methods including QT dispersion (QTd), corrected QT dispersion (cQTd) and transmural dispersion of repolarization. QT interval remains the most widely

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used index for assessing the propensity to ventricular arrhythmias [4].

In these days, new indexes such as T wave peak to T wave end (TpTe) interval and the TpTe/QT ratio have been suggested to be a more accurate measure for the dispersion of ventricular repolarization compared to QTd and cQTd that are independent of alterations in heart rate [5].

Despite the fact that previously ventricular repolarization was evaluated by using QT interval measurements in patients with MetS [6], the novel repolarization indices are presumed to be TpTe interval and the TpTe/QT ratio is not studied yet in these patient groups.

In this study, we aimed to evaluate the repolarization dispersion measuring TpTe interval and TpTe/QT ratio in the 12- lead surface electrocardiogram (ECG) in the patients with MetS and normal coronary arteries at angiography.

Materials and Methods

The study was approved by the Hospital Ethics Committee (20 January 2009, approval number: 2009–1/67). Between 2009 and 2010, the patients, who underwent coronary angiography in Department of Cardiology, patients with MetS and normal coronary arteries were included in the study. For this retrospective study, the data were obtained from archive files. They were all diagnosed with MetS in accordance with the criteria established in the 3rd report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment in Asian population (Adult Treatment Panel III) as the presence of three or more of the following risk factors [7]: waist circumference (WC) >88 cm in women or >102 cm in men, triglycerides (TG) ≥150 mg/dL, high-density lipoprotein (HDL-c) <50 mg/dL in women or <40mg/dL in men, blood pressure (BP) ≥130/85 mmHg, fasting blood glucose (FBG) ≥110 mg/dL.

The blood pressure records of the patients were noted. The patients having a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg and those taking antihypertensive drugs were accepted as hypertensive. The patients using oral antidiabetic drugs or insulin or those having two measurements of fasting blood glucose level ≥126 mg/dL were accepted as diabetic.

Patients with CAD, chronic renal failure, chronic liver disorders, chronic lung disease, moderate or severe valvular heart disease, diabetes mellitus, congenital heart disease, left ventricular systolic dysfunction on echocardiography, recent acute coronary syndrome, anemia, pregnancy, obstructive sleep apnea, secondary hypertension, hematological disorders, known malignancy, hypercholesterolemia, electrolyte imbalance, bundle branch block, atrioventricular conduction abnormalities on ECG and ECGs without clearly analyzable QT segment were excluded from the study. All of the patients were in sinus rhythm and none of them were taking medications such as antiarrhythmics, tricyclic antidepressants, antihistamines and antipsychotics.

All patients had angiographically normal coronary arteries. Angiographic findings were reviewed by three invasive cardiologists not blinded to reports. Normal coronary angiogram was defined as absence of any visible angiographic sign of atherosclerosis and thrombosis.

Height, weight, blood pressures, clinical and laboratory analysis results were obtained from the files. Fasting plasma glucose, serum triglycerides (TG), serum total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and thyroid stimulating hormone (TSH) were tested using an auto biochemistry instrument. Plasma fasting insulin level was tested by radioimmunoassay. Body mass index (BMI) was calculated as weight in kilograms dividing by height squared in meters (kg/m^2). Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as insulin reading (μIU/mL) multiplied by plasma glucose level (mmol/L) and diving by 22.5 [8].

Echocardiography

A Vivid 7 pro echocardiographic unit (Vivid Seven, GE Vingmed Ultrasound, Horten, Norway) with 3.5 MHz probe was used. Echocardiographic study was performed in left lateral decubitus position. According to the recommendation of the American Echocardiography Association, left ventricular end-diastolic (LVEDD) and left ventricular end-systolic dimensions (LVESD) were measured. We used the Teichholz method to determine the left ventricular ejection fraction [9].

Electrocardiography

For analysis of the electrocardiographic parameters, lead II was recorded at a paper speed of 50 mm/s (Nihon Kohden, Tokyo, Japan) the rest was used in the supine position. QT interval and TpTe interval were measured manually. The QT interval was defined as extending from the beginning of the QRS complex to where T waves descend onto the isoelectric baseline [6].

When a U wave interrupted the T wave before returning to baseline, the QT interval was measured to the nadir of the curve between the T and U waves. The QTc interval was calculated using the Bazett formula: QTc (ms)=QT measured/√RR (sec). Extended QTc interval was defined as a duration of >440 ms. The QT dispersion (QTd) value was determined as the difference between the longest and shortest QT intervals observed from the 12 ECG leads [10].

The TpTe interval was defined as the interval from the peak of T wave to the end of T wave. Measurements of TpTe

Table 1. Comparison of biochemical and echocardiographic variables in MetS Patients and Healthy Controls

	MetS group (n=30)	Control group (n=20)	P
Age (years)	52±7.8	54±9.3	NS
Gender (male/female)	4/26	8/12	p=0.044
BMI (kg/m^2)	31.6±4.6	27.9±4.5	p=0.003
Waist circumference (cm)	102±11.7	92.7±6	p=0.005
Smoking (%)	36.7	30	NS
Glucose (fasting)(mg/dL)	104.1±18	83.5±4.9	p<0.001
TC (mg/dL)	222.4±45.2	205.6±57.1	NS
HDL-C (mg/dL)	43.1±7.5	52.4±12.2	p<0.001
LDL-C (mg/dL)	135.8±37.5	134.3±49.9	NS
TG (mg/dL)	216.7±94.6	107.8±27.2	p<0.001
HOMA-IR	2.96±2	1.5±8	p=0.007
TSH (mIU/mL)	1.42±0.53	1.40±0.44	NS
LV ejection fraction (%)	63.4±7.5	62.2±6.5	NS
LVEDD (mm)	49.1±3.5	46.7±3.7	NS
LVESD (mm)	31±1.3	30±0.8	NS
Heart rate (beats/min)	75±8	73±7	NS
Systolic blood pressure (SBP)(mmHg)	136.3±14	109.5±6.8	p<0.001
Diastolic blood pressure (DBP)(mmHg)	80±10.5	70±5.1	p=0.04

BM: body mass index; TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; HOMA-IR: homeostasis model assessment of insulin resistance; LVEDD: left ventricular end diastolic diameter; LVESD: left ventricular end systolic diameter; EF: ejection fraction; Data are presented as means±SD.; NS: nonsignificant

interval were performed using the precordial leads [11]. The TpTe/QT ratio was calculated using these measurements.

Statistical analysis

Statistical Package for Social Sciences for Windows 16.0 was used for statistical analyses. We expressed variables as mean values with standard deviations. Mean values of continuous variables were compared between groups using the Student T test or Mann–Whitney U test, according to whether normally distributed or not, as tested by the Kolmogorov–Smirnov test. The chi-square test was used to assess differences between categorical variables. We accepted p<0.05 values as statistically significant for our analyses in our study.

Results

30 patients with MetS (4 male, mean age 52±7.8 years) and 20 patients without MetS serving as control group (8 male, mean age 54±9.3 years) were included. A summary of biochemical and clinical characteristics according to the presence of the MetS is shown in Table 1. MetS group had higher levels of BMI, waist circumference, HOMA-IR, serum TG and fasting glucose, as well as lowered HDL levels than control subjects. In the group with MetS, systolic pressures and diastolic pressure were higher than control group (Table-1). ECG parameters of the groups are shown in Table 2. The QTc, QTd, TpTe intervals and TpTe/QT ratio were significantly increased in MetS group compared to the control group (all p=0.01, Table 2).

Discussion

MetS is one of the major public health problems worldwide because of its frequency. Individuals with MetS are at increased risk for cardiovascular heart disease [12]. A prolonged QT interval reflects the myocardial refractoriness and electrical instability of myocardium and has been associated with adverse cardiovascular outcomes including ventricular fibrillation and sudden death [13]. A recent study demonstrated that MetS was associated with increased QTd [14].

Table 2. Comparison of electrocardiographically features of MetS Patients and Healthy Controls

	MetS patients (n=30)	Control (n=20)	p
QT interval (ms)	410±28	398±33	NS
QTc interval (ms)	433±10	405±4	p=0.01
QTd interval (ms)	44±14	30±12	p=0.01
TpTe interval (ms)	112±10	91±10	p=0.01
TpTe/QT ratio	0.25±0.02	0.22±0.01	p=0.01

QTc: corrected QT; QTd: QT dispersion; TpTe: T wave peak to T wave end; Data are presented as means±SD; NS: nonsignificant

In the study of Soydinc et al. QTc and QTd was significantly increased in patients with uncomplicated MetS when compared to the subjects without MetS [15]. Similarly, in our study, we found QTc and QTd increased in patients with MetS and normal coronary arteries.

Insulin resistance is reported to have a crucial role in MetS. Hyperinsulinemia has been reported to increase QTc and QTd in healthy subjects [16]. In our opinion, one of the reasons of the increased QTc and QTd is possibly due to insulin resistance.

The TpTe interval and TpTe/QT ratio have emerged as novel electrocardiographic markers of increased dispersion of ventricular repolarization [5]. Increased dispersion of repolarization between the base and apex of the heart intramurally or in the region of interventricular septum predisposes to ventricular arrhythmias, especially in the presence of ion channel diseases including long QT syndrome, short QT syndrome, Brugada syndrome, and polymorphic catecholaminergic ventricular tachycardia [17, 18]. TpTe also increased in acute coronary syndrome including ST- and non–ST-elevation myocardial infarction [19].

These markers may be used as an electrocardiographic index of ventricular arrhythmogenesis and sudden cardiac death [11]. We demonstrated in our study that both the TpTe interval and TpTe/QT ratio are higher in patients with MetS.

Our results showed that the association between the TpTe interval and TpTe/QT ratio with MetS denotes that cardiac repolarization abnormalities might exist not only in diabetic and ischemic patients with MetS but also they may be present in healthy subjects with MetS. Perhaps, the insulin resistance that increases cell membrane refractoriness and induces hypokalemia is the mainstay of the mechanism of the impairment of cardiac repolarization in patients with MetS. Beside the QTc and QTd, the TpTe interval and TpTe/QT ratio should be investigated for ventricular arrythmogenicty in patients with MetS.

To our knowledge, there is no study available in the literature about the association between the metabolic syndrome and TpTe interval, TpTe/QT ratio.

The most important limitation of our study is that we based normal coronary artery definement on angiographic findings. Due to lack of information obtained by coronary angiography compared to intravascular US, the intravascular US performing may be more appropriate in our study. The second important limitation is the small number of patients in both groups. Another limitation is the fact that we did not assess the association between ventricular arrhythmias with the TpTe interval and TpTe/QT ratio. Also, the study population was not followed-up prospectively for ventricular arrhythmic episodes. Further studies are required to determine the relation between the TpTe interval and TpTe/QT ratio and ventricular arrhythmia in MetS. In conclusion, our study revealed that the TpTe interval and TpTe/QT ratio had increased in patients with MetS. The TpTe interval and TpTe/QT ratio should be measured in healthy subjects with MetS in order to investigate the probability of ventricular arrhythmia. We believe that these variables may have clinical impact in the field of MetS in healthy subjects.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Uludag University Medical Faculty/ 2009-1/67.

Informed Consent: Informed consent was obtained from the participants who participated in this study.

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