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Evaluation of Tp-e/QTc Ratio in Obesity

Obezitede Tp-e/QTc Oranının Değerlendirilmesi

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ABSTRACT

Aim: We aimed to detect simple findings that might predict sudden cardiac death in electrocardiography recordings in obese patients.

Materials and Methods: Patients were included in our study retrospectively. Two groups with body mass index (BMI) ≥30 kg/m^2 (Group 1) and BMI <30 kg/m^2 (Group 2) were sampled from the study population with similar baseline characteristics, biochemical and echocardiographic features. Ventricular repolarization parameters were compared between the two groups. The Tp-e interval was defined as the period of time between the T waves' peak and their end. Tp-e/QTc ratio was calculated.

Results: This study included 190 participants. There were no differences between the two groups in terms of age (p=0.42), diabetes (p=0.238), hypertension (p=0.877), smoking (p=1.000), medical treatment used, laboratory parameters, left ventricular ejection fraction (p=0.673), and left ventricular mass index (p=0.089). The QTc interval was similar between the groups (416.4±11.6 ms, and 422.1±14.8 ms; p=0.081). Tp-e, and Tp-e/QTc ratio were greater in Group 1 (93.1±6.2 ms, and 67.7±2.5 ms; p=0.00; 0.22±0.02, and 0.15±0.01; p=0.001). Twelve months after the first examinations, six deaths were noted in the obese group (p=0.001).

Conclusion: Our study results showed that the Tp-e interval and Tp-e/QTc ratio were significantly increased, and sudden cardiac death was more common in patients with BMI ≥30 kg/m^2.

Keywords: Arrhythmias, ventricular tachycardia, electrocardiography, sudden cardiac death, Tp-e interval, Tp-e/QTc

ÖZ

Amaç: Obez hastalarda elektrokardiyografi kayıtlarında ani kardiyak ölümü öngörebilecek basit bulguları saptamayı amaçladık.

Gereç ve Yöntem: Çalışmamıza hastalar retrospektif olarak dahil edildi. Hastalar vücut kitle indeksi (VKİ) ≥30 kg/m^2 (Grup 1) ve VKİ <30 kg/m^2 (Grup 2) olacak şekilde iki gruba ayrıldı. İki grup da benzer temel özelliklere, biyokimyasal ve ekokardiyografik özelliklere sahipti. İki grup ventriküler repolarizasyon parametreleri açısından karşılaştırıldı. Tp-e aralığı, T dalgasının zirvesi ile sonu arasındaki süre olarak tanımlandı. Tp-e/QTc oranı hesaplandı.

Bulgular: Çalışmaya 190 hasta dahil edildi. İki grup arasında yaş (p=0,42), diyabet (p=0,238), hipertansiyon (p=0,877), sigara kullanımı (p=1,000), kullanılan medikal tedavi, laboratuvar parametreleri, sol ventrikül ejeksiyon fraksiyonu (p=0,673), sol ventrikül kitle indeksi (p=0,089) açısından anlamlı fark saptanmadı. QTc aralığı gruplar arasında benzerdi (416,4±11,6 ms ve 422,1±14,8 ms; p=0,081). Tp-e ve Tp-e/QTc oranı Grup 1'de daha yüksekti (93,1±6,2 ms ve 67,7±2,5 ms; p=0,00; 0,22±0,02 ve 0,15±0,01; p=0,001). İlk muayenelerden 12 ay sonra obez grupta altı ölüm kaydedildi (p=0,001).

Sonuç: Çalışma sonuçlarımız VKİ ≥30 kg/m^2 olan hastalarda Tp-e aralığı ve Tp-e/QTc oranının anlamlı olarak arttığını ve ani kardiyak ölümün daha sık olduğunu gösterdi.

Anahtar Kelimeler: Aritmiler, ventriküler taşikardi, elektrokardiyografi, ani kardiyak ölüm, Tp-e aralığı, Tp-e/QTc

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INTRODUCTION

A higher incidence of cardiac arrhythmias and sudden cardiac death (SCD) has been associated with obesity[1]. The risk of arrhythmias rises with obesity. The most common arrhythmias with obesity are premature atrial and ventricular contractions, ventricular and supraventricular tachycardia[2]. Obese patients may experience cardiac arrhythmias due to hypoxia, hypercapnia, obstructive sleep apnea, electrolyte imbalances, coronary heart disease, elevated catecholamine levels, and left ventricular hypertrophy[3]. Repolarization in the myocardium can be assessed using variables including the QT interval, corrected QT interval, and QT dispersion. The Tp-e interval, the time interval between the T wave peak and the endpoint, is considered as the distribution index of repolarization. Compared to other measurements, the ratio of the Tp-e interval to the QT interval is considered a more accurate predictor of arrhythmogenesis. Tp-e/QT is unaffected by changes in heart rate and can be used as a reliable indicator[4-6]. This study aimed to evaluate the risk of arrhythmias in obese patients using the Tp-e interval and Tp-e/QT ratio.

MATERIALS AND METHODS

Study Population

Body mass index (BMI) was calculated with the formula of body weight in kilograms/height in meters squared. In Group 1, 44 men and 52 women with a BMI more than 30 kg/m^2 were included. Group 2 (BMI less than 30 kg/m^2) included 42 men and 52 women. A BMI of 18.5 to 24.9 kg/m^2 was regarded as the range for normal, and ≥30 kg/m^2 was considered obese.

Patients were classified as hypertensive if they were taking antihypertensive drugs or if blood pressure was ≥140/90 mmHg. Diabetes was defined as having fasting blood glucose more than 126 mg/dL or the use of anti-diabetic drugs or insulin. To rule out systemic disorders, blood biochemistry studies, medical histories of patients, and physical examinations were reviewed in each group. Patients with coronary artery disease, recent acute coronary syndrome, severe valvular disease, chronic renal failure, ventricular systolic dysfunction, electrolyte imbalance, and bundle branch block were excluded. None of the patients were on any antiarrhythmic, tricyclic antidepressant, antihistamine, or antipsychotic drugs, and all were in sinus rhythm.

Electrocardiography (ECG) and echocardiography procedures were performed at the first examination. Twelve months after the first examinations, the death status of the patients and the cause of death were noted with ID number interrogation. Ethical committee approval was received from the University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital Local Ethics Committee (approval no: 2022/03-18, date: 15.03.2022).

Electrocardiography

ECG was performed at 50 mm/s (Nihon Kohden, Tokyo, Japan). ECGs were taken using a 10-mm 1 mV calibration electrode. The patient's resting heart rate was calculated. The QT dispersion (QTd) refers to the difference between the maximal and minimal QT intervals in ECG[7]. QT duration and Tp-e were calculated using the precordial lead V5 in all patients. The Bazett formula was used to determine the QTc interval, calculated between the beginning of the QRS complex and the termination of the T wave and adjusted for heart rate. The Tp-e interval was defined as the period between the T waves' peak and their end. Precordial V5 ECG lead was used to measure the Tp-e interval. Calculations were made for the Tp-e/QTc ratio.

Echocardiography

The patients underwent echocardiographic evaluation (Philips EP-Q 7) and the calculation of each parameter involved average of three subsequent cycles. The left ventricular end-diastolic diameter, interventricular septal end-diastolic thickness, and left ventricular posterior and anterior wall end-diastolic thickness were measured from the left sternal margin, and apical four-chamber sections under M mode. Body surface area was calculated as [0.0061 × height (cm) + 0.0128 × body mass (kg) - 0.1529]. LV mass of patients was calculated with the Devereux formula.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) version 24.0 for Windows was used to perform the statistical analysis (SPSS Inc., Chicago, IL). The distribution of the variables was evaluated using the Kolmogorov-Smirnov test. Comparison of parametric data was performed using the Student's t-test, non-parametric variables were evaluated using the Mann-Whitney U test, and categorical variables were compared using the chi-square test. For non-parametric variables, the median (minimum-maximum) represents the data, but the mean and standard deviation are used for parametric variables. Statistical significance was defined as a p value of <0.05.

RESULTS

Data from patients in our study population of 321 patients were reviewed. Since the cardiac mass index is associated with mortality in obese patients, patients with similar cardiac mass index were included in the study and 79 patients were excluded from the study. Fifty two patients were excluded from the study to reduce confounding factors, and patients with similar basic clinical features and laboratory measurements were included in the study. As a result, 190 patients were included in the study.

The obese group included 96 patients and the mean age was 54.2±3 years. The control group included 94 patients and the mean age was 53.1±2 years. No significant difference was observed between the two groups in terms of antihypertensive medications, hypertension, age, gender distribution, diabetes mellitus, and smoking status (Table 1). Laboratory analyses of the groups except total cholesterol were similar. Total cholesterol level was significantly higher in the obese group (p=0.029) (Table 2). There were no significant differences in left ventricular dimensions and ejection fraction (p>0.05) (Table 2).

The ECG parameters are summarized in Table 3. The QTc interval was similar between the groups (416.4±11.6, and 422.1±14.8; p=0.081). Tp-e, and Tp-e/QTc ratios were greater in the obese group (93.1±6.2 ms, and 67.7±2.5 ms; p=0.00; 0.22±0.01, and 0.15±0.02; p=0.001). There was no difference in cardiac mass index between the two groups.

Twelve months after the first examinations, six deaths were noted in an obese group with ID number interrogation (p=0.001). The non-cardiac cause of death was not noted in the death reporting system.

DISCUSSION

The BMI ≥30 kg/m^2 group in our study had a higher Tp-e interval and Tp-e/QTc ratio. The literature review indicates

Table 1. Baseline characteristics of the patients

Baseline clinical features	Group 1 n=96	Group 2 n=94	p value
Age (years)	54.2±3	53.1±2	0.42
Sex (female), n (%)	52 (52)	52 (52)	1.000
Body mass index (kg/m^2)	35.6±2.5	22.3±1.5	0.001
Smoking, n (%)	5 (5)	5 (5)	1.000
Hypertension, n (%)	44 (45)	43 (44)	0.877
Diabetes mellitus, n (%)	24 (25)	17 (18)	0.238
Angiotensin-converting enzyme inhibitors, n (%)	31 (32)	33 (34)	0.564
Angiotensin receptor blockers, n (%)	11 (12)	11 (12)	0.912
Diuretics, n (%)	24 (25)	31 (33)	0.413
Calcium channel blockers, n (%)	10 (11)	5 (6)	0.198
Sudden cardiac death at 12 month, n(%)	6 (6)	0	0.001

Table 2. Biochemical and echocardiographic features

	Group 1	Group 2	p value
Fasting glucose, (mg/dL)	106.7±24.1	102.4±2.3	0.155
Creatinine, (mg/dL)	0.9±0.1	0.9±0.2	0.134
Total cholesterol, (mg/dL)	208.1±38.6	201.5±27.3	0.049
Hemoglobin, (g/dL)	13.4±1.4	12.5±1.1	0.625
Na, (mmol/L)	139.5±2.0	137.7±2.3	0.347
K, (mmol/L)	4.4±0.4	4.5±0.5	0.350
Ca, (mg/dL)	9.8±0.5	9.7±0.4	0.097
Mg, (mg/dL)	2.0±0.2	2.0±0.1	0.452
TSH, (mIU/mL)	1.8±0.8	1.7±0.8	0.511
AST, (U/L)	20.7±5.5	19.2±5.0	0.761
ALT, (U/L)	20.9±7.3	20.2±7.1	0.432
LV ejection fraction, (%)	64.5±1.9	64.5±1.3	0.673
Left ventricular end-diastolic diameter, (mm)	48.0±1.5	47.2±2.1	0.249
Left ventricular end-systolic diameter, (mm)	29.3±1.1	27.8±1.2	0.837
LVPWT, (mm)	10.3±2.8	10.4±2.1	0.911
LVAWT, (mm)	11.2±2.3	10.1±1.8	0.892
LV mass index, (g/m^2)	92.2±9.2	89.4±8.5	0.089

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, TSH: Thyroid-stimulating hormone, LV: Left ventricular, LVPWT: Left ventricular posterior wall end-diastolic thickness, LVAWT: Left ventricular anterior wall end-diastolic thickness

Table 3. Electrocardiographic features

	Group 1	Group 2	p value
Heart rate, beats/min	74.2±7.1	73.2±9	0.064
QRS duration, ms	91.4±5.2	84.6±6.4	0.071
QT interval, ms	363.2±18.8	379.2±14.4	0.591
QTc interval, ms	416.4±11.6	422.1±14.8	0.081
Tp-e, ms	93.1±6.2	67.7±2.5	0.001
Tp-e/QTc ratio	0.22±0.01	0.15±0.02	0.001

that this study is the first to demonstrate how ventricular depolarization and repolarization are out of balance in obese individuals. The recording of three cardiac deaths in the obese group in the 12-month follow-up period in our study may suggest that ECG parameters may be clinically important in obesity.

Patients with morbid obesity have a higher risk of SCD before heart disease develops[8]. In SCD patients with anatomically normal hearts, obesity is a significant comorbidity[9]. The main causes of arrhythmia and SCD in obese people are cardiomyopathies, which include myocyte hypertrophy, mononuclear cell infiltration, abnormal cardiomyocyte lipid deposits, and cardiac fibrosis[10,11]. Fatty infiltration alters the parallel orientation of cardiac bundles; thus, affecting ventricular activation and leading to uneven repolarization[9]. Increased intracellular lipid content can cause ventricular tachycardia and abrupt cardiac death due to a decrease in potassium channel levels and impaired repolarization[12]. Adipocytokines from the epicardial fat of cardiomyocytes lengthen action potentials and increase triggered activity immediately after depolarization by decreasing delayed rectifier outward currents[13].

Premature ventricular contractions are common in obese patients, and this is unrelated to hypertension or concentric ventricular hypertrophy. Conduction system problems in obese people are uncommon[12]. The conduction system may play a part in sudden death in obese young people, according to a study by Bharati and Lev[14] These researchers have found enlarged and hypertrophied hearts, focal mononuclear cells in and around the conduction system, fibrosis of the left bundle branch and atrioventricular bundle, and fibrosis in the interventricular septum[15]. Patients who were mild to moderately obese had a higher amount of fibrosis/fat than those who were very obese. Because of the irregularities in sympathovagal balance, obese people have their heart rate variable between faster and lower, which is a factor increasing the risk of myocardial infarction and SCD[16]. Resting heart rate was higher in patients with BMI ≥30 kg/m^2 in our study.

Obese women who lost weight had a significantly shorter QTc interval and QT dispersion which was linked to a regression of ventricular hypertrophy. The risk of potentially lethal arrhythmias and sudden death may be reduced by shortening the QT interval and increasing the cardiac parasympathetic activity[16]. Three months following sleeve gastrectomy in patients with morbid obesity, the QT interval was shorter. The ventricular depolarization and repolarization periods are included in the QT and QTc intervals, and their lengthening is linked to malignant ventricular arrhythmias. The dispersion of QT and QTc represents electrical heterogeneity in the myocardium. These could be useful in predicting obesity in patients. QTc dispersion, a marker of a significantly increased risk of ventricular arrhythmia, is associated with obesity. Longer QT interval was linked to higher sympathetic and lower parasympathetic tone in obese people.

In normal and obese women, the QTc interval was associated with a free fatty acid level, and fatty infiltration could enhance the dispersions of action potential length, thus, increasing the chance of reentry circuits[11,16]. Plasma epinephrine and norepinephrine concentrations were all shown to be correlated with QTc intervals by Corbi et al.[16] suggesting that autonomic nervous system dysfunction may be the cause of prolonged QTc intervals in visceral obesity. The sympathetic nervous system is stimulated by higher plasma-free fatty acid levels.

Finally, it is possible to identify the elevated risk of unfavorable cardiovascular events linked to obesity using the Tp-e interval and Tp-e/QT ratio measurements. We discovered that obese patients had higher Tp-e intervals and Tp-e/QTc ratio than non-obese patients. Our findings, which point to higher ventricular repolarization heterogeneity in obese patients, may help us better understand the pathophysiological causes of the higher prevalence of arrhythmias. Prolonged transmural dispersion may explain the increased ventricular arrhythmia frequency.

Study Limitations

Patients could be followed with a long-term rhythm Holter or loop recorder for ventricular arrhythmic events. To assess the predictive ability of the longer Tp-e interval and higher Tp-e/QTc ratio in this population, large-scale prospective investigations are needed.

CONCLUSION

Obesity has a higher risk of ventricular arrhythmogenesis because obese patients have higher Tp-e/QTc ratio and longer Tp-e intervals. In the twelve-month follow-up, SCD was found to be higher in the obese group.

Ethics

Ethics Committee Approval: Ethical committee approval was received from the University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital Local Ethics Committee (approval no: 2022/03-18, date: 15.03.2022).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: M.K., Concept: A.D., Design: U.U., Ş.A., Data Collection or Processing: U.U., M.K., Analysis or Interpretation: C.A., A.D., Ş.A., Literature Search: A.D., Writing: U.U., C.A., A.D., M.K., Ş.A.

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