ORIGINAL ARTICLE

Medical Journal of Western Black Sea
Batı Karadeniz Tıp Dergisi

Med J West Black Sea 2024;8(2): 129-134
DOI: 10.29058/mjwbs.1397031

Evaluation of the Risk of Malignant Arrhythmia Through Electrocardiography Parameters in Patients with Urinary Stone Disease

Üriner Taş Hastalığı Olan Hastalarda Malign Aritmi Riskinin Elektrokardiyografi Parametreleri ile Değerlendirilmesi

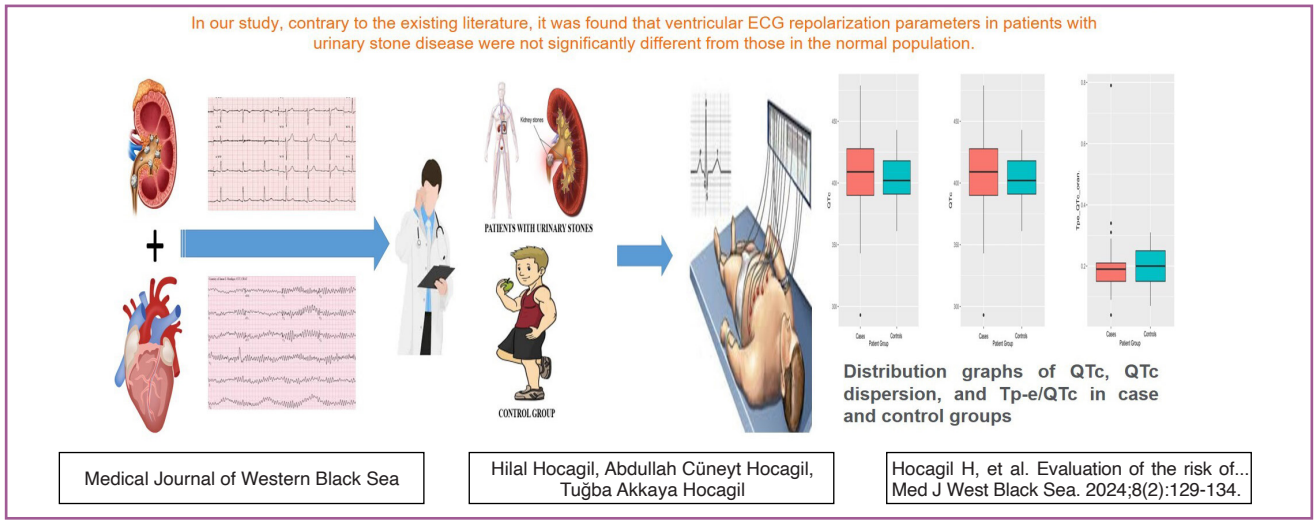
Hilal HOCAGİL[1], Abdullah Cüneyt HOCAGİL[1], Tuğba AKKAYA HOCAGİL[2]

[1]Zonguldak Bulent Ecevit University, School of Medicine, Department of Emergency, Zonguldak, Türkiye
[2]University of Waterloo, Department of Statistics and Actuarial Science, Postdoctoral Research Fellow, Ontario, Canada

ORCID ID: *Hilal Hocagil 0000-0001-7314-752X, Abdullah Cüneyt Hocagil 0000-0002-1675-9754, Tuğba Akkaya Hocagil 0000-0003-3603-4491*

Cite this article as: *Hocagil H et al. Evaluation of the risk of malignant arrhythmia through electrocardiography parameters in patients with urinary stone disease Med J West Black Sea. 2024;8(2):129-134.*

GRAPHICAL ABSTRACT



ABSTRACT

Aim: This prospective observational study aims to assess ventricular repolarization parameters using electrocardiography, which serve as risk markers for malignant arrhythmias in individuals diagnosed with urinary stone disease.

Material and Methods: A total of 178 participants were included in the study, comprising 118 patients with urinary system stone disease and 60 healthy volunteers. All patients underwent 12-lead electrocardiography. The electrocardiographys were evaluated for QTc interval, QTc dispersion, and Tp-e/QTc, and compared with the control group.

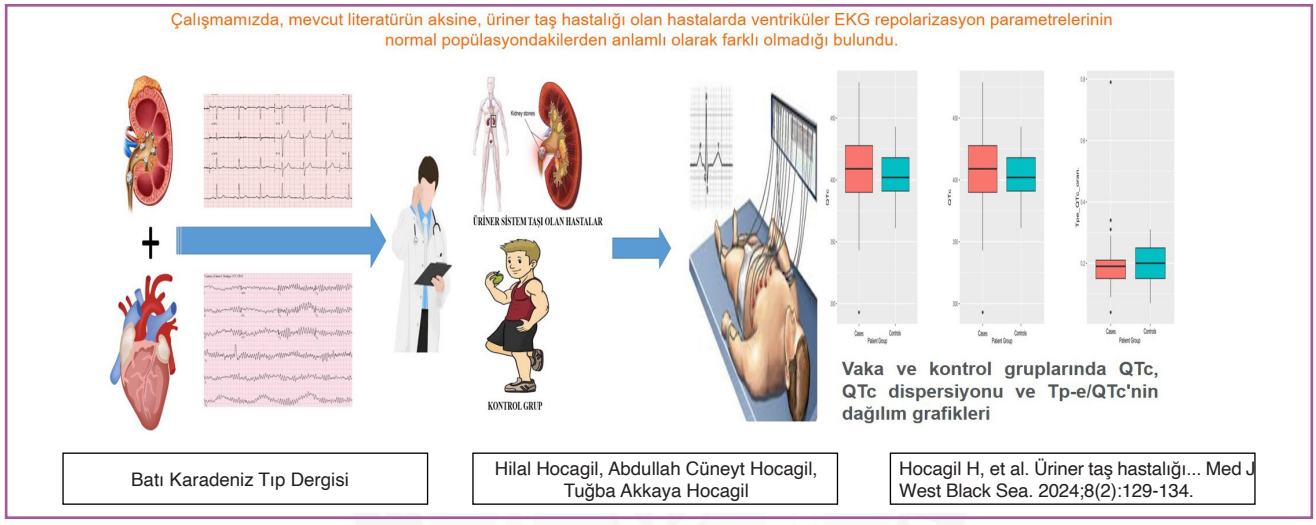
Corresponding Author: Hilal Hocagil ✉ drhocagil@gmail.com
Received: 28.11.2023 **Revision:** 17.07.2024 **Accepted:** 09.08.2024

Results: When comparing the QTc interval (406.0 ms to 413.0 ms), QTc dispersionand (41.7 ms to 40.0 ms) Tp-e/QTc (0.19 ms to 0.19 ms) results between the patient and healty control groups, no statistically significant difference was detected as a result of the comparison (p=0.233, p=0.663, p=0.077).

Conclusion: In our study, contrary to the existing literature, it was found that ventricular ECG repolarization parameters in patients with urinary stone disease were not significantly different from those in the normal population. The validity of this finding could be further investigated with larger case groups and longer-term studies. According to the findings of this research, we recommend that in the follow-up of patients with urinary stone disease, potential risk factors other than ECG parameters for malignant arrhythmias should also be examined.

Keywords: Electrocardiography parameters, risk of ventricular arrhythmias, risk of sudden cardiac death, urinary stone disease, malignant arrhythmia

GRAFİKSEL ÖZET



ÖZ

Amaç: Bu prospektif gözlemsel çalışma, üriner taş hastalığı olan hastalarda malign aritmiler için risk göstergesi olan ventriküler repolarizasyon parametrelerini elektrokardiyografi kullanarak değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntemler: Çalışmaya 118'i üriner sistem taş hastalığı olan, 60'ı sağlıklı gönüllülerden oluşan toplam 178 hasta dahil edildi. Tüm hastalara 12 derivasyonlu elektrokardiyografi çekimi yapıldı. Elektrokardiyografiler QTc aralığı, QTc dağılımı ve Tp-e/QTc açısından değerlendirilerek kontrol grubuyla karşılaştırıldı.

Bulgular: Hasta ve kontrol grupları QTc aralığı (406.0 ms'ye 413.0 ms) , QTc dağılımı (41,7 ms'ye 40,0 ms) ve Tp-e/QTc (0,19 ms'ye 0,19 ms) parametreleri karşılaştırıldı. İstatistiksel açıdan karşılaştırma sonucunda anlamlı bir fark tespit edilemedi (p=0,233, p=0,663, p=0,077).

Sonuç: Çalışmamızda, mevcut literatürün aksine üriner taş hastalığı olan hastalarda ventriküler EKG repolarizasyon parametrelerinin normal popülasyondan anlamlı derecede farklı olmadığı bulundu. Bu sonucun geçerliliği daha geniş vaka grupları ve daha uzun dönemli çalışmalarla araştırılabilir. Biz bu çalışmanın sonucuna dayanarak üriner taş hastalığı olan hastaların takibinde malign aritmiler ile ilgili EKG parametrelerinin yanında diğer potansiyel risk faktörlerinide incelemelerini öneririz.

Anahtar Sözcükler: Elektrokardiyografi parametreleri, ventriküler aritmi riski, ani kalp ölümü riski, üriner taş hastalığı, malign aritmi

INTRODUCTION

Urinary stone disease is a significant cause of comorbidity, with a lifetime prevalence of 10-15% and a recurrence rate reaching up to 50% within 10 years (1). Recently, it has become widespread knowledge that urinary system stone disease is not only confined to kidney stone development but is also linked to cardiovascular disease and a variety of other illnesses (2-4). The vascular endothelium is hypothesized to be damaged by urinary stone disease, leading to coronary artery disease (CAD) (5).

Sudden cardiac death and ventricular arrhythmias (malignant arrhythmias) are both caused by CAD. Although many studies have shown that urinary system stone disease is a risk factor for CAD, no electrocardiographic parameters have been evaluated in this patient group.

A prolonged QT interval, increased QT dispersion, and T peak-end (Tp-e) intervals on the electrocardiogram (ECG) can be used as noninvasive predictors of sudden cardiac death and ventricular dysrhythmia. The QT interval signifies the period during which the ventricles undergo both depolarization and repolarization, while QT dispersion reflects the variability in myocardial repolarization. Tp-e interval is recognized as an indicator of the dispersion of ventricular repolarization, and corrected QT (QTc) interval and QTc dispersion may be utilized to ensure that these parameters remain unaffected by heart rate (6-9). The Tp-e/QTc ratio is considered a more refined indicator of ventricular repolarization and the potential for arrhythmia (10).

In this study, we aimed to assess the ECG to assess ventricular repolarization parameters, including QTc interval, QTc dispersion, Tp-e interval, and Tp-e/QTc, which are risk indicators for malignant arrhythmias in patients with urinary stones.

MATERIAL and METHODS

This study was carried out as a prospective observational investigation at Zonguldak Bülent Ecevit University, Department of Emergency Medicine, between February 2, 2016, and October 10, 2016. Patients diagnosed with urinary stone disease by abdominal computerized tomography and healthy volunteers were conducted in our study. This study included 178 adults, including 118 patients with urinary tract stones and 60 healthy volunteers. Patients' age, gender, height, weight, cigarette and alcohol consumption were recorded. All patients in the study had their 12-lead ECG recorded using the same device at a rate of 25 mm/sec and an amplitude of 10 mm/mV. The ECGs were evaluated for QTc interval, QTc dispersion, Tp-e interval, and Tp-e/QTc and checked with the control group. All measurements was taken by the same researcher who not known of patient groups.

QTc Interval and QTc Dispersion Determination: The QT interval was determined from the beginning of the QRS complex to the conclusion of the T wave on the twelve-lead ECG of the patients. By means of Bazett's method, the QTc interval was computed ($QTc = QT/\sqrt{RR}$).

The longest corrected QT interval documented in the 12-lead ECG was noted as the maximum QTcintervals. The shortest corrected QT interval recorded in the 12-lead ECG was noted as the minimum QTc intervals.

QTc dispersions were measured as the variation between the maximum and minimum QTc intervals across all leads (11).

Tp-e Measurement: The distance from the apex to the termination of the T wave was assessed in lead V2 and documented as the Tp-e interval. Tp-e/QTc ratios were computed based on the Tp-e and QTc measurements.

Body Mass Index (BMI): BMI was determined from the recorded height and weight of the patients. The patients were grouped into four categories based on BMI. Those with a BMI less than 18.5kilogram per square meter (kg/m^2) were classified as underweight. Patients whose BMI ranges from 18.5 to 24.9 (kg/m^2) were considered to have a healthy weight. Individuals with a BMI ranges from 25(kg/m^2) to 29.9(kg/m^2) were categorized as overweight. Finally, patients with a BMI of 30 and above were classified as obese (12).

The Exclusion Criteria: The exclusion criteria included patients with hypertension and those diagnosed with high blood pressure upon admission to the hospital; those with diabetes mellitus, chronic renal failure, metabolic diseases, and electrolyte disorders; those with heart failure, coronary artery disease (CAD), valve disease, and rhythm disorders; those with malignancy; those with urinary system infection; those taking drugs that influence ECG parameters; and those under the age of 17.

Statistical Analysis: Version 20 of IBM SPSS (Statistical Package for the Social Sciences, Chicago, IL, USA) was utilized for all statistical analyses. Classified data were expressed as counts and percentages. Chi-square analysis or Fisher's exact test, whichever was suitable, was employed to compare these categorical variables. The Shapiro-Wilk method for assessing normality was employed to test the normality assumption for quantitative variables. For normally distributed continuous variables, the data were expressed as mean ± standard deviation conversely, data with a non-normal distribution were expressed as median and interquartile range. For comparisons of normally distributed continuous variables, Student's t-tests were applied, Mann-Whitney U tests were utilized for continuous variables that did not exhibit a normal distribution. Statistical significance was indicated by a p-value below 0.05.

RESULTS

This study included 178 adults, including 118 patients with urinary tract stones and 60 healthy volunteers. Patients had an average age of 44.8±14.0 years, in the control group, by comparison, it was 36.4±14.7 years. Among the patients participating in the study, 57 (48.3%) were women, while in the control group, there were 30 (50%) women (p=0.952).

When comparing gender, body mass index, and habits between the patient and control groups, there were no significant differences noted (p=0.936). (Table 1).

When the parameters of the QTc interval, QTc dispersion and Tp-e/QTc were evaluated and compared between the patient and healty control groups, no statistically significant differences were identified (p=0.233, p=0.663 p=0.077). (Table 1). Figure 1 illustrates the distribution graphs of QTc, QTc dispersion, and Tp-e/QTc in case and control groups.

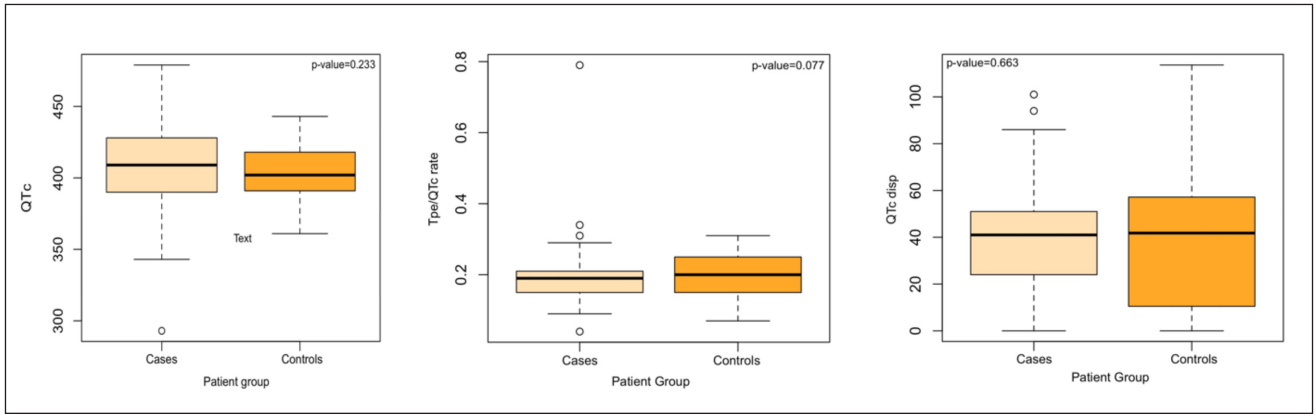


Figure 1: Distribution graphs of QTc, QTc dispersion, and Tp-e/QTc in case and control groups.

Table 1: Gender, bady mass index and habits, QTc, QTc disp and Tp-e/QTc rate parameters of the groups.

Caracteristics	Cases (n=118)	Controls (n=60)	p
Gender*			
Male	61 (51.7)	30 (50)	0.952**
Female	57 (48.3)	30 (50)	
Bady Mass Index Categories*			
<18.5 (Underweight)	3 (2.6)	3 (5.0)	
18.5-24.9 (Healthy weight)	36 (30.8)	28 (46.7)	0.936**
25-29.9 (Overweight)	49 (41.9)	21 (35.0)	
>30 (Obese)	29 (24.8)	8 (13.3)	
Habits*			
Alcohol	1 (0.8)	1 (1.7)	
Smoking	40 (33.9)	21 (35.0)	0.937**
Smoking+Alcohol	10 (8.5)	4 (6.7)	
No	67 (56.8)	34 (56.7)	
QT parameters			
QTc	406.0 (34.5)	413.0 (39.5)	0.233
QTc disp	41.7 (16.5)	40.0 (35.0)	0.663
Tp-e/QTc rate	0.19 (0.05)	0.19 (0.05)	0.077

*Data are shown as n(%), **Chi squared test, **QTc:** Corrected QT, **QTc disp:** Corrected QT Dispersion, **IQR:** Inter Quantile Range, **Tp-e:** The interval from the peak of the T wave to the end of the T wave.

Statistical analysis did not reveal a significant difference between the ECG parameters of female patients and women in the control group. When comparing ECG parameters in female patients by age, there was no significant difference. It was found that obesity had no effect on ECG parameters in either the patient or control groups (p=0.936).

When the ECG parameters of male patients and the control group were compared, the Tp-e/QTc ratio was significantly higher in the healty control group (p = 0.002).

Table 2: EKG parameters by gender in patients

	Male (n=61)		Female (n=57)		p-value
	Mean	SD	Mean	SD	
QTc	399.8	23.3	416.8	32.8	0.001*
QTc max	421.2	31.8	435.1	34.4	0.020*
QTc min	383.5	26.7	398.3	31.3	0.007*
	Median	IQR***	Median	IQR	
QTc disp	41.7	16.5	40.0	35.0	0.880**
Tp-e/QTc rate	0.19	0.05	0.19	0.05	0.890**

QTc max: Corrected QT maximum, **QTc min:** Corrected QT minimum, **QTc disp:** Corrected QT dispersion, **IQR:** Inter Quantile Range, **Tp-e:** The interval from the peak of the T wave to the end of the T wave. *Student's t-test, **Mann Whitney U test ***Data are shown as median (interquarte range, IQR).

When ECG parameters were compared in the patient group based on smoking habits, nonsmokers had a significantly higher QTc. However, in the control group, Between smokers and non-smokers, no statistically significant difference was found (p=937).

DISCUSSION

Our study is the first to use ECG parameters to determine the risk of developing malignant arrhythmias in patients with urinary stones. When comparing patients with urinary stone disease to healthy subjects, we discovered that ECG parameters indicating ventricular repolarization were not significantly different. This means that patients with urinary stone disease do not have an additional risk of malignant arrhythmias.

In a meta-analysis, Cheungpasitporn et al. discovered that individuals with kidney stones have a 1.24-fold higher risk of CAD than people without kidney stones (13). Other meta-analyses have found that people with kidney stones have a higher risk of myocardial infarction and CAD (14).

The ineffectiveness of calcification inhibitors in individuals with urinary stone disease has been hypothesized to increase the risk of myocardial infarction by inducing renal stone formation and coronary calcification. The fact that the composition of vascular plaques is the same as that of Randall plaque, the nidus of stone formation, supports this view. The concomitant coronary calcification in 80% of patients with renal stone disease and the increased risk of urinary stones and myocardial infarction in patients receiving high-dose calcium replacement therapy also support this mechanism (15,16).

According to Rule et al. patients with kidney stones have a 31% greater risk of myocardial infarction. However, when patients with additional comorbidities were removed from the study, the increased risk of myocardial infarction was statistically insignificant (15). Instead of urinary stone disease predisposing to heart disease, this could be interpreted as comorbidities including hypertension, obesity, and dyslipidemia. Furthermore, it can be said that chronic renal failure, which can develop due to urinary stone disease, is a risk factor for CAD (14).

When assessing the correlation between urinary stone disease and CAD, it is important to remember that the risk of both conditions rises with age independently.

Since patients with comorbidities were excluded from our study, it was possible to evaluate more precisely whether urinary stone disease poses a risk for malignant arrhythmias, and it was concluded that it might not pose a risk.

Ferraro et al. reported that the relationship between kidney stones and coronary artery disease was significant in women but not in men in a survey study (17). This could be due to the fact that women are more prone to having comorbid conditions associated with urinary tract stone disease (18,13).

In the study by Shu et al, CAD, stroke, and cholelithiasis were common in women with urinary stone disease, while hypertension was more common in men (19). Although urinary tract stone disease and CAD are both more common in men, CAD is surprisingly more common in female stone disease patients. However, the underlying pathophysiology is unknown. There is a need to investigate risks for CAD such as weight, diet, genetics, estrogen-progesterone ratio, and pregnancy (20).

Like age, obesity is a common risk factor for both diseases. Many studies have found that patients with a BMI of more than 28 kg/m^2 had a higher risk of urinary stone disease (21). In another study comparing obese and non-obese subjects, a significant correlation was found between BMI and maximum QTc interval and QTc dispersion (22). However, obesity had no statistically significant effect on ECG parameters in both the patient and control groups in our study. This could be due to the insufficient number of obese individuals in this study.

In both the patient and control groups, female patients had a significantly higher QTc value compared to male patients, but still within normal limits in our study. This is because the normal range of QTc values is higher in female patients as opposed to male patients. When QTc > 450 in males and QTc > 470 in females, it has been identified as an independent predictor of sudden cardiac death (23).

A relatively small sample size and the lower age of the control group compared to the patient group are the limitations of our study.

In our study, contrary to the existing literature, it was found that ventricular ECG repolarization parameters in patients with urinary stone disease were not significantly different from those in the normal population. The validity of this finding could be further investigated with larger case groups and longer-term studies. Drawing from the outcomes of this study, we recommend that in the follow-up of patients with urinary stone disease, potential risk factors other than ECG parameters for malignant arrhythmias should also be examined.

Acknowledgment

We thanks to Cardiologist Prof. Dr. Ahmet Avcı for his invaluable comments and suggestions and thanks to Nurse Handan Durmuş and Nurse Vildan Ergün for EKG imaging.

Author Contributions

Conception, design, data collection, literature search, writting, approval: **Hilal Hocagil**, Conception, design, literature search, writting, approval: **Abdullah Cüneyt Hocagil**, Analysis and interpretation of data, writting, approval: **Tuğba Akkaya Hocagil.** All co-authors have had the opportunity to review the final manuscript and have provided their permission to publish the manuscript.

Conflicts of Interest

There is no conflict of interest among the authors.

Financial Support

The authors did not receive financial support for the study.

Ethical Approval

The research was approved by the Research Ethics Committee at Zonguldak Bülent Ecevit University (certificate number 2015-141-30/12). Informed consent was obtained from all patients in the study.

Review Process

Extremely peer reviewed.

REFERENCES

1. Wilcox CR, Whitehurst LA, Cook P, Somani BK. Kidney stone disease: an update on its management in primary care.Br J Gen Pract. 2020;70:205-6.
2. Pak CY, Sakhaee K, Moe O, Preminger G M, Poindexter J R, Peterson RD,Pietrow P, Ekeruo W. Biochemical profile of stone-forming patients with diabetes mellitus. Urology 2003;61:523-27
3. Zimmerer T, Weiss C, Hammes H P, Braun C, Hesse A, Alken P, Knoll T. Evaluation of urolithiasis: a link between stone formation and diabetes mellitus? Urol Int 2009;82:350-55.
4. Domingos F, Serra A. Nephrolithiasis is associated with an increased prevalence of cardiovascular disease. Nephrol Dial Transplant. 2011;26:864-68.
5. Kovacevic L, Lu H, Caruso JA, Kovacevic N, Lakshmanan Y. Urinary proteomics reveals association between pediatric nephrolithiasis and cardiovascular disease.Int Urol Nephrol. 2018;50:1949-54.
6. Cosgun A, Oren H. Variation of the T-wave peak-end interval and heart rate variability values in healthy males and females at various hours of the same day, and relationship of them. J Arrhythm. 2020;36:118-26.
7. Franz MR, Zabel M. Electrophysiological basis of QT dispersion measurements. Prog Cardiovasc Dis. 2000;42:311-24.
8. Rosenthal TM, Masvidal D, Abi SFM, Bernard ML, Habit S, Polin GM,Rogers PA, Xue JQ, Morin DP. Optimal method of measuring the T-peak to T-end interval for risk stratification in primary prevention Europace. 2018;20: 698-705
9. Ucar FM, Oztürk C, Yılmaztepe MA. Evaluation of Tp-e interval, Tp-e/QT ratio and Tp-e/QTc ratio in patients with acute myocarditis. BMC Cardiovascular Disorders. 2019; 19: 1-7.
10. Zehir R, Karabay CY, Kalaycı A, Akgün T, Kılıçgedik A, Kırma C. Evaluation of Tpe interval and Tpe/QT ratio in patients with slow coronary flow. Anatol J Cardiol. 2015; 15: 463-67
11. Hocagil AC; Hocagil H. Evaluation of Electrocardiography Parameters in Renal Colic Patients Admitted to the Emergency Department. Eurasian J Emerg Med. 2022, 21.1: 68-72.
12. Aksoydan E, Çakır N. Adölesanların beslenme alışkanlıkları, fiziksel aktivite düzeyleri ve vücut kitle indekslerinin değerlendirilmesi. Gulhane Medical Journal 2011; 53:264-270.
13. Cheungpasitporn W, Thongprayoon C, Mao MA, O'Corragain OA, Edmonds PJ, Erickson SB. The Risk of Coronary Heart Disease in Patients with Kidney Stones: A Systematic Review and Meta-analysis. N Am J Med Sci. 2014;6:580-85.
14. Peng JP, Zheng H. Kidney stones may increase the risk of coronary heart disease and stroke: A PRISMA-Compliant meta-analysis. Medicine (Baltimore). 2017;96:e7898.
15. Rule AD, Roger VL, Melton LJ, Bergstralh EJ, Li X, Peyser PA, Krambeck AE, Lieske JC. Kidney stones associate with increased risk for myocardial infarction. J Am Soc Nephrol 2010; 21: 1641-44.
16. Khan SR, Rodriguez DE, Gower LB, Monga M. Association of Randall plaque with collagen fibers and membrane vesicles. J Urol. 2012;187:1094-100.
17. Ferraro PM, Taylor EN, Eisner BH, Gambaro G, Rimm EB, Mukamal KJ,Curhan GC. History of kidney stones and the risk of coronary heart disease. JAMA. 2013;310:408-15.
18. Reiner AP, Kahn A, Eisner BH, Pletcher MJ, Sadetsky N, Williams OD, Polak JF, Jacobs Jr DR, Stoller ML.Kidney stone and subclinical atherosclerosis in young adults: The CARDIA study. J Urol.2011;185:920-25
19. Shu X, Cai H, Xiang YB, Li H, Lipworth L, Miller NL, Zheng W, Shu XO, Hsi RS. Nephrolithiasis Among Middle Aged and Elderly Urban Chinese: A Report from Prospective Cohort Studies in Shanghai. J Endourol. 2017;31:1327-34
20. Shadman A, Bastani B. Kidney Calculi: Pathophysiology and as a Systemic Disorder Iran J Kidney Dis. 2017;11:180-91.
21. Luo W, Zhou Y, Gao C, Yan P, Xu L. Urolithiasis, Independent of Uric Acid, Increased Risk of Coronary Artery and Carotid Atherosclerosis: A Meta-Analysis of Observational Studies. Biomed Res Int. 2020;2020:1026240.
22. Seyfeli E, Duru M, Kuvandik G, Kaya H, Yalcin F. Effect of obesity on P-wave dispersion and QT dispersion in women. Int J Obes (Lond). 2006;30:957-61.
23. Straus SMJ, Kors JA, De Bruin ML, Van der Hooft CS, Hofman A, Heeringa J, Deckers JW, Kingma JH, Sturkenboom MCJM, Stricker BHCh, Witteman JCM. Prolonged QTc interval and risk of sudden cardiac death in a population of older adults. J Am Coll Cardiol. 2006; 47: 362-67