ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA MAKALESİ

Investigation of the Presence of QT Dispersion and its Relationship with Electrolyte Imbalance in Patients with Acute Kidney Injury

Akut Renal Yetmezliği Olan Hastalarda QT Dispersiyon Varlığının ve Elektrolit Dengesizliği ile İlişkisinin Araştırılması

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ABSTRACT

Aim: This study aims to investigate the relationship between QT dispersion and electrolyte imbalance in patients with acute kidney injury (AKI), and whether QT dispersion is associated with the severity of AKI.

Material and Methods: A total of 400 patients over the age of 18 presenting to a tertiary emergency department over a 3-month period were prospectively examined. While 200 of the participants were diagnosed with AKI, 200 were in the control group. Presence of QT dispersion, potassium values, age and sex data, and blood urea nitrogen (BUN) /Creatinine (Cr) ratio parameters were examined and comparisons were made.

Results: The mean age of patients diagnosed with AKI was 55.9±16.7 years, while it was 54.8±18.2 in the control group. QT dispersion was significantly higher in the AKI group (p<0.001). While the potassium value was 4.9±0.8 mEq/L in the AKI group with QT dispersion, it was 4.3±0.5 mEq/L in the control group. Potassium values were significantly higher in AKI patients with QT dispersion (p<0.001). When patients with AKI were compared in terms of QT dispersion, no significant difference was found between age, gender, electrolyte imbalances, and BUN/Cr ratios.

Conclusion: Age and gender are not predictive parameters for QT dispersion in patients. Hyperkalemia is significantly higher in AKI patients with QT dispersion. High BUN/Cr ratio is not a predictive parameter for the presence of QT dispersion in patients with AKI. The frequency of QT dispersion is high in AKI patients. We think that QT dispersion in AKI follow-up may help the clinician predict possible complications and mortality.

Keywords: Emergency medicine, acute kidney injury, electrolyte imbalance, QT dispersion

ÖZ

Amaç: Bu çalışma, akut renal yetmezliği (ARY) olan hastalarda QT dispersiyonu ile elektrolit dengesizliği arasındaki ilişkiyi ve QT dispersiyonunun ARY şiddeti ile ilişkili olup olmadığını araştırmayı amaçlamaktadır.

Gereç ve Yöntemler: Üçüncü basamak acil serviste 3 aylık bir süre içinde başvuran 18 yaş üstü toplam 400 hasta prospektif olarak incelendi. Katılımcıların 200'ü ARY tanısı alırken, 200'ü kontrol grubundaydı. QT dispersiyonu varlığı, potasyum değerleri, yaş ve cinsiyet verileri ve kan üre nitrojen (BUN)/Kreatinin(Cr) oranı parametreleri incelendi ve karşılaştırmalar yapıldı.

Bulgular: ARY tanısı alan hastaların yaş ortalaması 55.9±16.7 yıl, kontrol grubunda ise 54,8±18,2 idi. ARY grubunda QT dispersiyonu anlamlı olarak daha yüksekti (p<0,001). Potasyum değeri QT dispersiyonlu ARY grubunda 4,9±0,8 mEq/L iken kontrol grubunda 4,3±0,5 mEq/L idi. QT dispersiyonu olan ARY hastalarında potasyum değerleri anlamlı olarak yüksekti (p<0,001). ARY'li hastalar QT dispersiyonu açısından karşılaştırıldığında yaş, cinsiyet, elektrolit dengesizlikleri ve BUN/Cr oranları arasında anlamlı fark bulunmadı.

Sonuç: Yaş ve cinsiyet hastalarda QT dispersiyonu için prediktif parametreler değildir. QT dispersiyonu olan ARY hastalarında hiperkalemi anlamlı olarak daha yüksektir. Yüksek BUN/Cr oranı, ARY'li hastalarda QT dispersiyonunun varlığını öngören bir parametre değildir. ARY hastalarında QT dispersiyonunun sıklığı yüksektir. ARY takibinde QT dispersiyonunun klinisyene olası komplikasyonları ve mortaliteyi öngörmede yardımcı olabileceğini düşünüyoruz.

Anahtar Kelimeler: Acil servis, akut renal yetmezlik, elektrolit imbalansı, QT dispersiyonu

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Introduction

Acute kidney injury (AKI) is a clinical picture with high mortality that results in the inability to remove urea and other nitrogenous waste products from the body due to the sudden loss of function in the kidney, and the deterioration of extracellular fluid volume and electrolyte content (1,2).

Although the frequency of AKI varies according to age, it is less than 1% in the general population, 2-7% in hospitalized patients, and 5-30% in intensive care patients. While the mortality rate in uncomplicated AKI is 5-10%, it is between 40-90% in patients hospitalized in the intensive care unit (2). When the literature is examined, QT dispersion has had prognostic importance and has been associated with electrolyte imbalance in the mortality related to kidney injury as well as sudden cardiac deaths in the last 20 years. The majority of the studies have been on patients with AKI who get or do not get renal transplant and dialysis treatment (1,2). It has been mentioned in a study that sudden ventricular arrhythmias are more common in patients with AKI receiving dialysis without a known history of cardiac disease and may be associated with electrolyte imbalance (3). Similarly, in a study on kidney transplant patients, QT dispersion, which is associated with sudden cardiac death, has been reported to be high in kidney transplant patients (4).

Regardless of the etiology, AKI is a picture with high mortality due to many possible complications. Electrolyte imbalances, especially in the course of AKI, and the resulting cardiac complications are among the main causes of mortality. Considering the information that QT dispersion is common in AKI patients and has an effect on mortality, we aimed to investigate the frequency of QT dispersion in patients with AKI, whether there is a relationship between electrolyte imbalance and QT dispersion in the course of AKI, and whether QT value and QT dispersion is affected by the parameters that constitute risk factors for AKI, such as age, gender, and advanced age. In addition, we aimed to investigate whether BUN/Cr ratio, a predictor of prerenal AKI severity to be used in the evaluation of treatment response, is a parameter that affects the presence of QT dispersion in AKI. Finally, we tried to emphasize the importance of QT dispersion associated with cardiac mortality in predicting cardiac complications and lay groundwork for future studies regarding the relationship between cardiac mortality and QT dispersion in AKI.

Material and Methods

This study was conducted at the emergency department of the University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital with the approval of the clinical research ethics committee of the 2011-KAEK-25-2019/03-21. We created the data through the Hospital Central Electronic Recording System. In this study, we prospectively examined patients over 18 years of age with a diagnosis of AKI who presented to the emergency department over a 3-month period. We excluded those under 18 years of age, whose voluntary consent could not be obtained, with a known history of cardiac conduction disorder, with a known history of electrolyte imbalance, with a history of drug use that may cause QT dispersion (antiarrhythmic, antiepileptic, antipsychotic, etc.), with a diagnosis of CNS disease or infection, with a diagnosis of congenital long QT syndrome, and with a diagnosis of hypothermia. Additionally, in this period, we excluded 16 out of 236 patients with AKI from the study because we could not properly measure their QT on the ECG, 18 were because of using drugs leading to QT dispersion, and 2 were due to the diagnosis of meningitis causing QT dispersion.

We included 400 patients in the study, 200 of whom had AKI while 200 presented to the emergency department for any reason without a diagnosis of kidney failure. We evaluated the age, gender, presence of QT dispersion, potassium values, and BUN/Cr ratio of the patients in both groups.

At least two physicians manually measured the max and min values of corrected QT in the ECG and evaluated by comparing and confirming the QTc measurements calculated for DII derivation by the Ge MAC 2000 12-lead ECG device. We used Bazet's formula to calculate corrected QT interval. We accepted the difference between QT max and min values as 50 ms and above based on the studies in the literature.

The normal value for potassium was 3.5-5 mEq/L; we grouped values above 5 mEq/L as hyperkalemia, while we grouped values below 3.5 mEq/L as hypokalemia. We calculated the BUN/Cr ratio and took the20 ratios used to distinguish between prerenal and renal kidney injury as reference. We compared all data of the control group and AKI group, especially the presence of QT dispersion.

Statistical analysis

Data were analyzed with IBM SPSS Statistics 17.0 (IBM Corporation, Armonk, NY, USA) package program. Unless stated otherwise, results were considered statistically significant for $p<0.05$. However, Bonferroni Correction was performed to control for Type I error in all possible multiple comparisons.

The Kolmogorov-Smirnov test was used to determine whether the distribution of continuous numerical variables was close to normal and whether the assumption of homogeneity of variances was met was investigated with Levene's test. Descriptive statistics were expressed as mean ± standard deviation (minimum – maximum) for continuous numerical variables and number of cases and (%) for categorical variables.

The significance of the difference between the groups in terms of continuous numerical variables in which parametric test statistics assumptions were met was evaluated with the Student's t-test, while the significance of the difference in terms of continuous numerical variables in which parametric test statistics assumptions were not met was evaluated with Mann Whitney U test. When the expected frequency was below 5 in at least one of the 2x2 crosstabs, the categorical data were evaluated with Fisher's exact probability test whereas Chi-Square test with continuity correction was used when the expected frequency was between 5-25. Pearson's Chi-Square test was used in other cases.

Results

We evaluated AKI and control group data in the study. The mean age was 54.8±18.2 in the control group while it was 55.9±16.7 in the AKI group. The population of patients over 65 years old constituted 34.5% of the AKI group and 33% of the control group. There was no statistically significant difference between the control and AKI groups (p=0.531).

When the gender distribution of the groups was examined, 45.5% of the AKI group was male and 54.5% was female, while 44.5% of the control group was male and 55.5% was female. There was no statistically significant difference between the groups in terms of gender (p=0.751 and p=0.841). The data regarding the age and gender of the patients are given in Table 1.

Age group	n	%
18-40	68	20.2
40-70	183	54.5
71 and over	85	25.3
Total	336	100
Comorbidities	**n**	**%**
DM	87	25.8
HT	144	42
CHF	12	3.5
CVD	65	19.3
CAD	27	8
Other	57	16.9

HT: hypertension, DM: Diabetes mellitus CAD: coronary artery disease, CHF:congestive heart failure, CVD: Cerebrovascular disease

Table 1. Age groups and comorbidities

In the study, the presence of QT dispersion was significantly higher in the AKI group than the control group (p<0.001). While 56% of the AKI group had QT dispersion, the dispersion rate was 26.5% in the control group. In addition, QT dispersion value and QT max level of the AKI group were statistically significantly higher than the control group (p<0.001 and p<0.001). While the QT max value in the control group was 436.1±39.3 ms, it was 458.6±46 ms in the AKI group. Although the QT min level of the AKI group was higher than the control group, there was no statistically significant difference between the groups (p=0.104). Potassium value was higher in the AKI group than the control group (p<0.001) (Table 2).

Comorbidities	With CIN	Without CIN	P value
DM	9	78	0.096
HT	13	131	0.111
CHF	3	9	0.037
CVD	2	63	0.272
CAD	3	24	0.404
BMI	26.05	26.85	0,74
Height	167.50	167	0,991
Weight	77	75	0,835

HT: hypertension, DM: Diabetes mellitus CAD: coronary artery disease, CHF: congestive heart failure, CVD: Cerebrovascular disease

Table 2. Data regarding CIN, Comorbidities, Height, Weight, and BMI

As the presence of QT dispersion was more common in the AKI group, we made comparisons between the groups with and without QT dispersion within the AKI group.

There was no statistically significant difference in terms of mean age, advanced age (≥65 years), and gender distribution (p=0.113; p=0.914 and p=0.991, respectively). There was no statistically significant difference according to Bonferroni Correction in terms of potassium value and distribution of potassium levels (p>0.025). There was no statistically significant difference in terms of BUN/Cr value and the ratio of those with BUN/Cr≥20 (p=0.346 and p=0.456) (Table 3).

Weight	With CIN	Without CIN	P
≤18 (underweight)	0	8	
19-25(normal weight)	7	97	0.886
25-30 (overweight)	9	118	
31≤ (obese)	6	91	

Table 3. Data regarding the relationship between CIN and Weight

In terms of QT dispersion, we found no significant difference between the control group and the AKI group in terms of age (p=0.272). Considering the gender distribution, there was no statistically significant difference between the control group with QT dispersion and the group with AKI (p=0.750).

There was no statistically significant difference in terms of QT max levels between the control group with QT dispersion and the AKI group (p=0.083). While the mean QT max value was 473±47 ms in the AKI group, it was 463±47.9 ms in the control group.

Potassium value was statistically significantly higher in the AKI group with QT dispersion compared to the control group (p<0.001). The incidence of hyperkalemia was significantly higher in the AKI group with QT dispersion compared to the

control group (p<0.001). While there was no statistically significant difference between the groups in terms of the frequency of low potassium levels (p=0.387), the rate of those with normal potassium levels was significantly lower in the AKI group (p<0.001).

Discussion

In this study, we aimed to investigate the presence of QT dispersion and the relationship between QT dispersion and electrolyte imbalance in patients with acute kidney injury. There are some studies in the literature on the relationship between QT dispersion and Chronic Kidney Injury, but there is no study investigating the relationship between AKI and QT dispersion in the literature.

Although the data regarding the gender ratio of AKI are not clear, male gender is considered to be a risk factor (1.2). However, in our study, 54.5% of the AKI group consisted of females. In their study, Bagshaw et al. claimed advanced age and male gender as important risk factors for AKI. The study especially mentioned that the frequency of cardiac comorbidities also increases in AKI for the elderly population (5). For this purpose, we calculated the frequency of the elderly population in our study and reached the aforementioned data. In another study including 605 patients with AKI, Mehta et al. associated advanced age and male gender with an increased risk of mortality (6). In this study, the patient population over 65 years of age with AKI was 33% of all patients, which is similar to our study. We randomly selected AKI and control groups in terms of age, gender, and proportion of patients aged 65 and over in our study. We think that the similarity of the ratios of these parameters in both groups and the lack of significant difference ensure the homogeneity of the groups and provide reliability in the comparison of other data.

Familoni et al. compared 42 patients with end-stage renal disease receiving hemodialysis treatment and 45 patients in the control group in terms of the effect of QT max value and presence of QT dispersion in ECG on cardiac mortality rates (7). In the group of patients with end-stage renal disease (ESRD) treated with hemodialysis, the rate of those with a QT max value above 440 ms was 71%, and the cardiac mortality rate of this group was 73% higher than that of the control group. In our study, the frequency of QT dispersion was significantly higher in patients with AKI. We also found that the QT max value of the AKI group was higher. There was no difference in QT min value between the two groups.

Investigation of the relationship between demographic data of patients and QT dispersion was another aim of our study. In a study investigating the effect of ACE gene polymorphism on QT dispersion, Toraman et al. mentioned that QT dispersion develops independently of gender and age (8). In the study of Raizada et al., there was no correlation between QT dispersion with gender and age (9). Similarly, in our study, when the AKI and control groups with QT dispersion were compared, we observed no significant difference between the groups in terms of age and gender.

In a study on the relationship between QT dispersion and ACE gene polymorphism in myocardial infarction (MI), Jeron et al. stated that the ratio of the elderly population did not differ significantly in QT dispersion, and there was no significant difference in the mean age between MI diagnosed patients with and without QT dispersion (10). In our study, the frequency of QT dispersion in the elderly population over 65 was not statistically significant compared to the control group.

In our study, there was no significant difference between the dispersed AKI and control groups in terms of QT max value. Unlike our study, many studies in the literature state that dispersion correlates with the QT maximum value. Quantitative values of QT max measurement vary in studies (7,11,12).

In this study, the potassium value was higher in the AKI group than the control group, and hyperkalemia rate was significantly more frequent in the AKI group. The fact that the frequency of hyperkalemia and the higher potassium level were significantly higher in the whole AKI group may lead to similar findings in the AKI group with QT dispersion. Regardless of the etiology, hyperkalemia is an expected electrolyte imbalance in AKI as a result of both the disruption of potassium tubular secretion mechanisms and metabolic acidosis (13). Kol et al. reported that QT dispersion may be a noninvasive predictor of cardiac mortality in the increased risk of sudden cardiac death and arrhythmia in patients with end-stage renal disease who have not yet started dialysis treatment, and there is a significant relationship between high potassium level and QT dispersion (14). In the aforementioned study, the mean potassium value was 5.1±0.79 and it was significantly higher in patients with QT dispersion, which is similar to our study.

Unlike our study, Nitta et al. found a significant relationship between QT dispersion and hypokalemia. They examined 700 healthy and 700 pediatric patients aged 11-14 years with left ventricular hypertrophy with ejection fraction (EF) between 35-50%. Fatal ventricular arrhythmia and sudden cardiac death rates were higher in the other group compared to the healthy group. Cardiac mortality was higher in the group with QT dispersion and hypokalemia was statistically significant in 72% (15).

When the patients with AKI with and without QT dispersion were compared in terms of gender, we found no significant difference. We examined many studies in the literature and most of these studies stated that QT dispersion was independent of gender (16-18). In a study investigating the variables affecting QT dispersion in patients with CKI, age and gender were not significant variables in the dispersed and non-dispersed groups, which is similar to our study, and

the mean age in the dispersed group was significantly higher, unlike our study (19). We think that this situation is related to the fact that the study was conducted in patients with long-term kidney injury rather than AKI. Although there is no clear data for the mean age of AKI in the literature, many studies show that the mean age is higher in CKI when AKI developing on the basis of CKI are excluded (20-22).

Cupisti et al. found no difference between sodium, potassium, and calcium levels in the electrolyte imbalance analysis between the AKI group with or without QT dispersion (23). In a study investigating the relationship between QT dispersion with electrolyte imbalance, basal Cr levels, and BUN levels in more than 500 CKI patients receiving hemodialysis treatment, electrolyte values were similar to our study. In the aforementioned study, hypocalcemia and hyperkalemia were significantly higher in patients with CKI with QT dispersion. In our study, we found that there may be a relationship between QT dispersion and hyperkalemia in AKI patients.

In the studies conducted, as well as the Cr increase rate according to the basal creatinine value, the BUN/Cr ratio, which is one of the practical parameters used in the prerenal/renal distinction, is also important in evaluating the early stage changes and the severity at the onset of AKI (24,25).

In a study conducted by Guillaume et al. in 2017 with a group of 2756 patients with prerenal and renal acute kidney injury with a Cr value above 1.5mg/dl during their 13-month follow-up, the BUN/Cr ratio was not significant in determining the prerenal and renal differentiation and the severity of the clinical course (26). Contrary to this study, a study in Pakistan in 2009 examined the improvement of clinical and laboratory parameters with fluid therapy in patients diagnosed with prerenal AKI with a BUN/Cr ratio above 20. The study found that the higher the BUN/Cr ratio is, the better and faster the response to fluid therapy and recovery becomes, and accordingly, it is a parameter that can give an idea about the severity and clinical course of AKI (27).

In our study, when BUN/Cr levels were examined in the AKI group with and without QT dispersion, we found no statistically significant difference between the groups in terms of BUN/Cr ratio. When the literature is examined, it seems that there is a need for studies investigating the relationship between dispersion and BUN/Cr ratio with more patients and the relationship between QT dispersion with AKI severity and mortality.

We also emphasize the importance of QT dispersion, which is associated with sudden cardiac death and cardiac mortality, in patients with AKI in terms of predicting cardiac complications. Thus, we think that there is a need for future studies on the relationship between long-term cardiac mortality and QT dispersion in the course of AKI, and that these studies may help the clinician to predict possible complications and mortality in the follow-up of AKI.

Limitations

It is a study conducted from a single center. Additionally, we could not retrieve basal creatinine levels at the first admission in some patients and thus excluded those patients. Moreover, at least two physicians calculated QT dispersion manually (lack of access to programs that calculate QT dispersion on digital images), which is another limitation of the study. Finally, we could not follow up cardiac mortality.

Conclusion

In our study, QT dispersion and QT max value in patients with AKI were significantly higher than in the control group without AKI. We evaluated the BUN/Cr ratio in the patient group with AKI and found no significance in terms of the presence of QT dispersion when the BUN/Cr ratio was 20 or higher. We think that QT dispersion may be helpful in predicting complications and mortality in AKI follow-up.

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All authors declared that they follow the rules of Research and Publication Ethics.

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