Analysis of QT Dispersion, Corrected QT Dispersion, and P-Wave Dispersion Values in Alcohol Use Disorder Patients With Excessive Alcohol Use

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ABSTRACT

Objective: To identify the changes in QT dispersion (QTd), corrected QTd (QTcd), and P-wave dispersion (Pd) values with long-term alcohol abuse that could lead to severe ventricular arrhythmia, atrial fibrillation, and sudden death in alcohol use disorder (AUD) patients with excessive alcohol use.

Methods: This cross-sectional study included 48 individuals diagnosed with AUD based on *DSM-5* criteria. Patients with a history of psychiatric diseases were not included. The control group comprised 48 individuals with no psychiatric diagnosis who did not abuse alcohol or other substances. Participants with body mass index > 24.9 kg/m^2 were excluded. Twelve-derivation electrocardiograms (ECG) were obtained from all participants.

Results: The mean ± SD age was 44.35 ± 10.24 years in the AUD group and 40.90 ± 13.45 years in the control group. There was no significant difference between the groups based on age (P = .108). There was a significant difference between the groups based on smoking status (P = .000). The mean ± SD period of alcohol use was 20.71 ± 12.04 years, and the alcohol intake was 5.88 ± 1.65 units/d. The AUD group demonstrated elevations in all ECG measures (QTd: 46.56 vs 26.67 ms, QTcd: 54.25 vs 30.88 ms, Pd: 44.69 vs 28.54 ms, all P = .000).

Conclusions: AUD patients with excessive alcohol use had a higher risk of arrhythmia and sudden death compared to the control group. Consideration of ECG and referral to cardiologic examinations would contribute to the follow-up and health of patients with AUD.

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Alcohol use disorder (AUD) is a psychoactive substance dependency that is highly prevalent worldwide. According to World Health Organization estimates, 6% of global deaths are caused by alcohol use, and the mortality rate due to alcohol-induced cardiovascular disease is 12%.[1] QT dispersion (QTd) is the difference between the maximum QT value and the minimum QT value measured with 12-derivation surface electrocardiogram (ECG). Corrected QT (QTc) refers to the QT interval adjusted for the heart rate. QTc dispersion (QTcd) is obtained by measuring the difference between the maximum QTc and the minimum QTc in milliseconds by any ECG derivation.[2] Prolongation in QT indicates cardiac autonomy imbalance and increases susceptibility to malignant ventricular arrhythmias.[3] QT prolongation was reportedly observed in 22%–46.9% of patients with AUD.[4] Age, female sex, left ventricular hypertrophy, ischemia, slow heart rate, and electrolyte imbalance could lead to QT prolongation.[5] Prolonged QT, a rare condition in healthy individuals (0.0017%–0.31%), could be observed as a result of alcohol use or hypomagnesemia caused by alcohol use and may lead to tachyarrhythmia and sudden death.[6] P-wave dispersion (Pd) indicates the difference between the maximum P (Pmax) and the minimum P (Pmin) value. Pd prolongation is a risk factor for atrial fibrillation.[7] Although there are a few studies[8–12] that investigated QTd changes in patients diagnosed with AUD in the literature, no studies were found on Pd. The present study aimed to identify the changes in QTd, QTcd, and Pd values with long-term alcohol abuse that could lead to severe ventricular arrhythmia, atrial fibrillation, and sudden death in AUD patients with excessive alcohol use.

METHODS

This cross-sectional study compared the ECG QTd, QTcd, and Pd values of patients with long-standing AUD with that of controls with no history of alcohol abuse from a hospital alcohol and substance addiction therapy and research center outpatient clinic in Turkey. All participants signed an informed consent form. The study was approved by the Ethics Committee of Fırat University. Procedures were strictly in accordance with the ethical standards of the Institutional and National Committee on Human Experimentation and with the Declaration of Helsinki.[13]

Subjects

Both the AUD and control groups were composed of men. The AUD group was aged between 21 and 66 years and the control group between 20 and 65 years. Exclusion criteria for both groups included history of any cardiologic (cardiac arrhythmias, unstable coronary heart disease, atrioventricular blocks or bundle branch blocks, heart failure), neurologic, endocrinologic, metabolic, or psychiatric disorders; any electrolyte imbalance; systolic blood pressure ≥ 140 mm Hg or diastolic

Clinical Points

- Patients with alcohol use disorder had significantly higher QT dispersion, corrected QT dispersion, and P-wave dispersion values compared to the control group.
- Patients with a long history of alcohol use disorder with excessive alcohol use had a higher risk of arrhythmia and sudden death compared to the control group.
- Electrocardiogram, which could be easily obtained, and subsequent referral to cardiologic examination would contribute to the follow-up and health of patients with alcohol use disorder.

blood pressure ≥ 90 mm Hg; and body mass index > 24.9 kg/m^2. All participants included in the study were normotensive.

AUD group. Sixty-five consecutive patients diagnosed with AUD and history of abuse for at least 10 years (per *DSM-5* criteria[14]) who applied to the outpatient clinic for treatment were invited to participate in the study. Seven patients declined to participate, 4 did not attend the appointment, and 6 did not meet further study criteria. A total of 48 individuals participated in the study.

Control group. The control group included 48 healthy individuals with no history of alcohol or substance abuse for the past year. The control group comprised men who were referred to the outpatient clinic by any official institutions to prove that they were free of substances of abuse based on urine analyses.

All participants completed a sociodemographic form, which included alcohol history. One unit of liquor was accepted to contain 8–10 g of alcohol (1 unit of liquor: 33 cl beer, 1 glass of wine, single raki, 1 shot of liquor).[15] Alcohol consumption parameters were as follows: 0.1–9.9 g ethanol/d was defined as low, 10–30 g ethanol/d as moderate, and > 30 g ethanol/d as heavy.[16]

Height and weight of all participants were measured, and BMI was calculated. Blood pressure of the participants was measured with an automatic sphygmomanometer (Omron HEM-7113, Omron Healthcare, Lake Forest, Illinois) in secant after 10 minutes of rest. The participants with systolic blood pressure ≥ 140 mm Hg and diastolic blood pressure ≥ 90 mm Hg were excluded in both groups. After 10 minutes of resting, 12-derivation ECG (Cardiofax S, Nihon Kohden, Japan) with 3 standard (I–III), 3 unipolar (aVR, aVL, aVF), and 6 precordial (V1–V6) at a 25 mm/s paper speed and 1.0 mV/cm amplitude standardization was applied. The results were evaluated manually by the cardiologist (S.K.) who was blind to the groups. The distance from the beginning of the Q wave to the end point where the T wave returned to the isoelectric line was measured in milliseconds as the QT interval. The lowest point of the combined section of the T wave and the U wave was accepted as the finishing point of the T wave if there was a U wave.[17] The mean of 3 consecutive QT intervals was accepted as the final value. QTd values were calculated by subtracting the minimum value from the maximum value after measurement of the maximum and minimum values within the 12 derivation of each interval. The QTc durations were calculated according to the Bazett formula: $QTc = QT/\sqrt{(R\text{-}R)}$.[18] The QTc was considered long (long QT) at ≥ 450 ms in men and ≥ 460 ms in women according to the guidelines.[19] The duration of the P-wave was found by measuring the line between the intersection of the starting point of the P-wave and the isoelectric line and the end point of the P-wave and the isoelectric line. Pd was calculated as the difference between the maximum P-wave duration and the minimum P-wave duration.[20]

Analyses

The χ^2 test was used for categorical variables. Since the groups did not exhibit normal distribution, Mann-Whitney U test was used for comparisons.

RESULTS

The mean ± SD age of the AUD group was 44.35 ± 10.24 years and of the control group was 40.90 ± 13.45 years. There was no significant difference between the 2 groups based on age ($P = .108$). There was a significant difference between the groups based on smoking status ($P = .000$); however, there was no significant difference between the groups based on the number of cigarettes smoked daily ($P = .743$). The sociodemographic characteristics of both groups are presented in Table 1. The mean ± SD period of alcohol use was 20.71 ± 12.04 years, and the alcohol consumption was 5.88 ± 1.65 units/d. Mean ± SD alcohol consumption in the AUD group was 5.88 ± 1.65/d, which indicates an excessive consumption rate of about 58 g of alcohol/d.

Patients in the AUD group had significantly higher QTd, QTcd, and Pd values compared to the control group (all $P = .000$), indicating that patients with a long history of AUD with heavy alcohol consumption have a high risk of arrhythmia and resulting sudden death risk. The QTd, QTcd, and Pd values of the groups are presented in Table 2.

DISCUSSION

In the present study, the AUD group's (including male, normotensive, excessive alcohol users) QTd, QTcd, and Pd values were statistically higher compared to those of the control group. Chronic alcohol use may lead to autonomous nervous system dysfunction and QT prolongation,[4] alcoholic cardiomyopathy, myocarditis, myocyte degeneration, and immune system damage.[9] Chronic alcohol use could cause arrhythmia and contractile dysfunction, leading to heart failure, myocardial infarction, and sudden death.[21] The most common cause of death due to cardiovascular disease in patients with AUD is arrhythmia.[22] QTd reflects regional heterogeneity of ventricular repolarization and is an important predictor of arrhythmia and sudden death risk.[23] There are studies[3,24–27] that investigated the effects of acute alcohol intake on QT dispersion in the literature. However, to our knowledge, only 1 study[9] has investigated QTd values in patients with a long AUD and excessive alcohol use

Table 1. Sociodemographic Parameters of the Groups

Parameter	Alcohol Use Disorder Group (n = 48)	Control Group (n = 48)
Highest educational level, n (%)		
Illiterate	1 (2.1)	0 (0)
Elementary school	16 (33.3)	7 (14.6)
Middle school	11 (22.9)	4 (8.3)
High school	14 (29.2)	10 (20.8)
University	6 (12.5)	27 (56.3)
Marital status, n (%)		
Married	32 (66.7)	25 (52.1)
Single	6 (12.5)	16 (33.3)
Divorced	8 (16.7)	4 (8.3)
Widowed	2 (4.2)	3 (6.3)
Smoking, n (%)	41 (85.4)	14 (29.2)

Table 2. QTd, QTcd, and Pd Values of the Groups[a]

Variable	Alcohol Use Disorder Group	Control Group	*P*
Age, y	44.35 ± 10.24	40.90 ± 13.45	.108
QTd, ms	46.56 ± 15.82	26.67 ± 9.53	.000
QTcd, ms	54.25 ± 17.12	30.88 ± 10.60	.000
Pd, ms	44.69 ± 18.14	28.54 ± 10.72	.000
Smoking (no. of cigarettes/d)	22.73 ± 12.68	20.71 ± 4.75	.743

[a]Data presented as mean ± SD (Mann-Whitney U test).
Abbreviations: QTd = QT dispersion, QTcd = corrected QT dispersion, Pd = P-wave dispersion.

history. The Pd indicates the difference between the Pmax and Pmin values. Pd prolongation is a risk factor for atrial fibrillation.[7] Our literature review revealed no study on the effects of alcohol on Pd.

A correlation between high blood alcohol concentration and QTd has been reported.[25] It was suggested that acute ethanol intoxication affects several physiologic mechanisms in the heart such as the autonomous nervous system, ion channels that play a role in action potential, and modulation of receptor proteins, and changes in these mechanisms lead to changes in QTd and Pd.[25] Murata et al[28] and Yokoyama[12] demonstrated that acute alcohol intake affected sympathetic activity, decreased parasympathetic activity, and prolonged QTc in their respective studies.

The results of studies that investigated chronic alcohol use toxicity in the heart were contradictory. It is possible that hypomagnesemia, hypopotassemia, and hypocalcemia,[29] which are common in chronic alcohol use, could play a role in ECG differences. In a study[30] that investigated the etiology of QT prolongation and increase in T-wave voltage in chronic alcoholic patients, it was reported that prolongation incidence, T-wave high voltage levels in V2, sinus tachycardia, and high QRS voltage continued after the 35-day abstinence period. However, QT prolongation did not correlate with any electrolyte level including calcium but did correlate with alcohol use period, consumption volume, and the abstinence period length. Thus, contrary to Härtel et al,[8] the authors[30] concluded that it was difficult to explain the cardiologic abnormalities observed in chronic alcohol use with electrolyte imbalance, and alcoholic myocardial damage could be a cause of QT prolongation.[30] However, in more recent years, it was reported that laboratory findings demonstrated that ethanol inhibited Kv1.5 channel currents and ventricular repolarization.[31,32] Thus, since QT interval and P-wave were determined by repolarization and depolarization mediated by the ion channels, it was concluded that alcohol use could lead to changes in QT and P-waves by causing electrolyte abnormalities.[11] It has also been shown that chronic alcohol use leads to prolongation in the QRS complex, and this finding demonstrates that left ventricular hypertrophy could indirectly lead to changes in QT interval and ST-T configuration and P-wave.[30] In another study,[10] no evidence of cardiac arrhythmia, especially atrial fibrillation, was determined in alcoholic patients; however, an increase in β-receptor density was reported. QTd > 50 ms in healthy individuals indicates high risk for arrhythmia.[33] In the present study, the mean AUD group QTd value was measured as 66.06 ms. The findings of a study by Li et al[11] were consistent with those of the present study. In the study by Li et al[11] conducted with 11,269 people, QTc was more prolonged in individuals with heavy alcohol consumption compared to those who did not consume alcohol, which is consistent with the findings of the present study. The authors[11] also noted a difference between the sexes, as QTc prolongation was 1.4 times higher in males and 2.3 times higher in females compared to healthy controls. In the present study, the AUD group included only male patients due to hospital conditions.

It is known that the alcohol consumption volume is significant in the development of cardiologic effects of alcohol. It was reported that moderate alcohol consumption is associated with increased QTd,[3] and high alcohol concentration leads to prolongation of the P-wave, PR interval, QRS complex, and QTc interval.[26] The present study group was considered to consume excessive alcohol with 58 g of alcohol consumption per day (5.88 ± 1.65/d) and included patients with at least 10 years of alcohol consumption history (mean ± SD of 20.71 ± 12.04 years). In a study[27] that investigated the effects of alcohol on ECG, alcohol injection prolonged the QRS complex period in all subjects and prolonged the P-wave period in some. Uyarel et al[3] reported that alcohol intoxication increased the P-wave period by 9.1%. Similarly, Aasebø et al[26] reported that P-wave and QTc were prolonged in patients with alcohol intoxication compared to the control group. In the present study, the Pd period was significantly longer in patients with long-term and excessive alcohol consumption compared to healthy controls ($P = .000$).

In a study conducted by Corovic et al[9] in patients with a history of excessive alcohol use for more than a decade, it was reported that the frequency of prolongation in QTc was more than 2-fold compared to healthy controls. It was demonstrated that 24.5% of patients had a QTc value of 480 ms, which is known as the threshold value for the development of malignant ventricular arrhythmias; however, the same increase was not observed in healthy controls. In the same study,[9] the QTcd was 50.0 ms in 34.7% of the AUD group, while the same rate was found in only 2.0% of controls. This finding was statistically significant.

Furthermore, QT interval, QTd, QT interval index, QTcd, and QTc interval index were significantly higher in the AUD group compared to healthy controls.[9] Smoking is another factor that affects the electrical stimulation of the heart. It was reported that heart rate, QTc maximum, and QTd were higher in smokers compared to nonsmokers, and adrenergic effects of smoking contributed to this prolongation.[34,35] In the present study, there was a significant difference between the groups based on smoking favoring the AUD group.

The present study has some limitations. The sample included only male subjects due to hospital conditions, which might prevent generalization of the findings to both sexes. Another limitation is that the mean age of the AUD group was higher than the mean age of the control group. Factors such as nutrition, regular exercise, and smoking were confounding variables that are difficult to exclude. The present study was conducted with a cross-sectional design. Prospective studies including both sexes and a larger patient sample and minimization of confounding factors may contribute further to the literature.

CONCLUSION

In the present study, significant differences were found between the groups based on QTd, QTcd, and Pd values favoring the AUD group. Patients with a long history of AUD with excessive alcohol consumption had a high risk of arrhythmia and resulting sudden death risk compared to the control group. ECG, which can be easily obtained during the follow-up period, and subsequent referral for cardiologic examination would contribute to the follow-up and health of patients with AUD.

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