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Evaluation of QTc Interval, Tp-e Interval, Tp-e/QT Ratio and Tp-e/QTc Ratio in Patients with Autosomal Dominant Polycystic Kidney Disease

Otozomal Dominant Polikistik Böbrek Hastalığı Olan Hastalarda QTc Aralığı, Tp-e Aralığı, Tp-e/QT Oranı ve Tp-e/QTc Oranının Değerlendirilmesi

ABSTRACT

Objective: Autosomal dominant polycystic kidney disease (ADPKD) is a complex, progressive condition that primarily involves the kidneys but may also affect other systems, namely the cardiovascular system. It is characterized by the growth of cysts, leading to decreased renal function and finally, to chronic kidney disease. While renal symptoms are the primary focus of treatment, cardiovascular complications play a significant role in morbidity and mortality and there is a paucity of information regarding the risk of arrhythmias in these patients. The evaluation of myocardial repolarization was conducted through a variety of methodologies, including Tp-e, QTc and QT interval assessment. An increasing amount of data suggests that malignant ventricular arrhythmias are linked to a higher Tp-e/QT ratio.

Method: This case-control study of 31 adult patients diagnosed with ADPKD was conducted between May 2021 and April 2024. Control group patients were selected using propensity score matching and were considered to minimize confounding factors. All participants underwent electrocardiography and transthoracic echocardiography studies.

Results: Patients with ADPKD had substantially higher QTc intervals, Tp-e intervals, Tp-e/QT ratio and Tp-e/QTc ratio, than the control group (all P = 0.001). Correlation analysis revealed significant negative correlations between estimated glomerular filtration rate (ml/min./1.73 m^2) and QTc interval (P = 0.002), Tp-e interval (P = 0.003), Tp-e/QT ratio (P = 0.042) and Tp-e/QTc ratio (P = 0.021) in patients with ADPKD.

Conclusion: According to resting ECG findings, patients with ADPKD were predisposed to sudden cardiac death.

Keywords: Autosomal dominant polycystic kidney, electrocardiography, arrhythmia, sudden cardiac death

ÖZET

Amaç: Otozomal dominant polikistik böbrek hastalığı (ODPBH), öncelikle böbrekleri tutan ancak başta kardiyovasküler sistem olmak üzere diğer sistemleri de etkileyebilen karmaşık, ilerleyici bir durumdur. Kistlerin büyümesi ile karakterize olup böbrek fonksiyonlarında azalmaya ve nihayetinde kronik böbrek hastalığına yol açar. Kardiyovasküler komplikasyonlar ODPBH hastalarında önemli bir morbidite ve mortalite nedeni olmasına rağmen, bu hastalarda aritmi ve ani kardiyak ölüm riskine ilişkin bilgiler sınırlıdır. Miyokardiyal repolarizasyon, Tp-e, QTc ve QT aralığı dahil olmak üzere çeşitli yöntemler kullanılarak değerlendirilmiştir. Giderek artan sayıda veri, malign ventriküler aritmilerin daha yüksek Tp-e/QT oranıyla bağlantılı olduğunu göstermektedir. Hipotezimiz ODPBH'li hastalarda kardiyak aritmi ve ani kardiyak ölüm riskinin artmış olduğudur.

Yöntem: ODPBH tanısı konan 31 yetişkin hastayı kapsayan bu tek merkezli vaka kontrol çalışması Mayıs 2021 ile Nisan 2024 tarihleri arasında gerçekleştirilmiştir. Kontrol grubu hastaları, karıştırıcı faktörleri en aza indirmek için eğilim skoru eşleştirmesi kullanılarak seçilmiştir. Tüm katılımcılara elektrokardiyografi ve transtorasik ekokardiyografi çalışmaları yapılmıştır.

Bulgular: ODPBH'li hastalarda QTc aralıkları, Tp-e aralıkları, Tp-e/QT oranı ve Tp-e/QTc oranı kontrol grubuna göre önemli ölçüde daha yüksekti (tümü P = 0,001). Korelasyon analizi, ODPBH'li hastalarda tahmini glümerül filtrasyon hızı ile QTc süresi (P = 0,002), Tp-e aralığı (P = 0,003), Tp-e/QT oranı (P = 0,042) ve Tp-e/QTc oranı (P = 0,021) arasında anlamlı negatif korelasyonlar olduğunu ortaya koydu.

Sonuç: ODPBH'li hastalar istirahat EKG bulgularına göre ani kardiyak ölüme yatkınlık saptanmıştır.

Anahtar Kelimeler: Aritmi, otozomal dominant polikistik böbrek, elektrokardiyografi, ani kardiyak ölüm

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

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Autosomal dominant polycystic kidney disease (ADPKD) is a chronic, multisystem disorder that primarily affects the kidneys, with an estimated global prevalence of 1:400 to 1:1000 in Caucasian individuals.[1] ADPKD is defined by the progressive formation of numerous cysts within the renal cortex and medulla. Cysts grow over time, causing progressive enlargement of the kidneys and contributing to the destruction of the normal renal parenchyma. End-stage renal disease (ESRD) typically manifests in about half of the affected individuals by the sixth decade of life, although this may vary depending on genetic and environmental factors.

The primary genetic basis of ADPKD is mutations in PKD1 (85% of cases) on chromosome 16p13.3 genes and PKD2 (15% of cases) on chromosome 4q22 genes.[1] These proteins play a role in maintaining the structural and functional integrity of renal tubules. Dysfunction of these proteins disrupts signalling pathways and cellular mechanics.[1] Non-renal symptoms mostly affect the liver, heart and vascular system. ADPKD patients have a markedly elevated risk of mortality from cardiac causes, with estimates indicating that this risk is approximately two- to threefold higher than that observed in the general population.[2] Cardiovascular manifestations typically present in the second and third decades and preceding the onset of renal failure.[3]

On resting 12-lead electrocardiography (ECG), the Tp-e interval [T peak (Tp) – T end (Te)] and Tp-e/QT ratio are increasingly being recognized as valuable markers for the assessment of ventricular repolarization heterogeneity and risk stratification for adverse cardiovascular events. The Tp-e interval appears to be relatively unaffected by changes in the heart rate (HR), making it a potentially more stable marker for assessing the distribution of repolarization. It is hypothesized that the Tp-e/QT ratio is a more accurate reflection of transmural dispersion of repolarization, capturing subtle shifts in myocardial repolarization that could be early indicators of increased risk for sudden cardiac death (SCD).[4]

Although cardiovascular complications in patients with ADPKD are well established, information on the risk of arrhythmias and SCD remains limited. The primary aim of the present study was to identify the relationship between ADPKD and early risk factors for cardiovascular complications that contribute to mortality, specifically arrhythmia and SCD. To the best of our knowledge, this is the first study to investigate resting ECG abnormalities in patients with ADPKD.

Methods

Patient Population

This case-control study was conducted between May 2021 and April 2024 with thirty-one adult patients diagnosed with ADPKD in our nephrology outpatient clinic and a 1:1 propensity score-matched control group in our cardiology outpatient clinics.

All participants underwent resting ECG and transthoracic echocardiography (TTE) investigations. A detailed physical examination, a history of chronic disease and medical treatment were performed. Height and weight were measured and body mass index (BMI) as well as body surface area (BSA) were calculated.

ABBREVIATIONS

ADPKD	Autosomal dominant polycystic kidney disease
BMI	Body mass index
bpm	Beats per minute
BSA	Body surface area
CAD	Coronary artery disease
CKD	Chronic kidney disease
DM	Diabetes mellitus
ECG	Electrocardiography
eGFR	Estimated glomerular filtration rate
ESRD	End-stage renal disease
HT	Hypertension
LVMI	Left Ventricular Mass Index
QTc	Corrected QT interval
SCD	Sudden cardiac death
TDR	Transmural dispersion of repolarization
TTE	Transthoracic echocardiography

The estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft–Gault formula: eGFR (ml/min/1.73 m^2) = (140–age) × (weight) × (0.85 if female) / (72×serum creatinine).[5] Patients with chronic kidney disease (CKD) at stage 5 (eGFR < 15), hemodialysis, QT-prolonging medications, electrolyte abnormalities, bundle branch blocks, atrial fibrillation, hypertrophic cardiomyopathy, aortic stenosis, LVEF < 30 and age under 18 years were excluded from the study.

All participants were informed of the purpose and protocol of the study in detail and were included after informed consent was obtained. The study design, protocol and inclusion criteria are shown in Figure 1. Approval for this study was obtained from Kocaeli City Hospital Scientific Research Ethics Committee (Approval Number: 2024-120, Date: 31.10.2024).

ECG Examinations

ECGs were recorded with an amplitude of 0.1 mm/mV and speeds of 25 and 50 mm/h. After scanning, ECG signals were transmitted to a computer. The wave voltage of each ECG signal was measured.

The term "normal heart rate" is defined as a range of 60 to 100 beats per minute (bpm). ECGs were classified in accordance with the previous reports[6] and the QT interval is the temporal period between the start of the QRS complex, the end of the T-wave and the return to the isoelectric line.[7]

The ECG data was analyzed with particular attention paid to the baseline intervals (Figure 2). The QT interval was measured manually on three occasions per lead using ECG callipers and a magnifying glass to ensure accuracy. The mean values of these measurements were used in the analysis. The corrected QT interval (QTc) was calculated using the Bazett formula (QTc = QT /√ (RR interval)). The Tp-e interval, which is the time from the peak to the end of the T wave, was measured in the precordial leads. Tp-e dispersion [Tp–e (d)] was determined by subtracting the corresponding maximum and minimum Tp e intervals. These measurements were taken over three consecutive beats to ensure consistency and reliability in the results.[8]

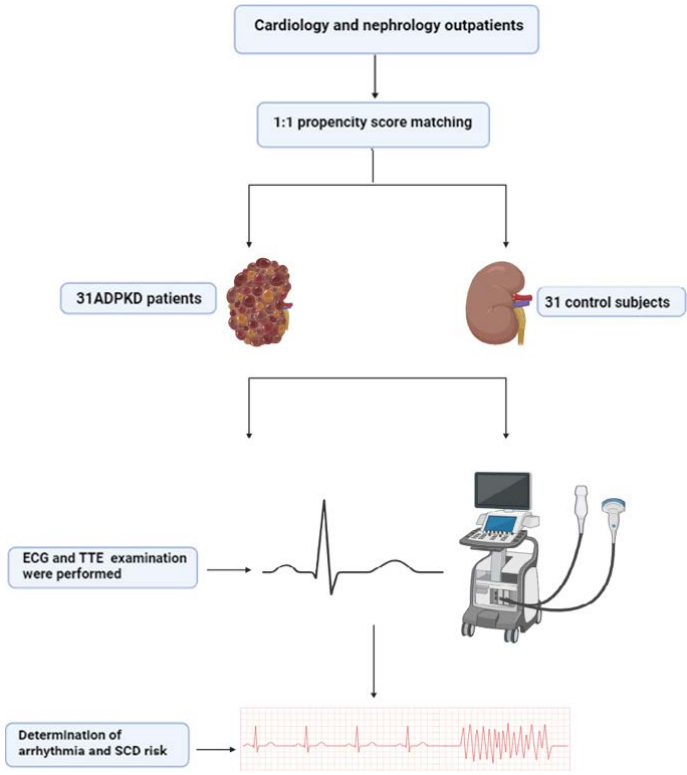

Figure 1. Study design, protocol and clinical pathway for subjects.

For additional analysis, the mean values of the measurements were recorded. The intra-and interobserver variances for the measurements were less than three percent. TTE imaging in the parasternal and apical planes was performed using standard techniques in accordance with the current guidelines.[9] LVH is defined by either an interventricular septum or posterior wall thickness of > 9 mm in women and > 10 mm in men.[9] Left ventricular mass index (LVMI) [g/m^2] was determined using LV mass/BSA.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (version 20.0; IBM SPSS Corp., Armonk, NY, USA). The acquired data was assessed for normality using the Kolmogorov-Smirnov test. Categorical variables were presented in numerical form and as percentages and were compared using Pearson chi-square tests. Continuous variables with a normal distribution were expressed as the mean ± standard deviation, while those with a non-normal distribution were expressed as the median (interquartile ranges, 25th–75th percentiles). Student's t-test and Mann-Whitney U test were employed to assess the statistical significance of differences between continuous variables with normal and non-normal distributions, respectively.

Propensity score matching calculations were performed in a 1:1 ratio to reduce the imbalance of the covariates between the groups and the following variables were included: age, sex, systolic and diastolic blood pressure, BMI, BSA, hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), hyperlipidemia and smoking status. We used 0.2 as a caliper for the propensity score matching method.

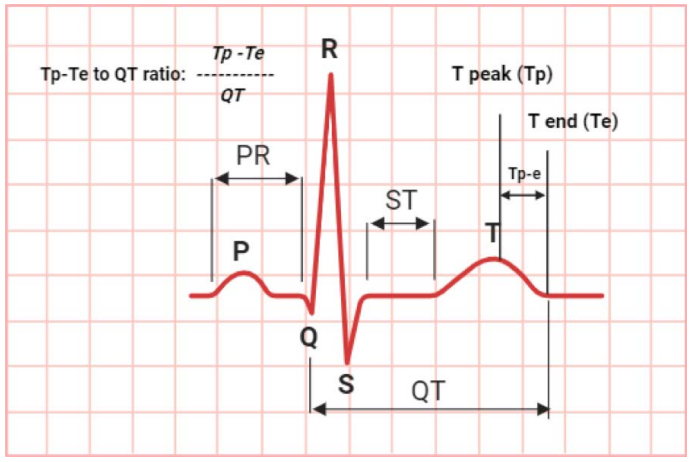

Figure 2. ECG parameters.

Pearson's correlation test was used to analyze the correlation between eGFR levels and ECG results in patients with ADPKD. Regression analysis was used to identify the independent determinants of QTc interval, QTc/QRS ratio, Tp-e/QT and Tp-e/QTc ratio in ECGs. We assessed the results with a 95% confidence interval and used two sited p-values < 0.05 were considered statistically significant.

Results

Sixty-two participants were enrolled, including thirty-one patients with ADPKD [17 men (54.8%); 14 women (45.1%)] and thirty-one propensity score index-matched controls [17 men (54.8%); 14 women (45.1%)] (Table 1). Serum hs-CRP, D-dimer, AST, ALT and fasting glucose levels were found to be similar in both groups. However, serum creatinine (P<0.001), BUN (P = 0.035) and uric acid (P = 0.015) levels were higher and eGFR (P<0.001) levels were lower, in the ADPKD patients (Table 1).

ECG and TTE Findings

Baseline HR, PR interval, QRS interval, QT interval, QT/QRS ratio, Tp-e (d) and QRS interval were similar between the groups. The QTc interval (P < 0.001), Tp-e interval (P < 0.001), Tp-e/QT ratio (P < 0.001), Tp-e/QTc ratio (P<0.001) and QTc/QRS ratio (P = 0.040) were significantly higher in patients with ADPKD, than in the control group (Table 2). Left atrium, LV dimensions and LVEF values were similar between groups (Table 2) but LVMI (P = 0.038), interventricular septal (P = 0.047) and posterior wall thickness (P = 0.021) were significantly higher in patients with ADPKD (Table 2).

TTE examination revealed LVH in twelve patients (38.7%) in the ADPKD cohort and thirteen patients (41.9%) in the control group (Table 3). Compared ECG findings of these patients showed that QTc intervals (P = 0.021), Tp-e intervals (P = 0.037), QTc/QRS ratio (P = 0.035), Tp-e/QT ratio (P = 0.040) and Tp-e/QTc ratio (P = 0.011) were significantly higher in the ADPKD patients (Table 3). Correlation analysis revealed a significant negative correlation between eGFR levels and QTc interval (r = 0.233, P = 0.002), Tp-e interval (r = 0.112, P = 0.003), Tp-e/QT ratio (r = 0.335, P = 0.042) and Tp-e/QTc ratio (r = 0.176, P = 0.021) in ADPKD patients (Figure 3 A–D).

Table 1. The Demographic, Clinical and Laboratory Characteristics of the Patients

	ADPKD (n = 31)	Control (n = 31)	P
Gender (Female), n (%)	14 (45.1)	14 (45.1)	[a]1.000
Age	52.14 (22–82)	53.04 (25–80)	[b]0.654
BMI	25 ± 3.2	24 ± 4.2	[b]0.657
BSA	2.0 ± 0.6	1.9 ± 0.9	[b]0.701
SBP (mm/ Hg)	144 ± 45	140 ± 36	[b]0.327
DBP (mm/ Hg)	88 ± 29	86 ± 19	[b]0.586
Smoking, n (%)	8 (25.8)	9 (29.0)	[a]0.159
Past medical history			
DM, n (%)	4 (12.9)	4 (12.9)	[a]1.000
HT, n (%)	16 (51.6)	15 (48.3)	[a]0.815
HL, n (%)	6 (19.3)	7 (22.5)	[a]0.602
Previous CAD, n (%)	2 (6.4)	3 (7.5)	[a]0.551
Laboratory values			
Creatinine mg/dL	2.12 ± 1.8	1.4 ± 0.9	[c]<0.001*
BUN	27.35 ± 10.5	19.04 ± 8.5	[c]0.035*
eGFR (ml/min/1.73 m^2)	50.1 ± 28.3	75.11 ± 18.4	[c]<0.001*
Hemoglobin, g/dL	12.5 ± 2.1	13.6 ± 3.7	[b]0.021*
Hematocrit	32.2 (23.2–50.4)	38.8 (25.0–48.8)	[b]0.017*
WBC x10^3/μL	6.69 (4.35–12.32)	7.23 (4.23–11.26)	[c]0.168
Platelet x10^3/L	237 ± 81	232 ± 128	[b]0.921
Glucose mg/dL	106.5 (75–242)	107 (78–244)	[c]0.827
AST mg/Dl	22 ± 14	24 ± 12	[c]0.510
ALT mg/Dl	26 ± 10	28 ± 11	[c]0.460
D-dimer ng/mL	0.7 (0.1–2.1)	0.7 (0.2–3.0)	[c]0.153
Uric acid mg/dL	6.2 (1.8–10.1)	3.6 (1.6–8.7)	[c]0.015*
hs-CRP mg/L	5.7 (0.4–15)	6.0 (0.01–14)	[c]0.527
LDL cholesterol mg/dL	133 (65–202)	125 (42–208)	[c]0.189
HDL cholesterol mg/dL	44 (21–67)	47 (23–53)	[c]0.528
Triglyceride mg/dL	139 (55–312)	143 (56–272)	[c]0.335
Medical treatments			
ACE-I/ARBs, n (%)	10 (32.2)	12 (38.7)	[a]0.205
B-Blockers, n (%)	5 (16.1)	6 (19.3)	[a]0.440
Diuretics, n (%)	7 (22.5)	6 (19.3)	[a]0.601
Ca channel blockers, n (%)	4 (12.9)	5 (16.1)	[a]0.406
ASA/anti-aggregant, n (%)	6 (19.3)	8 (22.5)	[a]0.570
Anti-arrhythmic, n (%)	3 (9.6)	3 (9.6)	[a]1.000
Anti- psychotropic, n (%)	–	–	
Other, n (%)	12 (38.7)	14 (45.1)	[a]0.121

Data is presented as numbers and percentages (%), mean (standard deviation) or median (interquartile range). P value was calculated using the student t-test or the Mann–Whitney U-test for continuous variables and the chi-square test for categorical variables as appropriate. *Statistically significant p values (P < 0.05). ACE-I, Angiotensin-Converting Enzyme Inhibitors; ARBs, Angiotensin 2 Receptor Blockers; ASA, Acetylsalicylic Acid; BMI, Body Mass Index; BSA, Body Surface Area; CAD, Coronary Artery Disease; CRP, C-Reactive Protein; DBP, Diastolic Blood Pressure; DM, Diabetes Mellitus; eGFR, Estimated Glomerular Filtration Rate; HL, Hyperlipidemia; HT, Hypertension; SBP, Systolic Blood Pressure; WBC, White Blood Cell; a Pearson Chi-Square, b Student-t test, c Mann-Whitney-U test.

Multivariate linear regression analysis revealed that serum creatinine (P = 0.029), HT (P = 0.015), age (P = 0.017) and LVMI (P < 0.001) were independent predictors of increased QTc interval in patients with ADPKD (Table 4). In addition, hematocrit (P = 0.030), hs-CRP (P = 0.011) and male gender (P = 0.009) independently predicted an increased QTc/QRS ratio, while platelet count (P = 0.002), age (P = 0.041) and DM (P = 0.015) were found to be independent predictors of an increased Tp-e/

Table 2. The Electrocardiographic and Echocardiographic Results of the Groups

	ADPKD group (n = 31)	Control (n = 31)	P
ECG results			
Heart rate (min)	74 ± 13	72 ± 14	0.201
Minor ECG anomaly	6	4	–
Major ECG anomaly	–	–	–
PR (msn)	157 ± 13	155 ± 15	0.608
QRS (msn)	92 ± 11	94 ± 13	0.660
QT (msn)	378 ± 43	363 ± 35	0.194
QTc (msn)	411 ± 34.2	387 ± 30.2	<0.001*
QT/QRS	4.1 ± 0.5	4.0 ± 0.6	0.552
QTc/QRS	4.48 ± 0.67	4.11 ± 0.90	0.040*
Tp-e (msn)	98.8 ± 7.6	84.4 ± 7.7	<0.001*
Tp-e /QT	0.25 ± 0.02	0.20 ± 0.01	<0.001*
Tp-e/QTc	0.23 ± 0.03	0.21 ± 0.02	<0.001*
Tp-e(d) (msn)	16 ± 4	15 ± 4	0.887
TTE results			
LVED (mm)	48.1 ± 4.7	48.9 ± 4.9	0.711
LVES (mm)	30.2 ± 3.1	31.6 ± 5.5	0.620
IVSD (mm)	11.9 ± 1.3	10.3 ± 1.4	0.047*
PW (mm)	11.3 ± 1.3	9.8 ± 0.9	0.021*
LAD (mm)	33.2 ± 4.2	33.6 ± 4.0	0.880
RVED (mm)	25.2 ± 2.8	23.3 ± 1.8	0.257
LV EF	65.2 ± 4.5	64.7 ± 3.7	0.687
LV mass index (g/m^2)	103 ± 10.3	97 ± 6.8	0.038*
Severe valve disease	–	–	–
MVP	1	–	–

IVSD, Interventricular Septal Diameter; LAD, Left Atrial Diameter; LVED, Left Ventricular End Diastolic Diameter; LVES, Left Ventricular End Systolic Diameter; LV EF, Left Ventricular Ejection Fraction; PW, Posterior Wall; RVED, Right Ventricular End Diastolic Diameter. *Statistically significant p values (p ≤ 0.05).

QT ratio. The Tp-e/QTc ratio was also found to be independently predicted by male gender (P = 0.012), hemoglobin level (P = 0.007) and HT (P = 0.018) (Table 4).

Discussion

In our study, resting ECG results were analyzed in ADPKD patients and a tendency to arrhythmias and SCD was observed in this group. ADPKD patients are at an elevated risk of cardiovascular disease, independent of their kidney function. Young individuals with ADPKD and normal renal function exhibit several cardiovascular complications, including endothelial dysfunction, diminished coronary flow velocity reserve, biventricular diastolic dysfunction and arterial stiffness.[3–10] Furthermore, valvular disease, pericardial effusion, cardiomyopathy, aortic root enlargement and aneurysms have been reported in various locations, including intracranial vessels.[11–13]

Abou Heidar et al.[14] conducted a study involving 71 531 hospital admissions and associated clinical data from adult patients with

Table 3. The Electrocardiographic Results of the LVH Patients

	ADPKD group (n=12, 38.7%)	Control (n= 13, 41.9%)	P
Heart rate (min)	75 ± 10	77 ± 15	0.550
Minor ECG anomaly	4	2	–
Major ECG anomaly	–	–	–
PR (msn)	160 ± 18	164 ± 14	0.327
QRS (msn)	98 ± 18	94 ± 12	0.578
QT (msn)	388 ± 52.2	374 ± 31.3	0.075
QTc (msn)	421 ± 43.1	402.5 ± 21.7	0.021*
QT/QRS	4.0 ± 0.4	4.2 ± 0.4	0.446
QTc/QRS	4.48 ± 0.67	4.09 ± 0.88	0.035*
Tp-e (msn)	99.7 ± 5.7	89.7 ± 8.4	0.037*
Tp-e /QT	0.25 ± 0.01	0.23 ± 0.01	0.040*
Tp-e/QTc	0.24 ± 0.02	0.22 ± 0.02	0.011*

*Statistically significant P values (P < 0.05).

Table 4. Multivariate linear regression analysis in ADPKD patients (n = 31)

	B coefficient	P
QTc interval		
Hypertension	-0.225	0.015
Creatinine	-0.288	0.029
Age	-0.285	0.017
LVMI	0.321	<0.001
QTc/QRS ratio		
Hematocrit	0.302	0.030
Hs-CRP	-0.265	0.011
Male gender	-0.248	0.009
Tp-e/QT ratio		
Platelet	-0.382	0.002
Age	0.297	0.041
Diabetes mellitus	0.151	0.015
Tp-e/QTc ratio		
Male gender	0.202	0.012
Hemoglobin	-0.223	0.007
Hypertension	-0.201	0.018

ADPKD, which revealed the presence of ischemic heart disease (19.3%), arrhythmias (14.2%) and heart failure (13.1%) in this cohort. After adjustment for confounding factors of sex, age and comorbidities, a 1.31-fold increased risk of atrial fibrillation was reported to be significantly associated in patients with ADPKD compared to the normal population.[15]

HT is a common initial and significant modifiable risk factor for ADPKD, with a strong correlation with the onset and progression of ESRD. Additionally, ADPKD causes blood pressure to lose its diurnal regularity. However, the precise mechanism underlying the QTc prolongation in HT remains unclear. Some reports have proposed that the aldosterone/

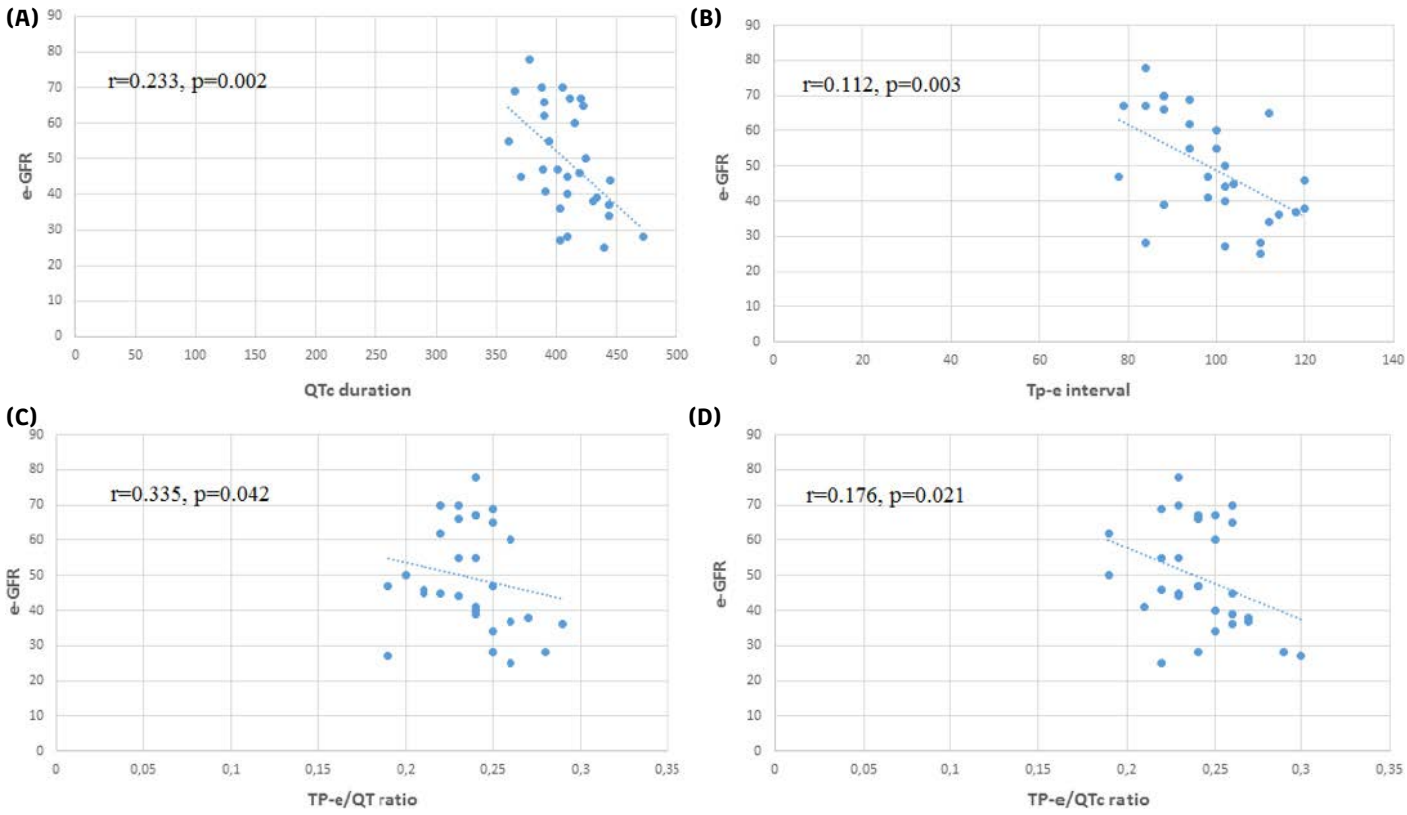

Figure 3. (A) Correlation analysis between eGFR and QTc interval, (B) Correlation analysis between eGFR and Tp-e interval, (C) Correlation analysis between eGFR and Tp-e/QTc ratio, (D) Correlation analysis between eGFR and Tp-e/QTc ratio.

active renin ratio may be linked to arrhythmic risk in HT.[16] Specifically, elevated aldosterone levels have been associated with repolarization abnormalities due to an increased density of myocardial capillaries, aberrant matrix proteins and elevated superoxide levels in mitochondria.[16]

LVH is an independent risk factor for cardiovascular disease.[17,18] An increased LVMI is associated with unfavourable clinical results in this patient population, according to the study by Imaizumi et al.[19] LVH introduces electrical heterogeneity due to fibrosis, ischemia and cellular remodelling. An increase in arrhythmia substrates was found in the ADPKD group in an ECG comparison of patients with increased LVH. Despite similar TTE results, it is clear that this finding indicates a disease-specific increased risk of arrhythmia in patients with ADPKD. Further studies are required to elucidate the exact underlying pathophysiology.

An increase in the QTc interval as CKD progresses, independent of other risk factors, has been shown in previous studies.[20] ADPKD may indirectly affect the QT interval and furthermore, numerous factors have been linked to QT prolongation, such as sex, age, electrolyte imbalances, thyroid disorders, genetic mutations, medications and HT.[4] Several techniques, including QT, QTc and transmural dispersion of repolarization (TDR), have been used to measure myocardial repolarization.[4,21] Increased QT and QTc are well-established markers for arrhythmogenic substrates and are linked to both ventricular arrhythmias and SCD,[22,23] particularly in conditions such as LVH.[22,23] Tp-e is thought to represent the difference in repolarization times among all myocardial layers: endocardium, myocardium and epicardium. Prolonged Tp-e and increased TDR have been strongly associated with ventricular tachyarrhythmias in various pathologies, including LVH, long QT syndrome and cardiomyopathies.[24,25]

The literature suggests that there is a delay in cardiac repolarization as CKD progresses, independent of other risk factors. This suggests a relationship between renal function and cardiac repolarization in patients with CKD, which may contribute to an increased risk of sudden cardiac death and susceptibility to drug-induced arrhythmias.[26] In a three-year follow-up study of patients with ADPKD, the QTc interval and heart rate exhibited a slight reduction compared to the baseline in the group treated with tolvaptan a short-acting vasopressin V2 receptor inhibitor. Conversely, the QTc interval demonstrated a significant increase in the control group.[26]

In our study, arrhythmic substrates were significantly higher in patients with ADPKD and this trend may have been exacerbated by the higher LVH, LV mass and LVMI in the ADPKD group. This finding aligns with previous reports in the relevant literature.[27]

As kidney function declines in ADPKD, the body's ability to maintain a proper electrolyte balance, which is crucial for normal heart rhythm, may be affected. An imbalance, particularly hyperkalemia or hypokalemia and fluid overload, may lead to malignant arrhythmias. In addition, hypocalcemia

and hypomagnesemia prolong the QTc interval. Patients with ESRD often require dialysis, which can also trigger arrhythmias due to shifts in electrolyte and fluid balances. Studies show that patients on dialysis are at a higher risk of QTc prolongation, especially during and after dialysis sessions.[28] In order to regulate blood pressure and address cardiac issues, patients may require the administration of pharmacological agents, including beta-blockers, diuretics and other cardiovascular therapies. The QTc interval may be prolonged by various pharmacological agents including antiarrhythmic drugs, certain antibiotics and antipsychotics. No discrepancy was observed between the groups with regard to medications. In the present study, a negative correlation was identified between eGFR and arrhythmic substrates in patients with ADPKD. These findings suggest that as renal function deteriorates in ADPKD, there is an increase in arrhythmia tendency.

Mitral and aortic valve calcifications and regurgitation increase as renal failure advances. The identification of these disorders is of crucial importance because they have the potential to induce systolic and diastolic dysfunction, heart failure (particularly mitral regurgitation) and arrhythmias. No significant valvular disease was detected in this study.

Limitations

A limitation of the present study is the small sample size and the use of experience from only a single center. Additionally, the absence of longitudinal follow-up (e.g., arrhythmic events and mortality data) limits the prognostic interpretation of the findings and creates a significant gap in the scope of the study.

Conclusions

In patients with ADPKD, especially those with declining kidney function, the QTc interval can be prolonged because of electrolyte imbalances, medications and other cardiovascular complications. Therefore, careful monitoring and proactive management are required to prevent serious cardiac events. Early treatment of cardiovascular risk factors is important for preventing arrhythmias in patients with ADPKD.

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References

1. Lee JJ, Cheng SJ, Huang CY, et al. Primary cardiac manifestation of autosomal dominant polycystic kidney disease revealed by patient induced pluripotent stem cell-derived cardiomyocytes. *EBioMedicine*. 2019;40:675-684. [CrossRef]
2. Helal I, Reed B, Mettler P, et al. Prevalence of cardiovascular events in patients with autosomal dominant polycystic kidney disease. *Am J Nephrol*. 2012;36(4):362-370. [CrossRef]
3. Sagar PS, Rangan GK. Cardiovascular Manifestations and management in ADPKD. *Kidney Int Rep*. 2023;8(10):1924-1940. [CrossRef]
4. Zhao D, Liang B, Peng J, et al. Tp-e and (Tp-e)/QT ratio as a non-invasive risk factors for malignant ventricular arrhythmia in patients with idiopathic ventricular premature complexes. *J Clin Lab Anal*. 2021;35(2):e23636. [CrossRef]
5. Michels WM, Grootendorst DC, Verduijn M, Elliott EG, Dekker FW, Krediet RT. Performance of the cockcroft-gault, MDRD, and new CKD-EPI formulas in relation to GFR, age, and body size. *Clin J Am Soc Nephrol*. 2010;5(6):1003-1009. [CrossRef]
6. Auer R, Bauer DC, Marques-Vidal P, et al. Association of major and minor ECG abnormalities with coronary heart disease events. *JAMA*. 2012;307(14):1497-1505. [CrossRef]
7. Beach SR, Celano CM, Noseworthy PA, Januzzi JL, Huffman JC. QTc prolongation, torsades de pointes, and psychotropic medications. *Psychosomatics*. 2013;54(1):1-13. [CrossRef]
8. Yıldız SS, Sutaşır MN, Sığırcı S, et al. Acute effects of synthetic cannabinoids on ventricular repolarization parameters. *Turk Kardiyol Dern Ars*. 2019;47(5):384-390. [CrossRef]
9. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2015;28(1):1-39.e14. [CrossRef]
10. Pietrzak-Nowacka M, Safranow K, Płońska-Gościniak E, et al. Cardiovascular involvement in patients with autosomal dominant polycystic kidney disease: A review. *Kidney Blood Press Res*. 2024;49(1):9-19. [CrossRef]
11. Righini M, Mancini R, Busutti M, Buscaroli A. Autosomal dominant polycystic kidney disease: Extrarenal involvement. *Int J Mol Sci*. 2024;25(5):2554. [CrossRef]
12. Dugar F, Pradella M, Kessel-Schaefer A, Kettnaker P, Haaf P. Cardiac manifestations of autosomal dominant polycystic kidney disease. *Eur Heart J Imaging Methods Pract*. 2025;3(1):qyaf003. [CrossRef]
13. Liu J, Fujikura K, Dev H, et al. Pericardial effusion on MRI in autosomal dominant polycystic kidney disease. *J Clin Med*. 2022;11(4):1127. [CrossRef]
14. Abou Heidar N, Chehab O, Morsi RZ, et al. Association of autosomal dominant polycystic kidney disease with cardiovascular disease: A US-National Inpatient Perspective. *Clin Exp Nephrol*. 2022;26(7):659-668. [CrossRef]
15. Yu TM, Chuang YW, Yu MC, et al. New-onset atrial fibrillation is associated with polycystic kidney disease: A nationwide population-based cohort study. *Medicine (Baltimore)*. 2016;95(4):e2623. [CrossRef]
16. Gouli A, Kaltsas G, Tzonou A, et al. High prevalence of autonomous aldosterone secretion among patients with essential hypertension. *Eur J Clin Invest*. 2011;41(11):1227-1236. [CrossRef]
17. Paoletti E, De Nicola L, Gabbai FB, et al. Associations of left ventricular hypertrophy and geometry with adverse outcomes in patients with CKD and hypertension. *Clin J Am Soc Nephrol*. 2016;11(2):271-279. [CrossRef]
18. Stewart MH, Lavie CJ, Shah S, et al. Prognostic implications of left ventricular hypertrophy. *Prog Cardiovasc Dis*. 2018;61(5-6):446-455. [CrossRef]
19. Imaizumi T, Fujii N, Hamano T, et al. Excess risk of cardiovascular events in patients in the United States vs. Japan with chronic kidney disease is mediated mainly by left ventricular structure and function. *Kidney Int*. 2023;103(5):949-961. [CrossRef]

20. Sherif KA, Abo-Salem E, Panikkath R, Nusrat M, Tuncel M. Cardiac repolarization abnormalities among patients with various stages of chronic kidney disease. *Clin Cardiol*. 2014;37(7):417-421. [CrossRef]
21. Alizade E, Avcı A, Fidan S, et al. The effect of chronic anabolic-androgenic steroid use on Tp-E Interval, Tp-E/Qt ratio, and Tp-E/Qtc ratio in male bodybuilders. *Ann Noninvasive Electrocardiol*. 2015;20(6):592-600. [CrossRef]
22. Zhao Z, Yuan Z, Ji Y, Wu Y, Qi Y. Left ventricular hypertrophy amplifies the QT, and Tp-e intervals and the Tp-e/ QT ratio of left chest ECG. *J Biomed Res*. 2010;24(1):69-72. [CrossRef]
23. Alonso MAG, Lima VACC, Carreira MAMQ, Lugon JR. Reproducibility and reliability Of QTc and QTcd measurements and their relationships with left ventricular hypertrophy in hemodialysis patients. *Arq Bras Cardiol*. 2017;109(3):222-230. [CrossRef]
24. Demir M, Uyan U. Evaluation of Tp-e interval and Tp-e/QT ratio in patients with non-dipper hypertension. *Clin Exp Hypertens*. 2014;36(5):285-288. [CrossRef]
25. Smetana P, Schmidt A, Zabel M, et al. Assessment of repolarization heterogeneity for prediction of mortality in cardiovascular disease: Peak to the end of the T wave interval and nondipolar repolarization components. *J Electrocardiol*. 2011;44(3):301-308. [CrossRef]
26. Demiray A, Ozan R, Özaytürk SG, et al. Evaluation of the renal and cardiovascular effects of long-term tolvaptan treatment in autosomal dominant polycystic kidney disease. *Cardiorenal Med*. 2024;14(1):167-177. [CrossRef]
27. Yılmaz M, Kayançiçek H. Elevated LV mass and LV mass index sign on the athlete's ECG: Athletes' hearts are prone to ventricular arrhythmia. *J Clin Med*. 2018;7(6):122. [CrossRef]
28. Bozaci I, Tatar E. Prolongation of QTc interval at the beginning and during dialysis is associated with hypervolemia and calcium and magnesium change in the first 2 h. *Int Urol Nephrol*. 2022;54(6):1399-1408. [CrossRef]