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Comparison of pathological electrocardiographic changes between long-term kidney transplant recipients and hemodialysis patients

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ABSTRACT

Aims: We aimed to reveal electrocardiographic changes in kidney transplant recipients (KTRs) compared with hemodialysis patients.

Methods: We included 70 KTRs who had underwent a kidney transplantation for more than one year and 84 patients who had been on hemodialysis for more than one year. We recorded age, sex, body-mass index (BMI) (kg/m^2), primary disease (makes chronic kidney disease) and duration of hemodialysis treatment. Standard measurements such as heart rate (HR), P wave, PR interval, P axis, QRS complex, QRS axis, T axis, QT interval and QTc interval were performed for all electrocardiography (ECG).

Results: KTRs were younger than the hemodialysis patients group (HPG) (31.5 vs. 54.5, p<0.001). The female gender was more common in the HPG (54.8% vs. 28.6%, p=0.001). Diabetes mellitus (DM) and hypertension (HT) were more common in the HPG (21.4% vs. 7.1% and 47.6% vs. 15.7% respectively, p<0.001). There was no statistically significant difference between KTRs and HPG in terms of heart rate, P axis, P-wave, QRS axis, QRS complex, RR interval, while T axis was higher in HPG (65o vs. 40.5o, p=0.001), PR interval was longer in HPG (152 msec vs 144 msec, p=0.020), QT interval was longer in HPG (385 msec vs 360 msec, p<0.001), QTc was longer in HPG (463 msec vs 415.5 msec, p<0.001).

Conclusion: In the long term after kidney transplantation, improvement of ECG pathologies such as prolonged QT and abnormal T axis seen in HPG may be the result of an improved uremic milieu and reduced inflammation in KTRs.

Keywords: Kidney transplant recipient, hemodialysis, prolonged QT

INTRODUCTION

Cardiovascular mortality is the most common cause of death in hemodialysis patients. Accelerated atherosclerosis in chronic kidney disease (CKD) leads to a higher incidence of cardiovascular disease in hemodialysis patients than in the general population, irrespective of the underlying CKD disease. Heart failure (HF) left ventricular hypertrophy (LVH), and coronary artery disease (CAD) are the most common cardiovascular diseases in hemodialysis patients.[1,2] However, not all cardiovascular mortality in hemodialysis patients is due to ischemic heart disease. In hemodialysis patients, 40% of deaths are sudden deaths, which occur more frequently than in the general population. Most sudden deaths are thought to be due to fatal arrhythmias.[3,4] In addition to HF, LVH and CAD, which are more common in dialysis patients compared to the general population, uremia, metabolic acidosis, hyperkalemia and electrolyte changes during hemodialysis as well as changes in body fluid composition can cause the development of fatal arrhythmias (bradyarrhythmia or tachyarrhythmia).[3]

The improvement of the uremic milieu, the electrolyte abnormalities, the metabolic acidosis and decrease in inflammation after kidney transplantation create favorable conditions with regard to cardiovascular disease compared to hemodialysis. However, cardiovascular mortality and complications after kidney transplantation are still higher than in the general population, even if they are lower compared to hemodialysis patients.[5]

ECG monitoring and follow-up in hemodialysis patients has been shown to be a useful tool for monitoring changes that may be predictive of mortality in this population. The best known of these ECG changes thought to be associated with mortality is the prolongation QT.[6]

In this study, we aimed to reveal the ECG changes that can be observed in kidney transplant recipients compared to hemodialysis patients.

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METHODS

The study was carried out with the permission of Gazi Yaşargil Training and Research Hospital Clinical Researches Ethics Committee (Date: 29.09.2023 Decision No: 524). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

We recorded patients' age, gender, body-mass index (BMI) (kg/m^2), primary disease makes chronic kidney disease, spending time on diaylsis. All ECG recordings were made at the beginning of the dialysis session in the first session of the week. ECG recordings were performed at a speed of 25 mm/s and an amplitude of 10 mm/mV using a Schiller AT 102 G2 12-lead/12-channel ECG machine. All ECGs were scanned at a resolution of 300 DPI and transferred to an electronic storage medium. The images were evaluated using the program "Adobe Photoshop CS2 Version 9.0" with a resolution of 1500 DPI and an accuracy of four milliseconds. Standard measurements such as heart rate (HR), P-amplitude, PR interval, P axis, QRS complex, QRS axis, T axis, QT interval and QTc interval were performed for all ECGs. The duration of the P wave was assessed as the duration between the initial deflection and its return junction to the isoelectric baseline. QT interval was calculated as the duration between the onset of the QRS complex and the end of T wave in the isoelectric baseline. QTc was measured using Bazett's formula ($QTc=QT/\sqrt{RR}$).[7,8]

Statistical Analysis

Variables with normal distribution are given as mean±standard deviation, variables without normal distribution as median (minimum-maximum). The p value obtained by comparing normally distributed numerical variables with the t-test for independent samples and the p-value obtained by comparing non-normally distributed numerical variables with the Mann-Whitney U test are indicated. The result of the chi-square test p is given by indicating the percentages of the categorical variables and taking into account the expected value. The statistical significance level was assumed to be $p<0.05$.

RESULTS

The demographic characteristics of the general population, KTRs and hemodialysis patients are shown in Table 1. The median age of all patients was 42 years and 42.9% of patients were female. The median BMI of all patients was 22.5 kg/m^2. The median number of months spending on hemodialysis was 16 months. Regarding the etiology of CKD, 33.1% (n=51) were HT, 14.9% (n=23) DM, 6.5% glomerulonephritis (GN) and 45.55% other diseases (n=70). Hemodialysis patients were older than KTRs (54.5 vs. 31.5, $p<0.001$). The HPG had a higher female sex ratio (54.8% vs. 28.6%, $p=0.001$). There was a difference between the groups regarding the etiology of CKD ($p<0.001$); HT was more common in the HPG (47.6% vs. 15.7%), DM was more common in the HPG (21.4% vs. 7.1%) and GN was less common in the HPG (2.4% vs. 11.4%).

The clinical characteristics of KTRs are listed in Table 2. Most patients (94.3%) underwent living kidney transplantation. Induction therapy was mostly (72.9%) administered as ATG, and the proportion of patients who did not receive induction therapy was 7.1%. The median mismatch rate was 3, the mean was 2.6, and the graft loss rate was 1.4%.

Table 1. Demographic characteristics of patients

	Whole population (n=154)	Kidney transplant recipients (n=70)	Hemodialysis patients (n=84)	p
Age	42 (15-88)	31.5 (15-61)	54.5 (19-88)	<0.001[a]
Gender, f/m (f%)	66/88 (42.9%)	20/50 (28.6%)	46/38 (54.8%)	0.001[b]
BMI, kg/m^2	22.5 (13.3-42.3)	22.2 (13.8-33.6)	22.8 (13.3-42.3)	0.519[a]
Spending time on dialysis, months	16 (0-204)	2 (0-197)	28 (4-204)	<0.001[a]
CKD etiology				
HT	51 (33.1%)	11 (15.7%)[a]	40 (47.6%)[b]	<0.001[b]
DM	23 (14.9%)	5 (7.1%)[a]	18 (21.4%)[b]	
GN	10 (6.5%)	8 (11.4%)[a]	2 (2.4%)[b]	
Others	70 (45.5%)	46 (65.7%)[a]	24 (28.6%)[b]	

[a]: Mann-Whitney U test, [b]: Pearson Chi-square test, BMI: Body-mass index, CKD: Chronic kidney disease, HT: Hypertension, DM: Diabetes mellitus, GN: Glomerulonephritis

Table 2. Clinical caharacteristics of kidney tranplanted recipients

Type of donor	
Deceased	4 (5.7%)
Living	66 (94.3%)
Induction regimen	
None	5 (7.1%)
IL-25 blockage	14 (20%)
ATG	51 (72.9%)
Number of missmatch	2.6±1.8 3 (0-5)
BPAR, y/n (y%)	4/70 (5.7%)
Graft loss, y/n (y%)	1/69 (1.4%)
Creatinin, mg/dL	
At discharging time	0.88 (0.78-1.92)
At second year	1 (0.89-1.22)
At fourth year	0.96 (0.9-2.21)
Last visit	1.01 (0.86-1.85)
ECG evaluation time, months	61.2±38.7 58.9 (8.1-130.3)

ATG: Anti-thymocyte globulin, BPAR: Biopsy proven acute rejection, ECG: Electrocardiography

Some clinical characteristics of the KTRs before and after kidney transplantation are shown in Table 3. Accordingly, high density cholesterol (HDL) increased after kidney transplantation (40 mg/dl vs. 37 mg/dl, $p<0.001$), there was no statistically significant change in triglycerides, low density cholesterol (LDL) and total cholesterol, the number of HT patients increased (46 vs. 17, $p<0.001$), the number of DM patients increased (14 vs. 3, $p=0.007$), and there was no statistically significant difference in terms of CAD and cerebrovascular event (CVE).

The ECG characteristics of the kidney transplant and HD patient groups are shown in Table 4. Accordingly, no statistically significant difference was found in terms of heart

rate, P axis, P wave, QRS axis, QRS complex and RR interval, while T axis was higher in the HD patient group (65° vs. 40.5°, p=0. 001), PR interval was longer in HD patient group (152 msec vs. 144 msec, p=0.020), QT interval was longer in the HD patient group (385 msec vs. 360 msec, p<0.001), QTC was longer in the HD patient group (463 msec vs. 415.5 msec, p<0.001).

Table 3. Clinical characteristics of kidney transplant patients before and after transplantation

(n=69), missing data=1	Pre-transplantation	Post-transplantation	p
Tryglicerid	164 (32-756)	132 (28-409)	0.268[a]
Total cholesterol	169 (105-314)	161 (90-288)	0.657[a]
HDL cholesterol	37 (14-98)	40 (18-100)	<0.001[a]
LDL cholesterol	92 (14-252)	87 (26-219)	0.146[a]
Hypertension, y/n (y%)	17/52 (24.6%)	46/23 (66.7%)	<0.001[b]
Diabetes mellitus, y/n (y%)	3/66 (%4.3)	14/55 (20.3%)	0.007[b]
Coronary artery disease, y/n (y%)	5/64 (7.2%)	4/64 (5.8%)	1.000[b]
Cerebrovasculary event, y/n (y%)	0/69 (0%)	0/69 (0%)	1.000[b]

[a]: Wilcoxon test, [b]: McNemar test, HDL: High density cholesterol, LDL: Low density cholesterol

Table 4. Electrocardiographical characteristics of patients

	Kidney transplant recipients (n=70)	Hemodialysis patients (n=84)	p
Heart rate	80.5±12.8	84.5±14.8	0.084[a]
P axis	+49.5° (-59°/+90°)	+49° (-63°/+180°)	0.793[b]
P wave, msec	105 (62-147)	107 (60-193)	0.687[b]
QRS axis	+30° (-47°/+98°)	+28° (-72°/+211°)	0.695[b]
QRS complex, msec	88 (72-140)	90 (66-173)	0.223[b]
T axis	+40.5° (-73°/+225°)	+65° (-67°/+266°)	0.001[b]
T axis classification			
Normal 15°-75°≤	50 (71.4%)[a]	38 (45.8%)[b]	
Borderline <15°-≥-15° and <75°-≤105°	8 (11.4%)[a]	20 (24.1%)[b]	0.006[c]
Abnormal <-15°-≥-180° and >105°-≤105°	12 (17.1%)[a]	25 (30.1%)[a]	
RR interval, msec	744 (537-1178)	703 (529-1273)	0.072[b]
PR interval, msec	144 (97-198)	152 (81-246)	0.020[b]
PR>200 msec, y/n (y%)	0/70 (100%)	4/79 (4.8%)	0.063[d]
QT interval, msec	360 (291-451)	385 (251-520)	<0.001[b]
QTc, msec	415.5 (354-496)	463 (299-551)	<0.001[b]

[a]: Independent sample t test, [b]: Mann Whitney U test, [c]: Pearson Chi-square test, [d]: Continuity correction

DISCUSSION

In our study, we found that ECG changes, which are risk factors for cardiovascular disease and mortality, improved in the long term after kidney transplantation compared to hemodialysis patients. We showed that QT duration was shorter and abnormal T axis changes were reduced in the long term after kidney transplantation compared to hemodialysis patients.

The risk of cardiovascular mortality is up to 100 times higher in the CKD population compared to the general population.[9] The functions of the kidney and heart are interconnected and interrelated. Impairment of the function of one of the two organs has a negative effect on the function of the other organ and leads to unfavorable clinical outcomes, which we define as cardiorenal syndrome. In addition to the contribution of the underlying disease causing CKD, such as HT and DM, to the development of cardiovascular disease in CKD patients, CKD-specific factors such as uremic toxins, inflammation, vascular calcification and thrombosis also contribute to the development of cardiovascular disease. Myocardial fibrosis and left ventricular hypertrophy, which develop as a result of collagen deposition between cardiomyocytes and capillaries in the myocardial region, are present in 70-80% of stage 5 CKD patients and are independent predictors of survival.[9] In patients with CKD, ischemic heart disease, heart failure, atrial fibrillation and arrhythmias are the most common causes of cardiovascular-related death.[1,2,10] Sudden cardiac death occurs up to twice as often in hemodialysis patients in the first 3 months than in peritoneal dialysis patients and is significantly more common in RRT recipients than in the general population. The fatal arrhythmias underlying sudden cardiac death are ventricular fibrillation, ventricular tachycardia, asystole and bradyarrhythmias.[3,11] Possible factors such as pre-existing hyperkalemia, acidosis, rapid potassium correction in dialysis, low calcium in the dialysate, and volume changes during hemodialysis can lead to cardiac electrical instability and potentially life-threatening arrhythmias.[3,11] The QT interval is used as a measure of ventricular depolarization and repolarization and has been shown to be prolonged in patients with CKD in many studies.[12-15] All-cause mortality and cardiovascular mortality are significantly increased in CKD patients with prolonged QT interval.[16,17] Many studies have shown that QT duration is shortened after kidney transplantation compared to hemodialysis patients and is still longer compared to the normal population.[12,18-20] Many of the etiologic risk factors for QT prolongation,[19] such as hypokalemia, hypocalcemia, hyponatremia, and low dialysate calcium intake, which are commonly seen in hemodialysis patients, disappear after renal transplantation. In addition, an improved uremic milieu and reduced inflammation as well as improved autonomic functions lead to better clinical outcomes in terms of cardiovascular disease in kidney transplant patients compared to hemodialysis patients. Akcay et al.[12] found a QTc value of 413.5 msec in renal transplant recipients and 421 msec in hemodialysis patients. Monfared et al.[18] found a maximum QTc of 436.3 msec in renal transplant recipients and 464.7 msec in hemodialysis patients. In another study, Monfared et al.[19] found 444.9 msec in renal transplant recipients and 471 msec before hemodialysis and 473 msec after hemodialysis in hemodialysis patients. In our study, similar to the literature, we found QT and QTc of 360 and 385 msec in renal transplant recipients and 415.5 and 463 msec in hemodialysis patients, respectively. Although there are studies showing that prolonged QT time is associated with mortality,[16,17] in a recent systematic meta-analysis that included 16 studies, the authors concluded that there is insufficient data to predict malignant ventricular arrhythmias

and cardiac arrest.[22] Limitations should be considered, such as the heterogeneity of the population in the studies included in this meta-analysis and the fact that the inclusion criteria represent only 2.3% of the relevant publications in the literature. In addition, only one study[13] from the CKD population was included in this meta-analysis, which did not include kidney transplant recipients, so it does not seem very appropriate to say that there is no association between prolonged QT and fatal arrhythmias and cardiovascular mortality in the CKD population. In our study, we evaluated the ECGs of KTRs after an average of 5 years and compared them with those of hemodialysis patients. Therefore, it was not possible to say whether the shortening of the QT interval occurred early after transplantation.

Scherer et al.[23] showed that a deviation of the T axis of more than 45° was associated with increased coronary artery calcification in elderly people of both sexes. In our study, we showed that the T axis regressed after kidney transplantation compared to hemodialysis patients (65° vs 40.5°). According to the classification of the T axis, the number of patients with borderline and abnormal T axis was higher in hemodialysis patients. This could be due to the fact that left ventricular hypertrophy, electrolyte abnormalities, pulmonary hypertension leading to right ventricular overload, and ischemic heart disease causing T axis abnormalities are more common in hemodialysis patients than in kidney transplant patients. In addition, vascular and coronary calcification are known clinical cardiovascular outcomes in hemodialysis patients. After kidney transplantation, this clinical process may improve.

Some sociodemographic differences in the study groups may have influenced the ECG differences between the groups. In the group of hemodialysis patients, the proportion of older patients, DM and HT was higher. DM, HT and advanced age are known risk factors for cardiovascular disease. Therefore, some ECG changes in our hemodialysis patient group could be due to these differences between the groups. Furthermore, since the ECGs of the patients were evaluated after a long period of time after transplantation, the presence of positive improvements in the lipid profile in the post-transplant period, such as higher HDL, as in our patients, may have influenced our results. These differences in the sample of our study make it difficult to make a clear causal interpretation of the results. Studies conducted in groups with similar sociodemographic characteristics and similar chronic diseases could help us to better understand cardiovascular disease and associated ECG changes in the post-transplant period.

Limitations

Due to the nature of this retrospective study, it was not possible to identify possible risk factors that may cause ECG abnormalities in both hemodialysis patients and KTRs. As this was a cross-sectional study, it was not possible to reflect the changes that may develop over time in the ECG of KTRs. As the aim of the study was to determine ECG changes after kidney transplantation, we were unable to detect the difference in these ECG abnormalities from healthy patients as a healthy group was not included in the study. As this was not a mortality and survival study, we could not detect the association between ECG abnormalities and survival in either group.

CONCLUSION

In conclusion, we have shown that renal transplant patients have shorter QT duration and lower T axis deviation during long-term post-transplant follow-up compared to hemodialysis patients. Prospective studies in KTRs are needed to demonstrate the impact of these ECG changes on cardiovascular clinical outcomes and patient survival.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Gazi Yaşargil Training and Research Hospital Clinical Researches Ethics Committee (Date: 29.09.2023 Decision No: 524).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Johansen KL, Chertow GM, Gilbertson DT, et al. US Renal Data System 2021 Annual Data Report: Epidemiology of Kidney Disease in the United States. *Am J Kidney Dis.* 2022;79(4 Suppl 1):A8-A12.
2. Ortiz A, Covic A, Fliser D, et al. Epidemiology, contributors to, and clinical trials of mortality risk in chronic kidney failure. *Lancet*. 2014;383(9931):1831-1843.
3. Genovesi S, Boriani G, Covic A, et al. EUDIAL working group of ERA-EDTA. Sudden cardiac death in dialysis patients: different causes and management strategies. *Nephrol Dial Transplant.* 2021;36(3):396-405.
4. Saran R, Robinson B, Abbott KC, et al. US Renal Data System 2018 Annual Data Report: Epidemiology of Kidney Disease in the United States. *Am J Kidney Dis*. 2019;73(3 Suppl 1):A7-A8.
5. Wilson GJ, Van K, O'Lone E, et al. Range and consistency of cardiovascular outcomes reported by clinical trials in kidney transplant recipients: a systematic review. *Transplant Direct*. 2022;9(1):e1398.
6. Di Iorio B, Bellasi A. QT interval in CKD and haemodialysis patients. *Clin Kidney J.* 2013;6(2):137-1343.

7. Goldberger AL, Goldberger ZD, Shvilkin A. Goldberger's Clinical Electrocardiography a Simplified Approach 8th ed. Elsevier Saunders, 2013.
8. Salles GF, Xavier SS, Sousa AS, Hasslocher-Moreno A, Cardoso CR. T-wave axis deviation as an independent predictor of mortality in chronic Chagas' disease. *Am J Cardiol.* 2004;93(9): 1136-1140.
9. Jankowski J, Floege J, Fliser D, Böhm M, Marx N. Cardiovascular disease in chronic kidney disease: pathophysiological insights and therapeutic options. *Circulation.* 2021;143(11):1157-1172.
10. Boriani G, Savelieva I, Dan GA, et al. Chronic kidney disease in patients with cardiac rhythm disturbances or implantable electrical devices: clinical significance and implications for decision making-a position paper of the European Heart Rhythm Association endorsed by the Heart Rhythm Society and the Asia Pacific Heart Rhythm Society. *Europace*. 2015;17(8):1169-1196.
11. Xu C, Tsihlis G, Chau K, Trinh K, Rogers NM, Julovi SM. Novel perspectives in chronic kidney disease-specific cardiovascular disease. *Int J Mol Sci.* 2024;25(5):2658.
12. Akcay M, Yıldırım U. Effect of dialysis and transplantation on myocardial repolarization parameters and P-wave dispersion in chronic kidney disease. *J Arrhythm*. 2021;37(2):348-355.
13. Genovesi S, Rossi E, Nava M, et al. A case series of chronic haemodialysis patients: mortality, sudden death, and QT interval. *Europace.* 2013;15(7):1025-1033.
14. Sherif KA, Abo-Salem E, Panikkath R, et al. Cardiac repolarization abnormalities among patients with various stages of chronic kidney disease. *Clin Cardiol.* 2014;37(7):417-421.
15. Oktavia D, Nasution SA, Setiati S. The clinical factors' prediction of increased intradialytic QT dispersion on the electrocardiograms of chronic hemodialysis patients. *Saudi J Kidney Dis Transpl.* 2013;24(2):274-280.
16. Hage FG, de Mattos AM, Khamash H, et al. QT prolongation is an independent predictor of mortality in end-stage renal disease. *Clin Cardiol.* 2010;33(6):361-366.
17. Beaubien ER, Pylypchuk GB, Akhtar J, et al. Value of corrected QT interval dispersion in identifying patients initiating dialysis at increased risk of total and cardiovascular mortality. *Am J Kidney Dis.* 2002;39(4):834-842.
18. Monfared A, Ghods AJ. Improvement of maximum corrected QT and corrected QT dispersion in electrocardiography after kidney transplantation. *Iran J Kidney Dis.* 2008;2(2):95-98.
19. Monfared A, Atrkar Roshan Z, Salari A, et al. QT intervals in patients receiving a renal transplant. *Exp Clin Transplant.* 2012; 10(2):105-109.
20. Durak MI, Algul Durak B. The comparison of QTc dispersion between renal transplant recipients and healthy individuals. *Cureus.* 2022;14(12):e32458.
21. Liu P, Wang L, Han D, Sun C, Xue X, Li G. Acquired long QT syndrome in chronic kidney disease patients. *Ren Fail.* 2020; 42(1):54-65.
22. Robison LB, Brady WJ, Robison RA, Charlton N. QT interval prolongation and the risk of malignant ventricular dysrhythmia and/or cardiac arrest: Systematic search and narrative review of risk related to the magnitude of QT interval length. *Am J Emerg Med.* 2021;49:40-47.
23. Scherer ML, Aspelund T, Sigurdsson S, et al. Abnormal T-wave axis is associated with coronary artery calcification in older adults. *Scand Cardiovasc J.* 2009;43(4):240-248.