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# Comparison of Tpe Changing on ECG, in Pre and Post Dialysis and Post Transplantation

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## Abstract

**Background:** High incidence of premature ventricular contractions (PVCS) and arrhythmia during and soon after dialysis have been demonstrated by Holter monitoring.
**Objectives:** In this study, the effects of dialysis and renal transplantation on Tpe, Tpec (corrected Tpe), QTc (corrected QT), QTd (QT dispersion), and Tpe/QT parameters as known factors in arrhythmogenicity, and also the correlation between electrolyte and arterial blood gas changing within these parameters will be assessed.
**Patients and Methods:** In a retrospective study, 42 renal transplant recipients were selected. Under the supervision of an electrophysiologist, information related to Tpe, Tpec, Tpe/QT, QTd, and QTc parameters before dialysis (pre-HD), after dialysis (post-HD), and two weeks after transplantation (RTX) were analyzed. Electrolyte and arterial blood gas information were also recorded. Bonferroni adjustment, repeated measures ANOVA, generalized linear models, and generalized estimating equations were used for analysis.
**Results:** Two weeks after transplantation, the mean Tpe decreased to $0.052 \pm 0.002$, which was significant compared to pre-HD ($P < 0.001$) and Post-HD ($P = 0.019$). The mean Tpec was $0.059 \pm 0.002$, which, just in comparison to pre-HD, was significant ($P = 0.005$). In addition, the mean Tpe/QT decreased to $0.143 \pm 0.005$, which was significant compared to pre-HD ($P = 0.018$). The mean QTd was $0.066 \pm 0.004$, which wasn't significant compared to before or after dialysis. The mean QTc decreased to $0.386 \pm 0.004$, which was significant compared to post-HD ($P = 0.0003$).
**Conclusions:** Taking the role of Tpe and Tpe/QT in arrhythmia into account and amending it by a successful transplantation can be considered as a factor that decreases arrhythmia after renal transplantation compared to ESRD patients.

*Keywords:* Tpe, Failure, ESRD, Hemodialysis, Transplant, Electrolyte

## 1. Background

Survival rates of renal transplant recipients compared with the general population are notably lower, for which the main reason is cardiovascular diseases. Furthermore, a successful transplantation in end-stage renal disease patients would improve their quality of life and major cardiac complications would be reduced (1). Although mortality in renal transplant recipients is higher than in the general population, it is lower than that of dialysis patients. The risk of cardiovascular complications could be increased in kidney transplant recipients in the long term due to medications (2) and continuation or occurrence of other cardiovascular risk factors after transplantation. In order to prevent morbidity and mortality in transplant patients, follow up assessment is recommended. The interval from the peak to the end of the T wave has been referred to as the Tpe interval. This parameter has been evaluated as a surface ECG measurement of the transmural dispersion of ventricular repolarization and also of arrhythmic risk (3, 4).

In addition, the ratio between the Tpe interval and the QT interval (Tpe/QT ratio) has been proposed as a noninvasive marker of the arrhythmic risk (3, 4).

These indexes were investigated in ESRD patients with high risk conditions. Despite numerous studies and research on QT changes in dialysis and transplant patients, Tpe and Tpe/QT changes have never been evaluated as the risk factor of arrhythmias in this population.

## 2. Objectives

In a group of dialysis patients who were candidates for transplantation, we decided to compare Tpe changes as well as Tpe/QT, Tpec and QTd changes before dialysis (pre-HD), after the last dialysis of the day before transplantation (post-HD), and after a successful transplantation (RTX).

## 3. Patients and Methods

In a retrospective study of patients who were transplanted in 2008 in an educational health care 42 cases were selected after excluding the criteria (atrial fibrillation, cardiac blocks, suspicious T waves, taking drugs that would prolong QT interval, antiarrhythmic drugs, and serum creatinine > 2 mg/dL).

Data such as ECG parameters and alb, BUN, Cr, Na, K, $HCO_3$, Ca, P, and Mg was extracted from patients' files that had been obtained pre-HD, post-HD, and two weeks after a successful RTX, (Cr < 2 mg/dL).

ECG parameters including Tpe, Tpec, Tpe/QT, QTd, and QTc (Tpe = T peak-T end interval, Tpec = corrected Tpe, Tpe/QT = T peak-T end/QT ratio, QTd = QT dispersion, and QTc = corrected QT) were measured by an electrophysiologist. The Tpe interval was measured in precordial leads. In the case of complex T waves (biphasic, triphasic, etc.), the interval from the nadir of the first component of the T wave to the end of the T wave were measured (5, 6).

### 3.1. Statistical Methods

The mean and the standard deviation were used for determining the amount of ECG factors and electrolytes in each stage of measurement (pre-HD, post-HD, and RTX). Bonferroni adjustment and repeated measures ANOVA were applied for comparing the changes of ECG factors in pre-HD, post-HD, and RTX. Generalized linear models and generalized estimating equations for assessing the correlation between changes in three levels of measuring (pre HD, post-HD, and RTX) were applied. The significant level of this study was $P < 0.05$ and a two-tailed test was used for assessing the tests.

## 4. Results

The mean age of patients was 39.11 ± 13.32 years. Out of 42 patients, 23 were male (54.8%) and 19 were female (45.2%). Electrocardiographic and electrolyte changes are shown in Table 1.

The mean pre-HD and post-HD Tpe were respectively 0.063 ± 0.002 and 0.058 ± 0.002, which weren't a statistically significant change (P = 0.087). However, two weeks after a successful transplantation, the mean decreased to 0.052 ± 0.002.The general linear model repeated measures demonstrated that there was a statistically significant difference between pre-HD with RTX (P < 0.0001) and post-HD with RTX (P = 0.19).

The mean pre-HD and post-HD Tpec were 0.0672 ± 0.003 and 0.0614 ± 0.002 respectively, which were statistically meaningful (P = 0.030), and 0.059 ± 0.002 after RTX. In comparison with post-HD, it wasn't significant (P > 0.05) but the changes were statistically significant (P = 0.005) in comparison with pre-HD.

The mean pre-HD and post-HD Tpe/QT were respectively 0.162 ± 0.006 and 0.146 ± 0.005, which were significant changes (P = 0.014). After RTX, the mean decreased to 0.143 ± 0.005, which was not significant in comparison with post-HD (P=1.000), but was significant in comparison with pre-HD (P = 0.018).

The mean pre-HD and post-HD QTd were respectively 0.073 ± 0.005 and 0.070 ± 0.004, which were not statistically significant (P = 1.000). After RTX, QTd reached 0.066 ± 0.004, which in comparison with pre-HD (P = 0.671) and post-HD (P = 0.932) were also non-significant.

The mean pre-HD and post-HD QTc were respectively 0.396 ± 0.005 and 0.403 ± 0.005, which weren't statistically significant (P = 0.319). After RTX, the mean decreased to (0.386 ± 0.004), which was significant in comparison with post-HD (P = 0.0003), but it was not significant in comparison with pre-HD (P = 0.312).

There was a significant correlation between Tpe changes and PH changes (P = 0.027) and also the change of k (P < 0.0001). Statistically, the most significant correlation was shown between Tpec changes and changes of bicarbonate (P = 0.010), Ca (P < 0.0001), and K (P = 0.011) levels. The most significant correlation between Tpe/QT level was shown with bicarbonate (P < 0.0001), phosphorus (P < 0.0001), and creatinine (P < 0.0001) changes. QTC changes had the most significant correlation with the change of bicarbonate (P < 0.0001), PH (P < 0.0001), and Ca (P < 0.0001), as well.

## 5. Discussion

Tpe is considered to be a new index for detecting possible arrhythmias. The interval from the peak to the end of the T wave is a representative of heterogeneity in transmural repolarization. Differences in the repolarization time in the three types of myocardial cells have been shown to contribute to the inscription of the T wave of the electrocardiogram (ECG). Voltage gradients developed as a result of the different time course of repolarization of phases 2 and 3 in the three types of cells give rise to opposing voltage gradients on either side of the M region, which are partly responsible for the inscription of T wave (1). In the case of an upright T wave, the epicardial response is the earliest to repolarize and the M cell action potential is the latest phase. In the coronary-perfused wedge preparation, repolarization of the epicardial action potential coincides with the peak of the T wave and repolarization of the M cells is coincident with the end of the T wave, so that the interval from the peak to the end of the T wave provides a measure of transmural dispersion of repolarization (TDR) (7, 8).

**Table 1.** Results of Mean Changes of Parameters Prior to Dialysis, Post Dialysis, and After a Successful Transplantation[a]

| Parameter | 1: Pre-HD | 2: Post-HD | 3: RTX | (1 - 2) PV | (1 - 3) PV | (2 - 3) PV | Coordination |
|---|---|---|---|---|---|---|---|
| **Tpe** | 0.063 ± 0.002 | 0.058 ± 0.002 | 0.052 ± 0.002 | 0.087 | 0.000 | 0.019 | PH-K |
| **Tpec** | 0.067 ± 0.003 | 0.061 ± 0.002 | 0.072 ± 0.002 | 0.030 | 0.005 | 1.000 | $HCO_3$-Ca-Cr-K |
| **Tpe/QT** | 0.161 ± 0.006 | 0.146 ± 0.005 | 0.142 ± 0.005 | 0.014 | 0.018 | 1.000 | $HCO_3$-P-Cr |
| **QTC** | 0.395 ± 0.005 | 0.403 ± 0.005 | 0.386 ± 0.004 | 0.319 | 0.312 | 0.003 | $HCO_3$-PH-Ca |
| **QTD** | 0.073 ± 0.005 | 0.070 ± 0.004 | 0.066 ± 0.004 | 0.1000 | 0.671 | 0.932 | P |
| **Bun** | 68.976 ± 19.40 | 54.532 ± 21.44 | 40.187 ± 48.14 | 0.01 | 0.0001 | 0.0001 | NA |
| **Cr** | 9.535 ± 8.028 | 5.754 ± 1.865 | 1.292 ± 0.405 | 0.791 | 0.03 | 0.02 | NA |
| **K** | 4.955 ± 0.802 | 4.378 ± 0.526 | 4.833 ± 0.547 | 0.001 | 0.715 | 0.001 | NA |
| **Mg** | 2.176 ± 0.416 | 2.101 ± 0.426 | 1.889 ± 0.353 | 0.006 | 0.005 | 0.035 | NA |
| **Ca** | 8.538 ± 1.277 | 8.842 ± 1.193 | 8.957 ± 0.871 | 0.611 | 0.225 | 0.095 | NA |
| **P** | 6.857 ± 1.799 | 6.002 ± 3.207 | 3.590 ± 2.990 | 0.001 | 0.001 | 0.001 | NA |
| **PH** | 7.328 ± 0.067 | 7.399 ± 0.069 | 7.401 ± 0.050 | 0.0001 | 0.0001 | 0.797 | NA |
| **$HCO_3$** | 21.254 ± 5.353 | 25.416 ± 6.405 | 25.397 ± 4.816 | 0.06 | 0.668 | 0.056 | NA |

Abbreviation: NA, not available.
[a](1 - 2) PV, Comparing before and after dialysis; (1 - 3) PV, Comparing before dialysis and after transplantation; (2 - 3) PV, Comparing after dialysis and after transplantation.

Prolonged Tpe is arrhythmogenic and there would be an increased risk of arrhythmias. As a result, the condition of the patients with ischemic heart disease can deteriorate. In a study of 813 men suffering cardiovascular disease during 16 years of follow up, QT and Tpe intervals in limb leads of electrocardiography were assessed. The most relevant factors in death were age, heart rate, and Tpe. The results of this study showed that prolonged Tpe would reflect the risk of cardiac death in the population due to any cause (8).

As body mass increases in various body sizes, QT interval and Tpe interval would increase across different species and the Tpe/QT ratio would remain relatively constant within a narrow range of values between 0.17 and 0.23. The Tpe/QT ratio was also reported to be relatively stable when the heart rate varied between 60 and 100 beats per minute (range 0.15 to 0.25, median 0.21, and mean 0.21 ± 0.003) (3).

Although Tpe and Tpe/QT vary along with body size (3), but not yet fully Tpe reflects the actual distribution of transmural dyspertion and may be other physiological factors are the reason. In addition, during an ischemic condition and when its range is normal, transmural repolarization varies greatly (9, 10). The effect of Mexiletin as an antiarrhythmic drug is conducted by shortening the Tpe interval; thus, it confirms that the prolongation of Tpe is arrhythmogenic (11).

In addition, an association between the Tpe interval or Tpe/QT interval ratio and arrhythmic risk is supported by other observations, such as: association between increased Tpe or Tpe/QT interval ratio and arrhythmic risk in long QT syndrome (LQTS) (11); association of Tpe interval prolongation with inducibility of ventricular arrhythmias during electrophysiology studies in patients with structural heart diseases (12, 13); association between Tpe and Tpe/QT indexes and quinidine-induced torsade de pointes (14); and correlation of the Tpe interval to the occurrence of sudden cardiac death or ventricular arrhythmias in patients with the Brugada syndrome and hypertrophic cardiomyopathy, and to all-cause mortality in patients undergoing primary PTCA for ST-segment myocardial infarction (15-18).

T wave changes are very dynamic and are represented in a variety of cardiovascular and noncardiac diseases, but we evaluated the same group of patients in three phases. Thus, with the exception of the effect of renal function, electrolyte, and PH alteration after RTX on T wave, the roles of other confounding factors were adjusted.

As shown in Table 1, arrhythmogenic factors such as Tpe, Tpec, and Tpe/QT decreased significantly after renal transplantation in comparison with ESRD patients before the hemodialysis session at ($P < 0.0001$), ($P = 0.005$), and ($P = 0.018$), respectively. These changes can be considered as factors that would decrease cardiovascular mortality in renal transplant recipients. Also, comparing RTX with ESRD patients after the hemodialysis session showed a significant reduction just in Tpe ($P = 0.019$) and QTc ($P = 0.003$), which might be the cause of a decrease in arrhythmia in renal transplant recipients compared to hemodialysis patients.

Significant alteration of the Tpe and Tpe/QT ratio toward reduction in renal transplant recipients compared to ESRD patients could be due to gradual correction of the uremic environment and also, as shown in this study, correction of electrolytes such as K, Ca, $HCO_3$, and P levels and arterial PH Values. The electrical conduction system of myocardium would definitely be disturbed by hyperkalemia and acidosis, and the reentry mechanism would be stimulated by blocks and due to dangerous ventricular tachycardia (VT) and ventricular fibrillation (VF) (19). The reason for improved survival with kidney transplantation compared to ESRD patients is unclear, but improvements of Tpe and Tpe/QT in renal transplant recipients may indicate the reduction of mortality due to cardiovascular diseases such as arrhythmia in this population. In addition, recovery of renal function with a functional renal allograft would decrease the inflammatory and/or oxidative stress found in chronic dialysis patients. These have been reported in some studies for elevated levels of C-reactive protein, tumor necrosis factor-alpha, and interlukin-6 (19).

Since most of the time cardiac symptoms in ESRD are silent and atypical, sensitive noninvasive parameters such as Tpe and other related parameters could be suggested in these patients, but more investigation and discoveries about the affecting factors may be needed.

Limiting factors in our study were: 1) the lack of sufficient knowledge about all the factors that can affect Tpe, especially drugs which were used in dialysis patients; 2) lack of an approved guideline for a more precise assessment of Tpe; and 3) lack of similar study about the effects of dialysis and renal transplantation on Tpe and Tpe/QT for a better analysis by the results.

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## Footnotes

**Authors' Contribution:** Study concept and design: Ali Monfared; acquisition of data: Ali Monfared, Mohammad Assadian Rad, Mohammadreza Feizkhah and Samaneh Esmaeili; analysis and interpretation of data: Ehsan Kazemnezhad and Samaneh Esmaeili; drafting of the manuscript: Ali Monfared, Mohammad Assadian Rad, Mohammadreza Feizkhah, Samaneh Esmaeili, and Nadia Rastjou Herfeh; critical revision of the manuscript for important intellectual content: Ali Monfared, Mohammad Assadian Rad, Mohammadreza Feizkhah, Samaneh Esmaeili, and Nadia Rastjou Herfeh; statistical analysis: Ehsan Kazemnezhad and Samaneh Esmaeili; administrative, technical, and material support: Ali Monfared, Mohammad Assadian Rad, Mohammadreza Feizkhah, and Razieh Hedayatsafa; study supervision: Ali Monfared, Mohammad Assadian Rad, and Mohammadreza Feizkhah.

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