

# Variation of serum potassium and electrocardiographic predictors of sudden cardiac death during hemodialysis

## Variation de la kaliémie et des paramètres électrocardiographiques prédictifs de mort subite cardiaque au cours des séances d'hémodialyse

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### Résumé

**Introduction :** La mort subite cardiaque (MSC) est une cause importante de mortalité chez les patients hémodialysés (HD), attribuable principalement aux dyskaliémies. Différents paramètres électrocardiographiques (ECG) prédictifs de MSC ont été évalués, avec des résultats divergents. De même, la cible de kaliémie la moins arythmogène reste encore à définir.

**Objectif :** Notre étude visait à évaluer les variations des paramètres ECG potentiellement arythmogènes ainsi que leur corrélation avec la kaliémie dans le but de déterminer l'approche optimale de baisse du potassium au cours des HD.

**Méthodes :** Etude transversale à propos de 60 malades hémodialysés chroniques chez qui on a pratiqué un ionogramme sanguin et un ECG immédiatement avant et après une séance d'HD. Ensuite, nous avons évalué les variations des paramètres ECG potentiellement arythmogènes et le potassium sérique le long des séances d'HD.

**Résultats :** L'âge moyen des patients était de 60 ans avec un sexe ratio à 2. Les séances d'HD étaient accompagnées d'une baisse significative de la kaliémie passant de  $5.09 \pm 0.66$  mmol/l en pré-dialyse à  $3.18 \pm 0.59$  mmol/l en post-dialyse ( $p=0.0001$ ). A l'ECG, l'onde T a diminué ( $p=0.0001$ ), l'onde R a augmenté ( $p=0.028$ ) et le rapport T/R a diminué ( $p=0.005$ ). La kaliémie en post-dialyse n'avait qu'une corrélation négative faible au rapport T/R en post-dialyse ( $r=-0.275$ ,  $p=0.037$ ). Cependant, la variation de la kaliémie au cours de l'HD ( $\Delta K$ ) avait une corrélation plus significative avec la variation de l'intervalle QT ( $\Delta QT$ ) [ $r=0.355$ ,  $p=0.006$ ].

**Conclusion :** Au cours des séances d'hémodialyse, on a démontré une baisse significative du rapport T/R ainsi qu'une majoration de  $\Delta QTc$  corrélée à  $\Delta K$  avec un potentiel risque de MSC.

### Mots-clés

Hémodialyse ; kaliémie ; mort subite cardiaque ; électrocardiogramme ; QT

### Summary

**Introduction :** Sudden cardiac death (SCD) is the leading cause of mortality in hemodialysis (HD) patients, attributed in part to serum potassium variations. Several electrocardiographic (EKG) predictors of SCD were evaluated, but with divergent results and the optimal least arrhythmogenic target of kalemia according to these EKG parameters is not yet consensual.

**Objective :** Our aim was to evaluate the variation potential EKG predictors of SCD in dialysed patients and their correlation to serum potassium variations in order to determine the optimal approach of decreasing the kalemia.

**Methods :** We conducted a transversal study in which 60 chronically dialysed patients benefited from a serum potassium dosage and EKG immediately before and after HD session. Then, we evaluated these potentially arrhythmogenic EKG parameters and serum potassium variations along HD.

**Results :** The mean age of our patients was 60 years old with a sex ratio of 2. Along HD sessions, a significant decrease of kalemia from  $5.09 \pm 0.66$  mmol/l to  $3.18 \pm 0.59$  mmol/l was detected ( $p=0.0001$ ), T wave decreased ( $p=0.0001$ ), R wave increased ( $p=0.028$ ) and T/R ratio decreased ( $p=0.005$ ). After dialysis, kalemia was not correlated to any ECG parameter, except a low negative correlation to T/R ratio ( $r=-0.275$ ,  $p=0.037$ ). However, the degree of variation of kalemia ( $\Delta K$ ) was more significantly correlated to the variation of corrected QTc interval ( $\Delta QTc$ ) [ $r=0.355$ ,  $p=0.006$ ].

**Conclusion :** According to our study, we noted a significant decrease of T/R ratio as well as a  $\Delta QTc$  increase correlated to  $\Delta K$  along HD sessions with a potential risk of SCD.

### Keywords

Hemodialysis ; kalemia ; sudden cardiac death ; electrocardiogram ; QT

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## INTRODUCTION

Cardiovascular diseases are the main cause of death in patients with chronic kidney disease undergoing hemodialysis (HD). Sudden cardiac death (SCD) accounts for about 60% of all cardiac deaths in this population (1). During the first year, cardiac arrest rate is about 93 event/1000 patients (2). It was already demonstrated that peaks of SCD occur in the last 12 hours before the next dialysis session especially due to hyperkalemia and during the first 12 hours after the index dialysis session mainly due to hypokalemia. Several previous studies identified electrocardiographic (EKG) predictors of SCD. In our study we aimed to evaluate the variations of predefined electrocardiographic predictors of SCD and those of kalemia during hemodialysis sessions and then to look into the optimal regimen of kalemia decrease.

## METHODS

We conducted a monocentric transversal study including 60 chronically dialysed patients in Nephrology department of La Rabta Hospital in January 2018. Patients were dialysed 3 times a week for at least 6 months. A kalemia dosage and a 12 lead ECG recording immediately before and after HD sessions were performed.

An independent experienced cardiologist who was blind to all clinical information interpreted the EKGs according to predefined criteria. T wave and R wave amplitudes were measured in the chest leads, and then T/R ratio was calculated. QT interval was measured and corrected (QTc) according to the Bazett's formula (QT interval/square root of R-R interval). QRS complex duration was measured and the presence of U wave was sought.

Depending on these EKG parameters studied, two approaches were compared according to the target to reach after HD: the absolute value of post HD kalemia versus the degree of variation of kalemia ( $\Delta K$ ) defined as the difference between the values of kalemia before and after HD.

### Statistical analysis:

Statistical analyses were performed using SPSS (SPSS Inc, Chicago, IL, USA) version 20 for Windows. Categorical variables were presented in absolute values and proportions. Continuous variables were presented as mean standard deviation as appropriate. To compare serum potassium and EKG parameters variations before and after HD, the Student *t*-test was used to compare means and the Pearson chi-square test was used to compare proportions. For analytical study, we evaluated the correlations between post HD serum potassium absolute value or  $\Delta K$  and EKG parameters by calculating

the Pearson linear correlation coefficient. A *p* value under 0.05 was considered statistically significant.

## RESULTS

The mean age of our patients was 60 years old (from 23 to 86 years old) with a sex ratio of 2. Patients were chronically dialysed for a mean duration of 66 months (12 to 456 months). Diabetic nephropathy was the leading cause of hemodialysis in 20% of cases.

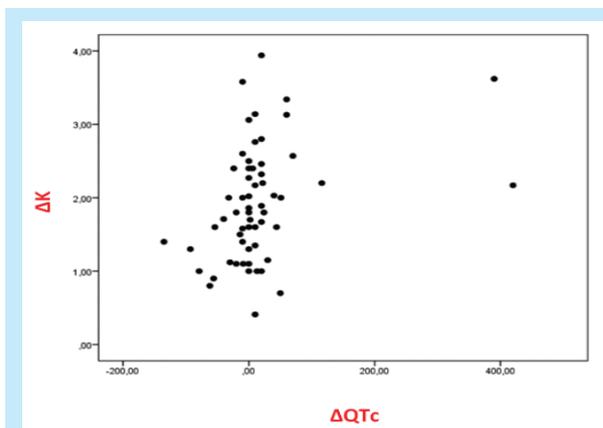
Along HD sessions, a significant decrease of kalemia from  $5.09 \pm 0.66$  mmol/l to  $3.18 \pm 0.59$  mmol/l was detected ( $p=0.0001$ ) with a mean variation of kalemia ( $\Delta K$ ) of  $1.91 \pm 0.78$  mmol/l.

In parallel, these EKG parameters significantly changed: T wave decreased, R wave increased and, as a result, T/R ratio decreased (table 1).

**Table 1:** EKG variations before and after hemodialysis (HD) sessions

EKG parameters	Before HD	After HD	P value
T wave amplitude (mm)	$5.77 \pm 3.3$	$4.31 \pm 2.9$	0.0001
R wave amplitude (mm)	$10.28 \pm 6.52$	$11.75 \pm 8.6$	0.028
T/R ratio	$0.84 \pm 0.78$	$0.59 \pm 0.69$	0.005
QTc interval (ms)	$415 \pm 84$	$429 \pm 34$	0.187
QRS duration (ms)	$83 \pm 21$	$84 \pm 19$	0.701
U wave	2 patients (0.03%)	19 patients (0.32%)	0.097

After dialysis, the absolute serum potassium value was not correlated to any of the above studied EKG parameter, except a slightly negative correlation to T/R ratio ( $r=-0.275$ ,  $p=0.037$ ). When comparing the variation of these EKG parameters to  $\Delta K$ , this latter was correlated to corrected QT interval variation,  $\Delta QTc$  ( $r=0.355$ ,  $p=0.006$ ) during HD (figure 1).



**Figure 1:** Correlation between  $\Delta K$  and  $\Delta QTc$  ( $r=0.355$ ,  $p=0.006$ )

## DISCUSSION

Our findings were consistent with variability of EKG predictors of SCD during HD sessions. In fact, T wave decreased, R wave increased and T/R ratio decreased. In the other hand, we demonstrated that variation of arrhythmogenic EKG parameters, QTc interval in our study, was more correlated to the degree of serum potassium variation ( $\Delta k$ ) than the absolute post HD value of kalemia itself, suggesting that during HD sessions, efforts should be made to decrease the rapidity and the degree of variation of kalemia to avoid arrhythmia and then SCD.

Optimal kalemia in chronically dialysed patients is controversial. In fact, hyperkalemia leads to less negative membrane potential, action potential shortening and altered conduction velocity while hypokalemia result in resting membrane hyperpolarization, action potential prolongation and increased automaticity (3). These electrophysiological effects could generate membrane instability and, thus, potential cardiac arrhythmia and SCD. These effects are translated into several EKG parameters which variations were demonstrated through previous studies. As found in our study, Tarif and al. also noted a significant decrease in T wave amplitude, an increase in R wave amplitude and, as a result, a decrease in T to R ratio along dialysis sessions (4). Darren and al. demonstrated the statistical relationship between T to R ratio variation and increased risk of SCD (5).

In addition, many studies noted a variation of QTc interval and QTc dispersion in dialysed patients (6,7). These variations were found to be an independent factor of complex ventricular arrhythmia (8). In our patients, we noted a decrease of QTc interval along HD but without being statistically significant.

As these different EKG predictors of SCD were mainly attributed to kalemia variations, we studied the correlation between EKG parameters and serum potassium variations during HD sessions. We found that the variation of QTc interval ( $\Delta QTc$ ) negatively correlated to  $\Delta K$  while post HD serum potassium value had a slight negative correlation to T/R ratio. This comparison supports that the arrhythmogenicity increases with rapid and deep variations of kalemia during HD. In fact, in a large cohort, lower post HD serum potassium level was an independent risk factor of mortality in dilysed patients. In addition, in this cohort, HD patients showed U-shaped survival pattern suggesting that both lower and higher potassium levels were deleterious (9).

At the light of these data, technical tools should be used to limit potassium variations. For this purpose, HD technique using Acetate Free Biofiltration with Potassium Profiled Dialysate (AFBK) was developed in order to control programed gradient between serum

potassium and dialysate potassium along dialysis leading to less variations of kalemia. When compared to the classical technique using Acetate free Biofiltration (AFB), several conducted trials proved a significant less variation of QTc interval and dispersion as well as less frequent and less severe premature ventricular beats and arrhythmia trend when less variation of kalemia was targeted, which was in favour of AFBK application (10-12).

### *Study limits:*

Few patients were studied in our series which did not allow designing our study in order to detect a significant rate of rhythm disturbances. As a result, the approach was to study EKG parameters which arrhythmogenic potential was already previously demonstrated by other studies. In the other hand, correlations found in our series was statistically significant ( $p < 0.05$ ) but low ( $r < 0.5$ ) may be because of our small sample. Observing correlations, considering the little number of patients, should motivate clinicians to pay more and more attention to the degree of variation of the kalemia during hemodialysis.

## CONCLUSION

According to our study, we noted a significant decrease of T/R ratio along HD sessions which may lead to a potential risk of cardiac arrhythmia and SCD. As well, we consider that, a most important attention should be paid to the degree of variation of the kalemia instead of the absolute target value of kalemia itself mainly because of the potential risk of prolonging the QTc interval with an imminent risk of cardiac arrhythmia. As a result, application and development of tools aiming to limit serum potassium variation during HD sessions is recommended in order to decrease HD related mortality.

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