Principal Component Analysis of the T Wave: 24 Hour Monitoring of Repolarization Complexity in Dialysis Patients

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Abstract

The 24-hour changes in the complexity of ventricular repolarization in hemodialysis (HD) patients were quantified by principal component analysis (PCA) of the T wave. The effects of dialysis sessions leading to different plasma potassium levels ('K_{low}' and 'K_{high}') were analyzed. Forty-six Holter recordings were collected from twelve patients. PCA was applied to the T waves extracted from each beat. Repolarization complexity was quantified by the ratio of the second to the first eigenvalue (PCA ratio). Hemodialysis caused a significant increase in the PCA ratio (+50% at the end of the sessions), which recovered to the basal value during the first hour post-dialysis. In the last two hours of dialysis PCA ratio was significantly higher in K_{low} sessions than in K_{high} ones. Results show a significant HD-induced increase of the T wave complexity, strongly related to the therapy-induced potassium depletion.

1. Introduction

Hemodialysis therapy has a strong impact on cardiac excitability and some patients experience a significant increase in the occurrence of ventricular ectopic beats during the session [1,2]. Dispersion of ventricular repolarization could be a cause of such HD-induced arrhythmogenic effect. In fact, QT dispersion increases during HD [3,4].

Patients with chronic renal failure regularly undergo, in the inter-dialysis period, a K^+ overload due to the dietary intake. To restore a physiological K^+ plasma concentration about 80-100 mEq of K^+ are acutely removed during the treatment. The QT dispersion increase seems to be related to such potassium removal [5].

However, some concerns have been raised about uncertainty of the QT dispersion measurement. In fact, the QT interval dispersion as a clinical index of the dispersion of ventricular repolarization is neither well defined yet nor fully understood. In addition, technical difficulties in measuring the QT interval often made the interpretation and the comparison of clinical results controversial [6].

Principal component analysis of the T wave applied to 12-lead ECG recording has been proposed as an approach to study the complexity of repolarization without the need to determine the end of T-wave [4,7,8]. The aim of this study was to assess and quantify the 24-hour changes in the complexity of ventricular repolarization in patients undergoing HD by means of principal components analysis. The effects of HD sessions leading to different plasma potassium levels were also assessed.

2. Methods

2.1. Subjects and dialysis treatments

Subjects were retrospectively selected within a multicentric study [9] addressed to investigate the clinical effect of two different K^+ removal rates during HD. Only those patients in whom premature ventricular complexes (PVC) were observed to increase with HD were selected in accordance with the following criteria [2]: (a) if the inter-dialysis number of PVCs/h was less than 2, at least a fourfold increase of PVCs/h during the "HD interval" (dialysis time and the subsequent four hours); or else (b) if the inter-dialysis number of PVCs/h was 2 or more, at least a twofold increase of PVCs/h during the HD interval.

The selected group consisted of 12 subjects with a mean age of 72 years (range: 63 to 86) undergoing three treatments per week and each treatment lasted about 4 hours.

Plasma K^+ concentration was measured at the beginning, after one hour and at the end of each treatment. Among four dialysis sessions per patient (except for one patients who had only 2 sessions) two were classified as 'K_{low}' and two as 'K_{high}' on the basis of the plasma K^+ concentration measured at the end of the treatment. Holter 12-lead 24-hour recordings (H-12 Holter, Mortara Instrument Inc., Milwaukee, Wisconsin, USA) were collected starting with the dialysis session. ECGs were sampled at 180 Hz and stored to a PC hard disk for subsequent analysis.

2.2. ECG data analysis

Principal components analysis was applied to the T wave automatically extracted from each sinus beat over I, II, V1 to V6 leads, and the degree of correlation between the 8 T-waveforms was determined. To this purpose, T wave interval, described as the interval from the end of QRS to beyond the end of T, was extracted from each beat. The end of T wave interval was defined by adding 0.1 second to the rate-expected end of T according to Bazzet's formula. T wave amplitude was evaluated from the baseline connecting the beginning of QRS block to the end of QT interval in each lead to create the matrix of samples (Y_{mk}). Subscript *m* represents one of considered eight leads while subscript *k* denotes one of the N time samples. The estimated covariance matrix ($Y_{mk'} \cdot Y_{mk}/N$) was calculated and then eigenvalues and eigenvectors were obtained. E1-T and E2-T are the largest eigenvalues (E1-T>E2-T), so that their related eigenvectors account for the most of wave signal energy. The index of repolarization complexity, PCA ratio, is then defined as:

$$\text{PCA ratio} = \text{E2-T/E1-T}.$$

The PCA ratio was then calculated every minute by averaging the beat-to-beat values over a two-minute window.

When repolarization is homogeneous the first singular value, accounting for the most of repolarization is largely prevalent on the second and the PCA ratio is low (see, e.g., Fig. 1). In contrast, inhomogeneous repolarization causes a relevant contribution of the second singular value and a decrease of the first one thus increasing PCA ratio (see, e.g., Fig. 1).

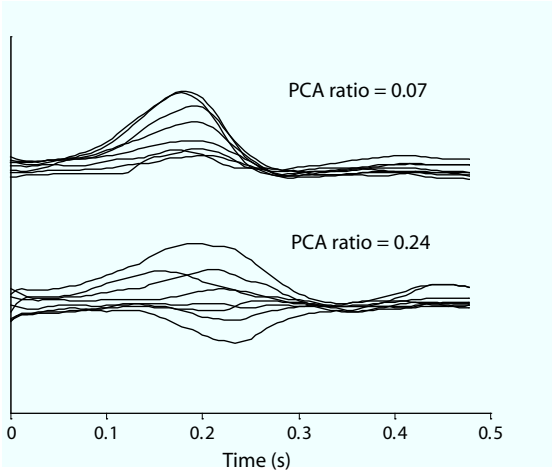

Figure 1. Examples of poorly and highly correlated T wave intervals over the 8 leads (I, II, V1 to V6 are superimposed), and the corresponding high and low PCA ratio values.

2.3. Statistical analysis

Analysis of variance for repeated measures and the Tukey-Kramer multiple comparison test were employed to assess differences in PCA ratio with respect to time and to the potassium level. All the results are expressed as mean±SD. The natural logarithm transformation of the number of PVC/h was performed in order to have a normally distributed variable.

3. Results

Hemodialysis caused a striking increase in the PCA ratio (averaged over all the ECG recordings) with respect to its basal value (Fig. 2). At the beginning of dialysis

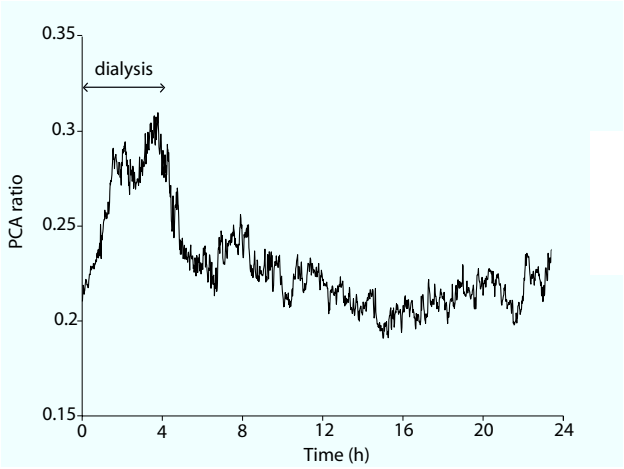

Figure 2. Average (12 patients, 46 recordings) time course of the PCA ratio during 24 hours

PCA ratio was 0.21± 0.12, it rapidly increased during the first two hours of dialysis (0.28± 0.18 after two hours, $p<0.05$), than it increased slightly reaching the maximal value towards the end of dialysis (0.31±0.16, after 220 min, $p<0.05$). The PCA ratio started decreasing just at the end of dialysis recovering almost to the basal value during the first hour post-dialysis (0.24± 0.11, after 5 hours) and remained quite stable during the subsequent hours (e.g., 0.22± 0.09, after 23 hours).

As expected, the HD-induced potassium decrease followed different time-courses in K_{low} and K_{high} sessions. At the beginning of HD K^+ plasma concentration was 4.9±0.8 mM in K_{low} vs 5.1±0.6 mM in K_{high} (NS). After the first hour of treatment patients reached a similar level in both treatments (4.0±0.5 mM in K_{low} and 3.8±0.6 mM in K_{high}, NS). The two treatments differed only during the last part of the sessions: plasma K^+ concentration was 3.0±0.5 mM in K_{low} and 3.3±0.4 mM in K_{high} ($p<0.001$) at the end of the dialisys. Patients started K_{low} and K_{high} sessions with similar PCA ratio (0.21±0.12 in K_{Low} and 0.22±0.12 in K_{high}, NS, see Fig. 3). The subsequent

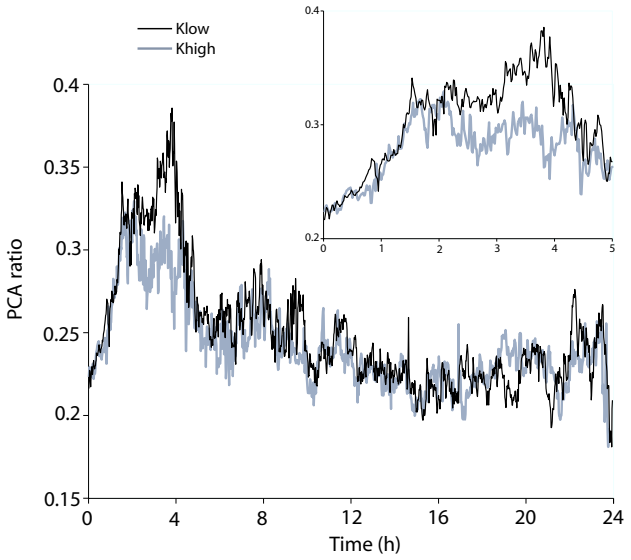

Figure 3. Time course of the PCA ratio during 24 hours in K_{low} (black line) and K_{high} (grey line) sessions. Significant difference ($p<0.05$) was found in the last part of the dialysis treatment (third to fourth hour, see inset).

increase was similar during the first two hours of dialysis (0.32±0.19 vs 0.30±0.20 after two hours, NS) but it was significantly higher in K_{low} sessions in the last two hours of dialysis (Fig. 3, inset), the difference reached its maximal value at the end of dialysis (0.38±0.20vs 0.28±0.16, $p<0.05$). The PCA ratio then rapidly decreased both in K_{low} and K_{high} (0.27± 0.10 vs 0.26± 0.12 after 5 hours, NS) and no significant differences were found between the two groups of Holter recordings in the subsequent hours, in which PCA ratio remained quite stable (e.g., 0.22± 0.09 vs 0.23± 0.10, after 23 hours).

The occurrence of PVCs in K_{low} vs. K_{high} dialysis sessions was also assessed (Fig. 4). A difference in the ventricular ectopic beats was pointed out, being the number of PVCs significantly higher in K_{low} sessions in the last three hours of treatment ($p<0.05$). This result correlates with the difference in the PCA ratio at the end of the dialysis.

4. Discussion and conclusions

In this study we quantified the 24-hour variations in the complexity of ventricular repolarization in patients undergoing HD by evaluating the PCA ratio index based on principal component analysis of the T wave. In our data, the PCA ratio was markedly sensitive to the hemodialysis treatment showing that hemodialysis significantly increases the T wave complexity. The strong impact on the cardiac cell activity was confirmed, as well as the role of the dispersion of ventricular repolarization in the arrhythmogenic effect of hemodialysis.

In spite of the great inter-individual variability of the absolute value of PCA ratio and of its "baseline" variability (see Figg. 2 and 3), such index was found clearly sensitive to the hemodialysis related cardiovascular stress. An increase of dispersion of repolarization occurred even when no critical end-dialysis plasma K^+ levels were elicited by the treatment. Nevertheless such an increase seems to be strongly related to the therapy-induced K^+ depletion, being greater the T wave complexity when lower K^+ levels are reached.

In a large prospective study [8] it was demonstrated that PCA ratio greater than 0.32 for women and 0.25 for men identified subjects with a nearly 3-fold increased risk of cardiovascular mortality. In the present study the average value of PCA ratio was lower than these critical

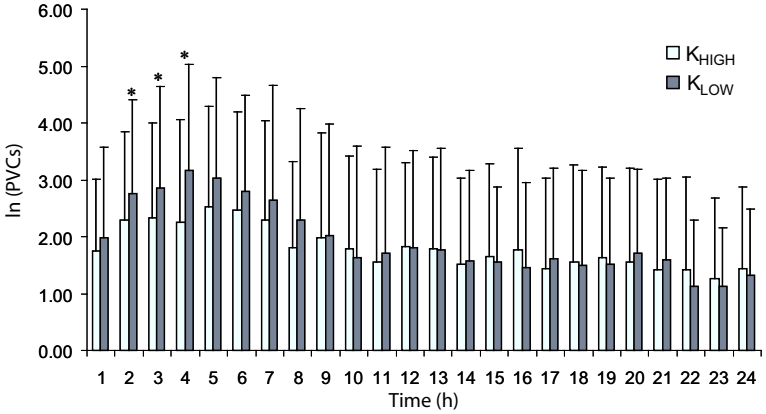

Figure 4. Time course of the premature ventricular complexes occurrence during 24 hours in K_{low} (grey) and K_{high} (white) sessions. Significant difference ($p<0.05$) was found in the last part of the dialysis treatment (second to fourth hour).

limits at the beginning of the therapy but it reached them at the end of the K_{low} one. Moreover, based on the significant difference in the occurrence of HD-induced premature ventricular beats it can be hypothesized that when repolarization dispersion overcome a critical level (maybe corresponding to a patient-dependent PCA ratio threshold) PVCs occurrence dangerously increases.

Further studies might address whether it is possible to identify the dialysis patients at highest arrhythmogenic risk by means of a careful analysis of PCA indexes and whether the documented electrocardiographic changes can be prevented by identifying the optimal K^+ removal for the individual patient.

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References

[1] Abe S, Yoshizawa M, Nakanishi N, Yazawa T, Yokota K, Honda M, Slomag G. Electrocardiographic abnormalities in patients receiving hemodialysis. Am Heart J 1996; 131(6):1137-1144.

[2] Redaelli B, Locatelli F, Limido D, Andrulli S, Signorini MG, Sforzini S, Bonoldi L, Vincenti A, Cerutti S, Orlandini G. Effect of a new model of hemodialysis potassium removal on the control of ventricular arrhythmias. Kidney Int 1996; 50(2):609-617.

[3] Lorincz I, Matyus J, Zilahi Z, Kun C, Karanyi Z, Kakuk G. QT dispertion in patients with end-stage renal failure and during hemodialysis. J Am Soc Nephrol 1999; 10(6):1297-1302.

[4] Severi S, Vecchietti S, Cavalcanti S, Mancini E, Santoro A. Electrocardiographic changes during hemodiafiltration with different potassium removal rates. Blood Purif 2003; 21(6):381-388.

[5] Cupisti A, Galetta F, Morelli E, Tintori G, Sibilia G, Meola M, Barsotti G. Effect of emodialysis on the dispersion QTc interval. Nephron 1998; 78(4):429-432.

[6] Malik M, Batchvarov V. QT Dispersion. In: Camm AJ, editor. Clinical approaches to tachyarrhythmias [12]. Armonk, NY: Futura, 2000.

[7] Priori SG, Mortara DW, Napolitano C, Diehl L, Paganini V, Cantu F, Cantu G, Schwartz PJ. Evaluation of the spatial aspects of T-wave complexity in the long-QT sindrome. Circulation 1997; 96:3006-3012.

[8] Okin PM, Devereux RB, Fabsitz RR, Lee ET, Galloway JM, Howard BV. Principal component analysis of the T wave and prediction of cardiovascular mortality in American Indians. Circulation 2002; 105:714-719.

[9] Santoro A, Mancini E, Gaggi R, Cavalcanti S, Severi S, Cagnoli L, Badiali F, Perrone B, London G, Fessy H, Mercadal L, Grandi F. Electrophysiological response to dialysis: the role of dialysate potassium content and profiling. Contrib Nephrol 2005; 149:295-305.

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