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Differences Between Model-based Electrocardiogram T Wave Features Before and After Haemodialysis

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***Abstract*— Electrolytes play an essential role in the regulation of the heart, and the electrocardiogram (ECG) can be a useful instrument for detecting metabolic disturbances. Hyperkalaemia, usually clinically silent, is a medical condition known for higher serum potassium levels and it is one of the causes of sudden cardiac deaths in chronic kidney disease patients. In order to develop a unobtrusive method capable of monitoring potassium changes remotely, our study investigated which ECG parameters are sensitive to fluctuations during the interdialytic period. Specifically, we evaluated 14 morphological and 5 model-based ECG features. Results show that T wave features: right slope, the ratio of the right slope and T wave peak amplitude, and lognormal fitting parameters show statistically significant differences if evaluated before and after haemodialysis.**

Keywords— electrolyte fluctuations; non-invasive, unobtrusive monitoring; weight scale; electrocardiogram signal processing; potassium changes; ECG feature extraction; T wave detection.

I. INTRODUCTION

Electrolytes play an irrefutable role in homeostasis. Electrolyte fluctuations are clinically silent and occur without warning, hindering the possibility of early detection in the absence of blood tests. Finding new ways to detect these imbalances by external means, preferably using unobtrusive and non-invasive methods is extremely important.

The dysregulation of potassium (K^+) homeostasis, mainly caused by end-stage renal disease (ESRD) or earlier stages of chronic kidney disease (CKD), can lead to an increase of extracellular serum K^+ levels, a condition also known as hyperkalemia. This asymptomatic condition is commonly associated with potentially sudden death since it causes life-threatening arrhythmias and cardiopulmonary arrest [1], [2]. Haemodialysis (HD) is usually performed on ESRD patients three times per week, with equal intervals between the procedures, to remove fluid and waste products from the blood, and also correct these electrolyte imbalances. Not surprisingly, the prevalence of electrolyte disturbances has a bigger incidence on the day after a long interdialytic interval. Early and, if possible, unobtrusive, remote detection of the variation of these levels may well save lives by ensuring a prompt treatment before the patient displays severe symptoms like Kussmaul respiration and metabolic acidosis [3]. Even though they don't primarily affect the heart, electrolyte disturbances play a fundamental role in the electrical activity of the heart [4]. The earliest changes associated with hyperkalemia can be detected when the concentration of K^+ rises above 5.5 mmol/l, and they are associated with peaked T waves in the electrocardiogram (ECG). As the K^+ concentration rises, the P wave flattens and widens, the PR segment lengthens, and P waves may disappear completely. This is followed by a widening of QRS complexes, which then begin to merge with the T wave, creating a sine wave [3]. Unfortunately, these changes are asymptomatic and are often undetected. Moreover, there aren't any current descriptive features that could be used to monitor electrolyte fluctuations unobtrusively.

In this study, we propose a novel approach to monitoring electrolyte fluctuations remotely, using a data acquisition equipment that is operator independent, simple, unobtrusive, and convenient to use at home. For that, we evaluated the most significant differences of the ECG before and after haemodialysis. Understanding which ECG features are influenced by electrolyte fluctuations can inform the development of a discriminating algorithm to remotely detect abnormal electrolyte fluctuations, particularly at higher levels of potassium.

II. MATERIALS AND METHODS

A. Data

Short term ECG signals (~1 min) of 33 patients were collected immediately before and after haemodialysis. The dataset was obtained (Fig. 1) by the CARRE Multiparametric body composition scale (KTU Biomedical Engineering Institute, Lithuania) capable to acquire 3 leads ECG from palms and feet [5]. The average age of the patients was 55.94±15.92 years, and the group was constituted by 17 females and 16 males.

Fig. 1. Multiparametric scale: scale (left), signal acquisition with scale (right).

B. *Signal Processing*

A discriminatory algorithm was used to choose the highest quality ECG from all leads. At the end, a set of 22 ECGs before and 23 ECGs after HD were used to evaluate significant differences. The flowchart of this procedure is shown in Fig. 2.

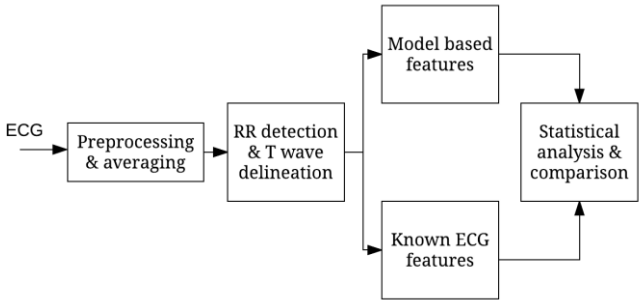

Fig. 2. Flowchart of the main steps performed during this study

The signals were filtered with a high-pass bidirectional 4th order Butterworth 0.5 Hz filter for baseline removal and a low pass filter with a cut-off frequency of f_c=25 Hz. The pre-processed signal needs to meet certain quality standards to be considered viable for analysis. A methodology proposed in [6] was used to estimate a signal quality index (SQI). Evaluating SQI is particularly important in ambulatory ECG recording devices, which are typically more noisy than clinical. This step guarantees that only signals without artefacts will be analyzed, thus decreasing the chances of including false alarms. RR peaks were detected using the Pan-Tompkins algorithm [7]. If several signals of the same patient passed the SQI test, the one with the highest number of detected RR peaks was given priority. If there were 2 leads with the same number of RR peaks, then the signal with the highest T/R amplitude ratio was chosen as the best ECG lead. Signal averaging of the highest quality ECG lead was the following step, using each R peak as the fiducial point. The detected ECG beats were then divided into two different segments: (1) to include 30% of the median RR interval before the fiducial point and (2) to include 70% of the median RR interval after the fiducial point. By estimating the means for two ensembles of intervals, it is possible to obtain a much more smooth and clean signal.

C. *Model-based T wave features*

Ambulatory ECG recordings are prone to more noise than clinical ECGs. Since model-based parametrizations are more robust to noise, this study evaluated the possibility of such parameters being used as discriminators for electrolyte imbalances. Moreover, since the asymmetry of the T-wave is strongly associated with potassium changes, it was hypothesized that the parameters of some functions could potentially be used to identify electrolyte fluctuations before and after HD. A lognormal function (1) was selected as a model for T wave because of its ability to obtain asymmetrical shape:

$$T_{LN}(x) = \frac{k}{(x-\tau)\sigma\sqrt{2\pi}} e^{-\left(\frac{(\ln(x-\tau)-\mu)}{2\sigma}\right)^2} + h \quad (1)$$

The final parameters from lognormal fitting evaluated in this work were, therefore, τ, σ, μ, k and h. Fig. 3 illustrates the impact of different values of μ and σ on the lognormal curve. The fitting was performed using MATLAB R2016b functions from the Optimization and Curve Fitting toolboxes.

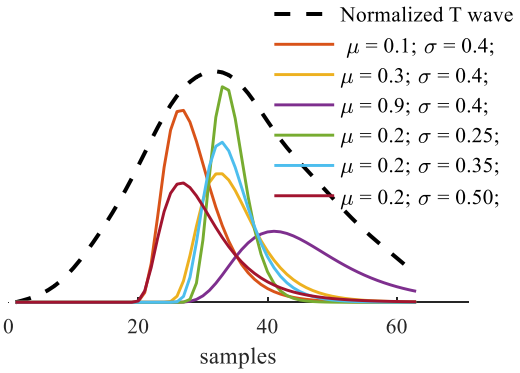

Fig. 3. Illustration of lognormal curve fitting

Usually, the right slope of T wave is steeper than the left slope. Therefore, we also took into consideration a mirrored T-wave and mirrored ST interval together with the T wave (ST segment is the ECG segment starting at S peak until the end of T wave). The coefficient of determination, R^2, was used to evaluate the goodness of fit. The statistical analysis and comparison were only performed in waves for which $R^2 \geq 0.51$.

D. *Other ECG features*

The averaged ECG intervals were then used to extract several parameters, including the 14 ECG features proposed by [8]. The extraction of such features was only performed in ECGs with positive T waves. The automatic detection of the T wave phase was performed by analyzing the part of the signal where the left slope of the T wave is expected to be. If the sum of the derivative in these points is positive, then the T wave is considered to be positive as well. This algorithm takes into consideration the sum of 20 samples after the ST interval. To properly detect the T wave limits, an algorithm proposed by [9] to detect the T wave end was used. After delineation of the T wave limits, the signal features such as amplitude of the T wave peak (T_{amp}) and P wave peak (P_{amp}), T right slope (RS) and T left slope (LS) (obtained by calculating the mean of the first derivative between T-peak and T-end point or T-beginning point, respectively), area underneath T wave (T-area), the T/R amplitude ratio, T/RS amplitude ratio (diving the T wave amplitude from the baseline by total amplitude from S to R), RT interval, ST interval, QRS duration, PR interval, the center of gravity of the T wave (T-COG), the center of gravity of the last 25% of the T wave (T4-COG), and $T_{S/A}$ were extracted. $T_{S/A}$ was obtained as follows:

$$T_{S/A} = \frac{RS}{\sqrt{T_{Amp}}} \quad (2)$$

III. RESULTS

Figure 4 exemplifies the results after each step of signal processing.

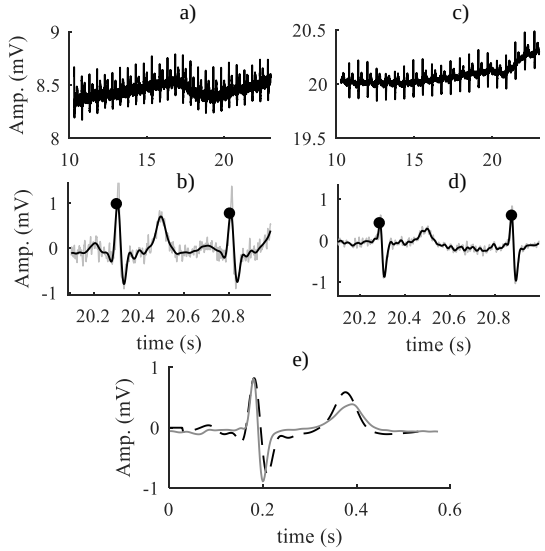

Fig. 4. Signal denoising steps:
(a) Raw ECG and (b) ECG after baseline wander removal (in grey) and ECG after low pass filtering (black) and RR peaks before HD,
(c) Raw ECG and (d) ECG after baseline wander removal (in grey) and ECG after low pass filtering (black) and RR peaks after HD,
(e) Averaged ECG before HD (dashed line) and after HD (solid line).

Figure 5 shows the lognormal fitting results of a normal (non-mirrored) T wave and a ST segment before and after HD. The results for the mirrored T wave and ST segment are portrayed in Fig. 6.

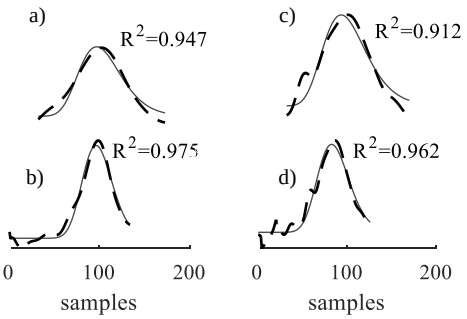

Fig. 5. Illustration of fitting results for non-mirrored T wave and ST segement: T wave (a) and ST segment (b) before HD,
T wave (c) and ST segment (d) after HD
(dashed line is T wave signal, solid one – fitted function)

An Anderson-Darling test was used to test whether the extracted features come from a normal distribution. Since our data wasn't normally distributed, the statistical significance of the differences before and after HD was performed using Kruskal-Wallis test.

As predicted, the goodness of the lognormal fitting in a mirrored T wave is much better, giving the traditional skewness of the lognormal probability density function. Strangely, only the non-mirrored T wave fitting manifested a sensible parameter to changes before and after HD: σ (p=0.0075, whereas p=0.4961 for a mirrored T wave).

Additionally, the *k* parameter of a non-mirrored T wave was also found significant with a p=0.046. Another parameter that could be a potential detector of alterations before and after HD is σ of a non-mirrored ST segment (p=0.0411). Oddly enough, the offset *h* of the mirrored T wave appeared to present a p-value (p=0.0029) sufficiently low to discard the hypothesis, thus could be used to detect changes before and after HD. The p-value results for this fitting are displayed in Table 1.

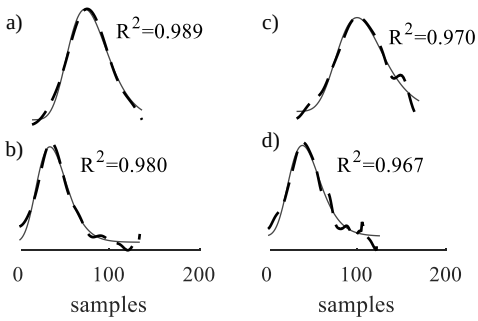

Fig. 6. Illustration of fitting results of mirrored T wave and ST segement:
(a) T wave and (b) ST segment before HD,
(c) T wave and (d) ST segment after HD
(dashed line is T wave signal, solid one – fitted function)

As explained before, 14 morphological ECG features were extracted as well. The statistical results of such features are displayed in Table 2.

TABLE I. P-VALUE RESULTS OF LOGNORMAL PARAMETERS

Model	**Lognormal**				
	k	***μ***	***σ***	***τ***	***h***
p α<0.05	*Non-Mirrored T wave*				
	0.046	0.091	**0.0075**	0.5573	0.2599
	Mirrored T wave				
	0.5573	0.1661	0.4961	0.7248	**0.0029**
	Non-Mirrored ST segment				
	0.0783	0.2222	**0.0411**	0.8144	0.4248
	Mirrored ST segment				
	0.2803	0.0744	0.888	0.1158	0.7963

Only 2, out of the 14 ECG features, demonstrated to be possible indicators of potassium variations before and after HD: T Right-Slope (RS) and $T_{S/A.}$ These parameters scored p<0.05 (p=0.0411, p=0.0189, respectively). As expected, the *T/R* amplitude ratio and *T/RS* amplitude ratios decrease after HD. However, both parameters scored a p>0.05 (p=0.2405 and p=0.1522 respectively) and thus it is impossible to conclude that there is a difference between these features before and after HD. The variation of the duration of the various intervals before and after HD were not significant either. Variation of the length of different intervals was observed, but without any statistical importance. Both the median and mean of the QRS duration shortened after HD.

TABLE II. KNOWN ECG FEATURES P-VALUE RESULTS

ECG Features	Median		Mean		p (α<0.05)
	Before	After	Before	After	
RT interval, ms	0.2650	0.2700	0.2659	0.2644	0.9345
ST interval, ms	0.1290	0.1340	0.1296	0.1322	0.6302
PR interval, ms	0.0640	0.0480	0.0605	0.0500	0.2086
QRS interval, ms	0.0660	0.0640	0.0712	0.0663	0.2298
T/R	0.3623	0.2422	0.3952	0.3087	0.2405
T/RS	0.2902	0.2270	0.3257	0.2579	0.1522
LS, mV	0.0433	0.0304	0.0457	0.0322	0.0821
RS, mV	-0.0437	-0.0257	-0.0476	-0.0317	**0.0411**
T_{Amp}*, mV*	2.0317	1.6939	2.1183	1.5945	0.1522
P_{Amp}*, mV*	0.7830	0.8616	0.7856	0.9029	0.44454
T-COG	0.6228	0.3003	0.5965	0.3277	0.1271
T4-COG	0.6396	0.5708	0.4741	0.5564	0.62214
T-Area	46.639	24.008	42.770	27.640	0.1967
$T_{S/A}$	-0.0283	-0.0247	-0.0312	-0.0252	**0.0189**

IV. DISCUSSION

The main goal of this study was to investigate, which ECG features could be used to distinguish electrolyte fluctuations before and after HD.

The results show that the number of statistically significant global parameters that are able to discriminate ECGs before and after HD is not high. On the one hand, the T/RS ratio does decrease as expected, and patients do demonstrate to have a quite peaked T wave before entering their HD session. However, these results lack statistical proof to indicate that there is strong evidence to support a difference before and after the dialytis, as many other previous studies demonstrated. This could be due to calcium fluctuations. On the other hand, the T wave right slope displays a considerable difference between the two groups, which could be explained by the fact that higher potassium concentrations disturb the typical symmetry of the T wave. Moreover, the feature $T_{S/A}$ proposed by Dillon et al. [8] shows some significance as well.

The lognormal model features σ for a non-mirrored ST segment and a non-mirrored T wave showed statistically significant differences before and after HD procedure. These two features, alongside the T wave features, have a good potential to be used as parameters for monitoring electrolyte variations. *h* offset of mirrored T wave also seems to display some sensitivity to these changes. The *k* parameter of a non-mirrored T wave also displays some significance. The mirrored features did not demonstrate to be detectors of electrolyte fluctuations.

It should be noted that this study is limited by the fact that no blood tests were made before and after HD, thus it can't certainly ascertain if the patients were in a hyperkalemic state or not. The study only intended to understand which electrocardiographic features could be the potential indicators of electrolyte fluctuations, particularly T wave related features.

As a future work, besides the blood tests, other fitting functions should also be tried, as well as evaluating other type of parameters such as heart rate variability. By knowing the exact electrolyte levels in the blood, it is also possible to construct a personalized estimator of the serum potassium levels.

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