Noninvasive Potassium Measurements from ECG Analysis during Hemodialysis Sessions

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Abstract

It is well known that blood potassium concentration [K^+] has a strong influence on ECG signal and particularly on T-wave morphology. No quantitative relations between parameters derived from ECG analysis and potassium levels in the blood have been established for clinical use. We developed a new method to quantify [K^+] from T-wave analysis in real-time and tested it on data from dialysis patients, in which [K^+] varies significantly during the session. The agreement between ECG-based potassium estimator and the reference potassium measurements was good (absolute error: 0.49±0.16 mM) for most of the sessions (30/39) except for 9 (absolute error: 1.17±0.36 mM) in which the presence of a systematic error all along the session did not allow reliable estimates. Bland-Altman analysis showed that the overall systematic error was almost null (-0.03 mM) whereas the standard deviation was 0.83 mM. The manual correction of the bias over each dialysis session resulted in excellent results for all patients. Preliminary results are promising although further investigation is required to understand the reason for session-dependent bias in some patients.

1. Introduction

Maintenance of normal potassium homeostasis is increasingly an important limiting factor in the therapy of several diseases and in particular for patients with heart failure (HF) [1,2] and patients with chronic renal failure maintained on hemodialysis (HD) therapy[3-5].

Electrocardiographic effects of potassium are well known since many years [6,7]: the earliest electrocardiographic manifestation of hyperkalemia is the appearance of narrow-based, peaked T waves; in addition QT segment duration (QTc) [8] and repolarization complexity [9] have also been associated with potassium levels in dialysis patients.

Several studies in the literature are focused on blood potassium concentration ([K^+]) measurement through ECG analysis [3,10-12]. Herzog et al. [3] showed that qualitative evaluation of electrocardiogram changes to diagnose potassium level resulted in poor sensitivity and specificity. Wrenn and colleagues [10] designed their study to determine whether physicians blinded to the serum potassium level can predict potassium concentration of more than 5.0 mmol/L from the ECG; the results showed the sensitivity and specificity of the readers were at most .43 and .86, respectively. In spite of preliminary positive observations [11], Aslam et colleagues showed that the height of T waves does not correlate with [K^+], even if normalized to QRS, especially in dialysis patients [12]. Frohnert et al. were the first to attempt a quantitative assessment of serum potassium level from ECG derived parameters (T-wave amplitude and maximum time) in patients with chronic heart failure [13]. However, this [K^+] estimator was not applied on data from additional patients to test the robustness and validity of the method and did not reach clinical application.

In this study we developed a new method to quantify [K^+] from T-wave analysis in real-time and tested it on data from consecutive dialysis patients, since they have wide fluctuations in serum potassium pre- and post-dialysis. The results of this testing are the subject of this paper.

2. Methods

Changes in extracellular potassium have significant effects on the time course of ventricular repolarization in a manner that profoundly alters the T wave amplitude and slope (figure 1A). We hypothesized a direct relationship between the ratio of the T wave slope to amplitude ($T_{S/A}$, figure 1B) and serum potassium.

Based on the relationship between $T_{S/A}$ and [K^+] we defined an estimator from which the [K^+] values were derived.

We retrospectively analyzed Holter ECG recordings (H12+, Mortara Instrument Inc.) acquired during 39 dialysis sessions on 13 patients (3 per patient for 3 weeks,

the same day of the week). ECG data were exported (SuperECG, Mortara Instrument Inc.). The most significant two eigenleads were used to calculate the slope and amplitude of the T-wave for each beat. The 2-minute window median value of the $T_{S/A}$ was used for the $[K^+]$ estimation at 15 minute intervals.

Reference values for $[K^+]$ as well as values of Na^+ and Ca^{2+} serum concentrations were obtained at the following times: 0, 30, 60, 120, 180, 240 minutes from the start of dialysis by blood samples (RapidLab 855, Bayer).

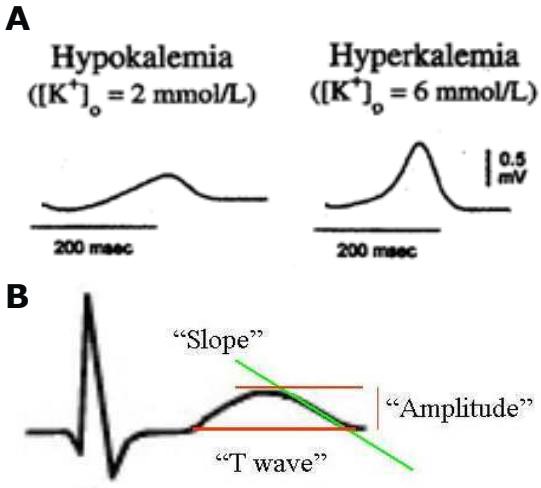

Figure 1. (A) Alterations in T-wave due to different potassium level [14]; (B) A typical QRS-T wave complex from a representative electrocardiogram together with the schematic explanation of the negative slope and the amplitude of the T wave used for $[K^+]$ estimation.

3. Results

A significant correlation ($r=0.63$, $p<0.0001$) was found between $T_{S/A}$ and $[K^+]$ (figure 2).

Based on these results an ECG-based potassium estimator (K_{ECG}) was defined as $K_{ECG}=1.21* T_{S/A}-0.69$ and compared with the reference potassium measurements.

The agreement was good (absolute error: 0.49±0.16 mM) for most of the sessions (30/39). An example of the results obtained in one patient is shown in figure 3.

In 9 sessions (absolute error: 1.17±0.36 mM) the presence of a systematic error (bias) all along the session did not allow reliable estimates. An example of a patient in which a systematic error in the $[K^+]$ estimates is shown in figure 4.

Bland-Altman analysis showed that the overall systematic (mean) error was almost null (-0.03 mM) whereas the standard deviation (sd) was 0.83 mM (figure 5). The manual correction of the bias over each dialysis session resulted in excellent results for all patients (mean=0.001 mM, sd=0.45 mM). An example of the result improvement following the manual correction, in one session is shown in figure 6.

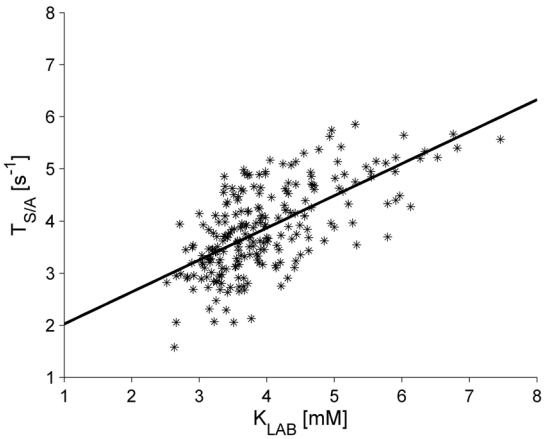

Figure 2. Linear regression between $T_{S/A}$ and $[K^+]$.

4. Discussion and conclusions

We proposed a new method for quantification of the blood potassium concentration in real-time from the ECG.

The treatment of several classes of patients could benefit from a non-invasive measurements of $[K^+]$. In HF patients a combination drug therapy may simultaneously improve clinical outcomes and enhance the risk of potassium-related adverse events; therefore an appropriate balance of benefit and risk depends heavily on careful patient selection and adequate surveillance of serum potassium [1]. In HD patients the restoration of plasma potassium concentration is one of the main goals of the therapy, but HD-induced changes in $[K^+]$ can lead to dangerous transient hypo or hyperkalemia [8,9].

In this framework, continuous potassium monitoring could be extremely useful in order to design dialysate potassium content tailored to the patient's specific needs or even to close the loop and personalizing each single therapy session through a real biofeedback system.

Preliminary results are promising although further investigation is required to understand the reason for session-dependent bias in some patients. Possible causes for this limitation could be session dependent factors such as serum calcium, initial hydration status, pH, heart rate and serum magnesium. Following a comprehensive validation, this method could be effectively applied to monitor patients at risk for hyper- and hypo-kalemia which are among the main risk factors for cardiac arrhythmias as well as being indicators for worsening of heart or kidney conditions.

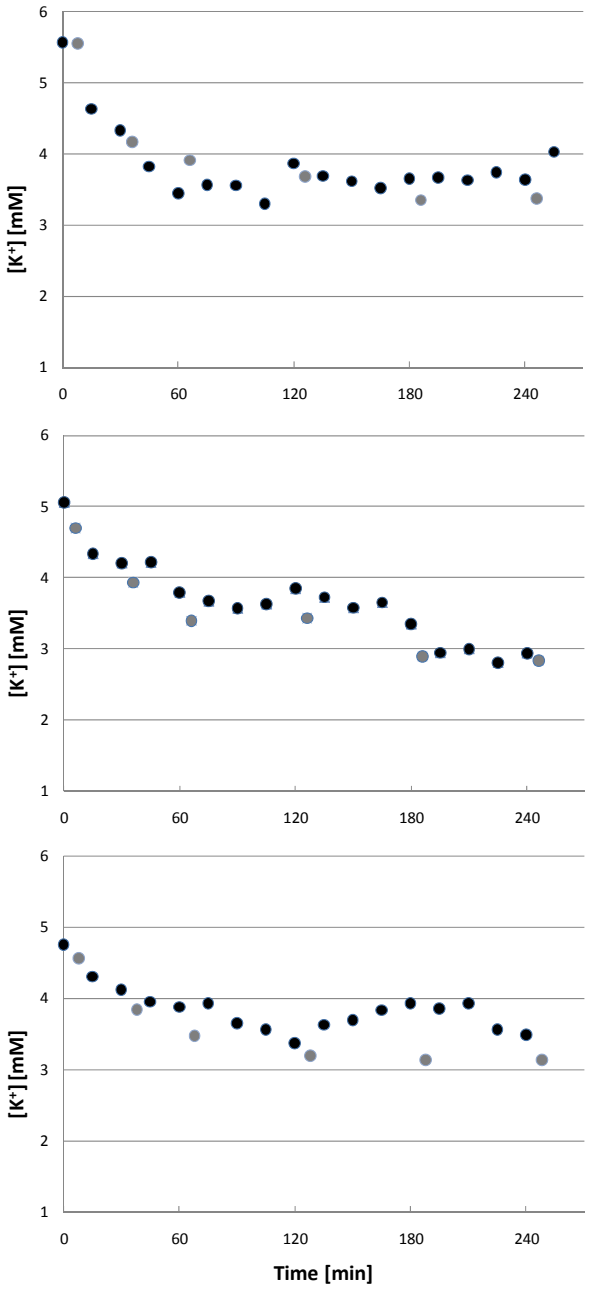

Figure 3. Example of a good agreement between the K_{ECG} (dark points) and reference potassium values (light points) in one patient in the three analyzed sessions.

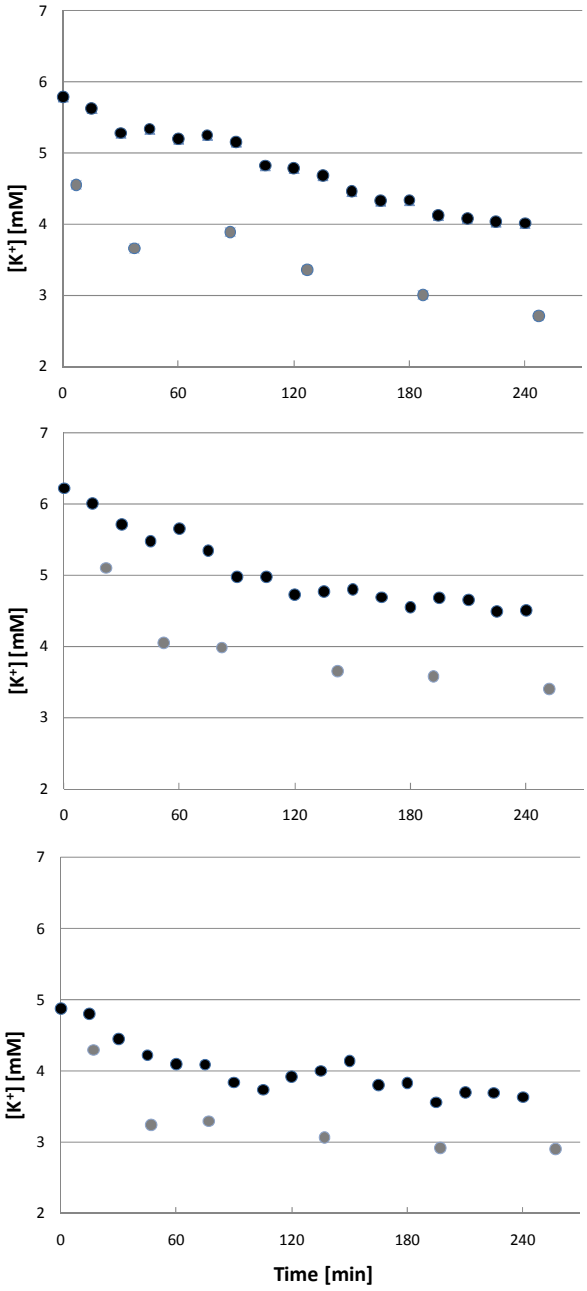

Figure 4. Example of the systematic error in the K_{ECG} measurements (dark points) and reference potassium values (light points) in one patient in the three analyzed sessions.

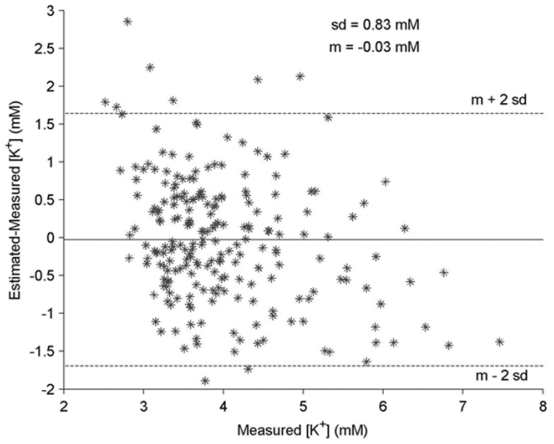

Figure 5. Bland-Altman plot of the estimated vs the reference values for $[K^+]$.

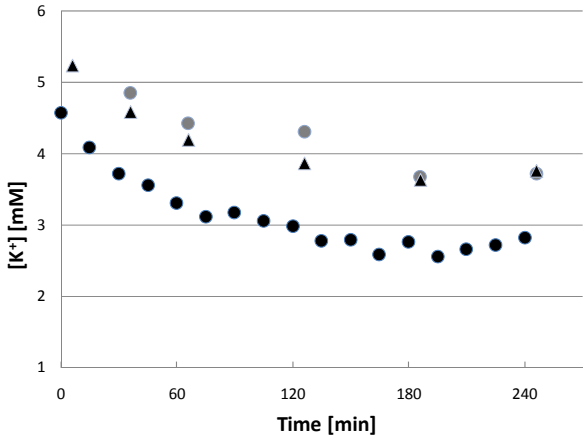

Figure 6. Example of the improvement (dark triangles) obtained in one patient applying manual bias correction to the K_{ECG} estimates (dark points) with respect to the reference potassium values (light points).

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