

Effects of Ca^{2+} and K^+ Changes during Dialysis on Ventricular Repolarization Duration: *in vivo* and *in silico* Analysis

STEFANO SEVERI¹, ELEONORA GRANDI¹, CHIARA PES¹, FABIO GRANDI² AND ANTONIO SANTORO³

¹ Biomedical Engineering Laboratory – Dept of Electronics, Computer Science and Systems, University of Bologna, Cesena, Italy. ² Hospal S.p.A., Bologna, Italy. ³ Malpighi Nephrology Division, Policlinico S. Orsola-Malpighi, Bologna, Italy

ABSTRACT: Alterations of ventricular repolarization duration, as measured by QT interval, are frequently observed in patients undergoing hemodialysis (HD) therapy. The nature and the sign of these alterations are not fully understood. HD-induced electrolyte changes are one of the main factors that can affect ventricular repolarization. Different levels of K^+ and Ca^{2+} concentrations in the dialysis bath, leading to different K^+ and Ca^{2+} end-dialysis plasma concentrations in the patient, have been tested in the present study. Each patient underwent two HD sessions differing for only one electrolyte concentration serving as his/her own control. Duration of heart rate corrected QT interval (QTc) was assessed on ECG recordings. The Ten Tusscher mathematical model of human cardiomyocyte action potential (AP) was used to assess *in silico* whether the changes in Ca^{2+} and K^+ concentration were able to justify at the cellular level the observed alterations of QTc duration.

The clinical study confirmed that QTc interval is prolonged in dialyses with low vs. high Ca^{2+} (424 ± 33 vs. 400 ± 28 ms, $p < 0.05$). For the first time we showed a similar effect by comparing dialyses with identical bath composition except for K^+ concentration (K^+ low: 420 ± 35 ms, K^+ high: 399 ± 36 ms, $p < 0.05$). These alterations were confirmed at the cellular level by the computational analysis showing end-dialysis prolongation of ventricular AP both at low Ca^{2+} (APD₉₀: 310 vs. 288 ms) and at low K^+ (APD₉₀: 318 vs 300 ms). Moreover, numerical simulation predicted a critically long AP when considering low K^+ and Ca^{2+} simultaneously, suggesting the concurrent lowering of Ca^{2+} and K^+ as a potential arrhythmogenic factor.

Results from previous studies on QTc in HD indicated that when both Ca^{2+} and K^+ change during the treatment, the overall result on QTc is not easily predictable. We suggest that numerical simulation of the ventricular AP may be useful to quantitatively predict the complex dependence of APD on simultaneous changes in Ca^{2+} and K^+ . We conclude that Ca^{2+} content in the dialysis bath should be designed so as not to critically lower serum Ca^{2+} , especially in sessions at risk of end-dialysis hypokalemia.

KEYWORDS: Hemodialysis, Ventricular repolarization, Action potential, Computational biology, Electrolytes

Address for correspondence: Stefano Severi PhD, Biomedical Engineering Laboratory - Dept. of Electronics Computer Science and Systems, University of Bologna, Cesena (FC), 47023, Italy,
Tel: +39054739202; Fax: +39054739208,
E-mail: sseveri@deis.unibo.it

