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Alterations of atrial electrophysiology related to hemodialysis session: insights from a multiscale computer model

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Abstract

Background: The prevalence of atrial fibrillation is increased in patients with end-stage renal disease. Previous studies suggested that extracellular electrolyte alterations caused by hemodialysis (HD) therapy could be proarrhythmic.
Methods: Multiscale models were used for a consequent analysis of the effects of extracellular ion concentration changes on atrial electrophysiology. Simulations were based on measured electrolyte concentrations from patients with end-stage renal disease.
Results: Simulated conduction velocity and effective refractory period are decreased at the end of an HD session, with potassium having the strongest influence. P-wave is prolonged in patients undergoing HD therapy in the simulation as in measurements.
Conclusions: Electrolyte concentration alterations impact atrial electrophysiology from the action potential level to the P-wave and can be proarrhythmic, especially because of induced hypokalemia. Analysis of blood electrolytes enables patient-specific electrophysiology modeling. We are providing a tool to investigate atrial arrhythmias associated with HD therapy, which, in the future, can be used to prevent such complications.

Keywords: Hemodialysis; Atrial electrophysiology; Multiscale cardiac modeling; Patient-specific modeling; P-wave

Introduction

The prevalence of atrial fibrillation (AF) in hemodialysis (HD) patients is much higher than in the general population, and AF is associated with greater total and cardiovascular mortality in these patients.[1] It has been shown that, during HD session, there is an increased occurrence of supraventricular ectopic beats that can be triggers for the onset of paroxysmal AF episodes.

Moreover, transmembrane ionic movements occurring during the HD session can induce changes in action potential (AP) of myocardial cells and contribute to increase AF susceptibility. A recent study combining single cell simulations and analysis of measured electrocardiograms (ECG)[2] revealed a correlation between changes in plasma electrolytes and intra-atrial conduction velocity (CV) related to HD therapy. We present a multiscale, multi-tissue simulation study to investigate the influence of HD-related electrolyte modifications on atrial electrophysiology from the cell level to the ECG.

Because many studies described the macroscopic effects of HD-induced electrolyte changes on atrial electrophysiology, we want to bridge the gap between single cell simulations and in vivo body surface ECG measurements and, thus, provide an insight into the underlying phenomena. This can be used to optimize the dialysis bath composition to reduce the risk of AF onset during the session.

An additional intention of the presented work is to show that models of cardiac electrophysiology can be personalized

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by the adaptation of model electrolyte parameters to individual plasma concentrations.

Methods

The influences of extracellular ion changes owing to HD therapy were evaluated on different levels of electrophysiologic modeling (Fig. 1). Severi et al[2] showed the impact of electrolyte alterations on isolated single cells using the Courtemanche-Ramirez-Nattel (CRN) AP model for human atrial myocytes.[3] Our study focuses on the simulation of coupled cells in homogeneous and heterogeneous tissues and organs using the CRN model as well as the computation of body surface potentials.

Patient data

The 6 different dialysis baths listed in Table 1, column 1, include the possible electrolyte combinations used in clinical practice: each of them produces different plasma electrolyte variations. Data are drawn from a previous study[5] in which 16 patients performed 3 HD sessions at a K^+ concentration of 2 mmol/L and 3 sessions at 3 mmol/L. Each of these HD

Table 1
Plasma ion concentration measured before and at the end of HD sessions with 6 different compositions of dialysis bath

Bath	$[K^+]_o$—pre (mmol/L)	$[K^+]_o$—post (mmol/L)	$[Ca^{2+}]_o$—pre (mmol/L)	$[Ca^{2+}]_o$—post (mmol/L)
K2Ca1.25	5.0 (0.4)	3.3 (0.2)	1.17 (0.11)	1.24 (0.12)
K2Ca1.50	5.0 (0.5)	3.4 (0.2)	1.16 (0.11)	1.37 (0.06)
K2Ca1.75	5.2 (0.6)	3.5 (0.3)	1.18 (0.09)	1.52 (0.07)
K3Ca1.25	5.1 (0.6)	3.7 (0.3)	1.17 (0.12)	1.19 (0.05)
K3Ca1.5	5.1 (0.6)	3.9 (0.4)	1.16 (0.10)	1.25 (0.12)
K3Ca1.75	5.1 (0.4)	3.9 (0.3)	1.21 (0.12)	1.37 (0.07)
Severi et al[2]	4.9 (0.5)	3.9 (0.4)	1.18 (0.09)	1.30 (0.07)

Data were taken from Genovesi et al,[5] except from the bottom row, which reflects the data collected in Severi et al.[2] Values are presented as mean (SD).

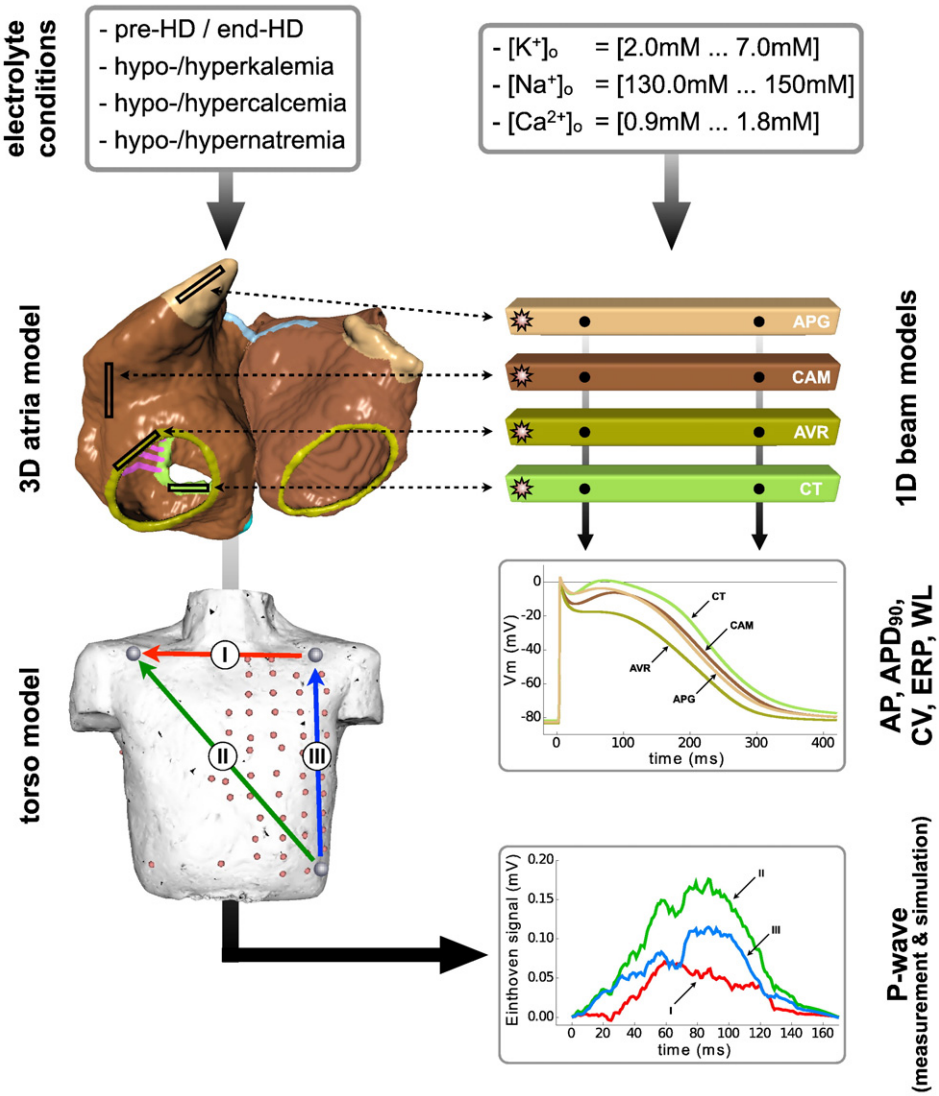

Fig. 1. Schematic overview of the multiscale modeling approach. Different electrolyte conditions (top row) were used to parameterize the CRN model of atrial electrophysiology. These model setups were used to run simulations in four 1D beam models and in combination in a 3D model of a single atrial anatomy. The results were used to evaluate the influence of electrolyte changes on the atrial AP, its duration (APD_{90}), CV, ERP, WL, and body surface ECG.