Cardiac Sensitivities to Biomechanical Changes in a Chronic Alcoholic Heart: A Case Study Using 3-Dimensional Electro-Mechanical Heart Modelling

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Abstract

Chronic excessive alcohol consumption impairs cardiac function through altered anatomy, material properties, and pre-/afterload. Understanding these mechanisms may improve diagnosis, patient selection, and therapy monitoring. We propose a multi-scale 3D electro-mechanical cardiac simulator, integrating patient data to identify key biomechanical factors affecting heart function. Patient-specific four-chamber anatomical models were created for a control and an alcohol-affected case, simulating cellular, tissue, and organ scale electrophysiology and mechanics within a closed-loop cardiovascular system. We evaluated the impact of myocardial stiffness, ventricular pressures, and vascular resistance through 100 simulations, employing Latin Hypercube (LH) sampling. Gaussian Process Emulators (GPE) were developed for ejection fraction, maximum ventricular pressures, and left ventricular (LV) end-diastolic volume outputs. Sensitivity analysis revealed LV end-diastolic pressure as the most influential parameter in both models, with LV stiffness significantly impacting right ventricle (RV) ejection fraction in the alcohol-affected model. Systemic resistance had a larger influence than pulmonary resistance, particularly in the alcoholic heart.

1. Introduction

Chronic alcohol consumption has a significant impact on cardiovascular health. Epidemiological evidence suggests a cardioprotective effect associated with light to moderate alcohol intake [1]. However, chronic alcohol consumption can have a negative impact on cardiac performance, potentially leading to alcoholic cardiomyopathy characterized by ventricular dilation and impaired cardiac function [2]. These pathological changes can consequently lead to reduction in ejection fraction and impaired heart tissue contractibility increasing the risk of stroke and hypertension [3].

While prior studies have investigated structural and functional changes due to chronic alcohol use, the dynamic mechanical response of the heart to such changes remains less explored. Current methods do not fully explain the biomechanical behaviour of the heart under the altered conditions brought about by chronic alcohol exposure. Thus, this study leverages the capabilities of 3D electro-mechanical heart modelling and integrates cine MRI imaging and sensitivity analysis to reveal the sensitivity of the cardiac performance to biomechanical changes in a chronic alcoholic heart.

2. Methods

Four-chamber multi-scale electromechanical patient specific cardiac models were created for a representative control and alcohol cardiomyopathy case. Models were created in three steps: image processing, mesh generation and fibre orientations, and electro-mechanics-simulations.

Global sensitivity analysis was then employed to examine the sensitivity of indexes of whole organ cardiac function to changes in cardiac biomechanics material properties, boundary conditions and initial conditions: myocardium stiffness, end-diastolic pressure, and systemic and pulmonary resistance.

2.1. Image acquisition

Cine MRI images with in plane resolution of 1.38x1.38 mm and the slice thickness of 6 mm were collected from

control subjects and those with chronic alcohol exposure. A short-axis MR image of the alcoholic subject has been shown in Figure 1A.

2.2. Segmentation, Mesh generation and fiber orientation

The 3D geometry of the heart was segmented with 30 distinct labels including blood pools, myocardium, outflow tracts and main blood vessels. Figure 1B shows a 2D segmented slice associated with a short axis image of the four chambers of the heart. Linear tetrahedral elements with average edge length of 0.8 mm were used to mesh the 3D reconstructed geometry of the heart (Figure 1C). Ventricular and atrial myofibre orientations were assigned to the mesh, following the Laplace-Dirichlet rule-based method defined by Bayer et al [4]. Myofiber orientations were calculated by extracting the epicardial surface of the ventricles and the endocardial boundaries of both the LV and RV within the mesh, which then used to define various Laplace solutions. Fibre and sheet angles at the endocardium and epicardium were defined at +60°/-60° and +65°/-25°, respectively [5]. For the atrial fibres, universal atrial coordinates [6] were used to map myofibre orientations from a human ex-vivo DTMRI dataset using the Cardiac Arrhythmia Research Package (CARP) [7]. Subsequently, an epicardial and endocardial layer of fibres were assigned based on a transmural Laplace solution [5]. Figure 1D demonstrates the myofibre directions assigned to the ventricles and atria.

2.4. Electromechanics simulation

To simulate the electrical activation of the heart, a reaction-eikonal model [8] was employed. Transversely isotropic conduction media were used to model the atrial and ventricular myocardium, with the preferred conduction direction being in line with the local myofibre orientation [5]. Additionally, two new regions were defined: one to replicate fast endocardial activation in the ventricular endocardium and the other to represent the Bachmann's bundle in the atria. The hyperelastic Guccione model [9] was used to model the atria and ventricles as a transversely isotropic, hyperelastic, and nearly incompressible material. Other tissues such as aortic wall, pulmonary artery and valve planes were modelled as neo-Hookean material. Normal springs were used to simulate the effect of the pericardium. A spring stiffness of 10 kPa/mm was scaled in space based on the method described in [10], [11]. The mechanical contraction was simulated with the Land model and coupled with a closed-loop model for the circulatory system using CircAdapt [12]. Unless otherwise stated default parameters are taken from [13], [14] and these values were assumed to be the same in both the control and alcohol induced cardiomyopathy case.

2.5. Global sensitivity analysis

The GSA was performed over physiological ranges for the stiffness of the LV, RV, and atria, as well as the end-diastolic pressures of the ventricles and systemic and pulmonary resistance (Table 1). Using the LH sampling method with N=100, a set of 100 value combinations was created for these parameters. Simulations were performed at all sampled points in both the control and alcohol induced cardiomyopathy case.

Table 1. Parameters' ranges used in sampling

Parameter	Range
a_ventricles [KPa]	0.5-2.5
a_atria [KPa]	1.5-2.5
EDP_lv [mmHg]	6-12
EDP_rv [mmHg]	3.6-7.6
a_lvrv [-]	1-2
Rsys [-]	1-4
Rpulm [-]	1-4

Upon the completion of all simulations, the values of the input parameters and output data, were utilized to train a GPE which was then used to perform a global sensitivity analysis.

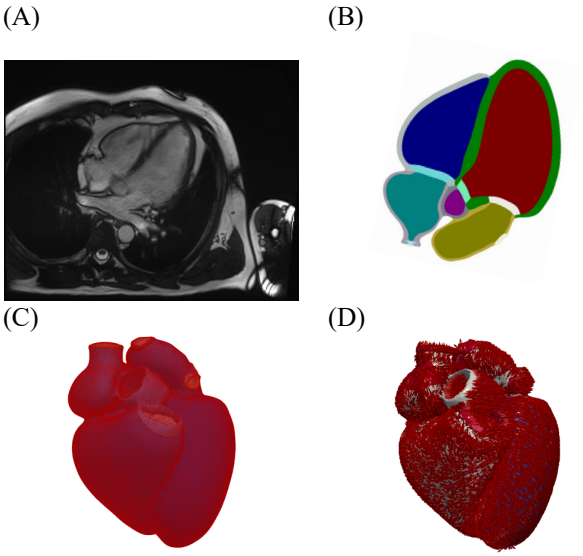

Figure 1. Image processing pipeline: (A) Short-axis view (B) Segmented labels (C) 3D meshed model (D) Myofibre directions assigned to the atria and ventricles.

3. Results

We made models from two cases (Table 2). Figures 2A and 2B show the sensitivity analysis of control and

alcoholic hearts, highlighting how seven main parameters influence five cardiac outputs, including ejection fractions, peak pressures of ventricles, and LV end-diastolic volume. In the control heart, the LV stiffness (a_ventricles) has the highest impact on LV maximum pressure (pmax_lv), while in the alcoholic heart, it notably affects RV ejection fraction (EF_rv). Atria stiffness shows a slightly higher influence on the ejection fractions of both ventricles in the control heart, with a comparable impact observed in the alcoholic heart. Moreover, the LV end-diastolic pressure has the highest influence on LV end-diastolic volume across both hearts. For the control heart, the end-diastolic pressure in the RV has the highest impact on the LV ejection fraction. This effect is similar in the alcoholic heart, where it equally affects the LV ejection fraction and the RV maximum pressure. Regarding the systemic and pulmonary resistance, it indicates that the systemic resistance primarily affects the LV ejection fraction, whereas the pulmonary resistance most significantly influences the RV maximum pressure, with these relationships holding true in both control and alcoholic hearts.

Table 2. Patients' demographic data

Feature	Control	Alcoholic
Age [years]	34	39
Height [cm]	175	183
Gender	male	male
LVS (LV size) [cm^{3}]	203	184
RVS (RV size) [cm^{3}]	186	161

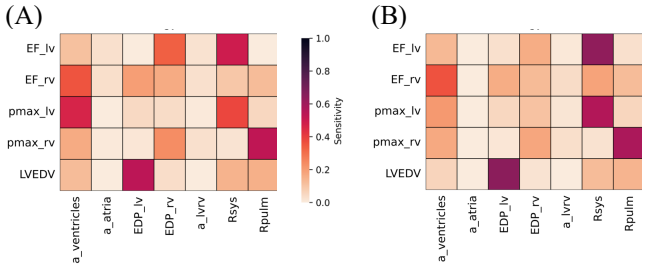

Figure 2. Normalized impact of input parameters (x-axis) on the outputs (y-axis), (A) control and (B) alcoholic

In Figures 3A and 3B, the total effects of input parameters on outputs are ranked for the control and alcoholic hearts, respectively. The graphs demonstrate that LV end-diastolic pressure is the most influential parameter affecting cardiac outputs in both heart conditions. In the control heart, pulmonary and systemic resistance rank as the second and third most impactful parameters. However, in the alcoholic heart, systemic resistance is the second most important parameter with a slightly higher influence than the pulmonary resistance. The RV end-diastolic pressure, while significant for the control heart, shows a lower effect on the alcoholic heart. Furthermore, the figures reveal that LV stiffness has significantly higher influence than atrial stiffness in both scenarios, with atrial stiffness having no impact on the output parameters of the alcoholic heart. This suggests different responses in cardiac mechanics between the control and alcoholic hearts to these specific physiological parameters.

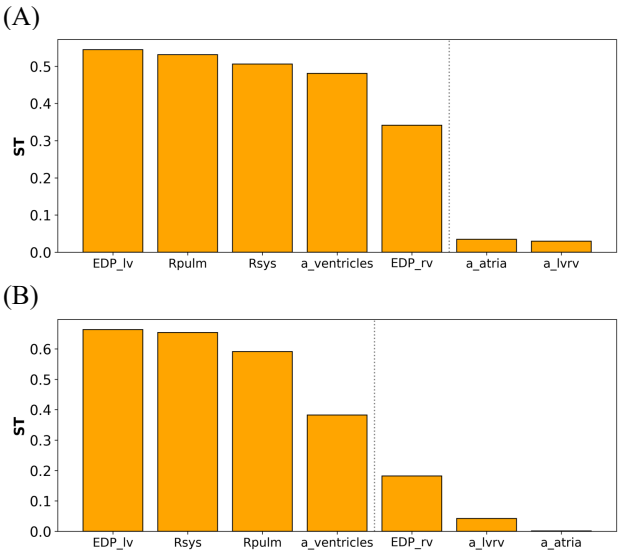

Figure 3. Ranked input parameters according to their total impact, (A) control and (B) alcoholic

The findings of this study underscore the pronounced impact of LV end-diastolic pressure and myocardial stiffness on cardiac function in chronic alcoholic hearts. These results align with previous research, indicating that chronic alcohol consumption exacerbates ventricular contractibility [15], which in turn negatively affects cardiac output and overall heart performance. Furthermore, the significant role of systemic resistance observed in our alcoholic heart model corroborates findings in [16], who reported enhanced vascular resistance as a critical factor in chronic alcoholism. Our study extends these insights by quantifying the relative influence of these parameters through advanced 3D electro-mechanical heart modeling.

5. Limitations

This is the first 3D multiscale electro mechanical heart model of the heart's response to chronic alcohol consumption. Its conclusions are derived from a single comparative case study. The study's scope, including one control and one alcoholic heart, sets a platform for broader research rather than offering statistically significant conclusions. The goal moving forward is to expand this research to a cohort of patient specific models

involving multiple cases of chronic alcoholic hearts, which would provide a more robust and statistically valid outcomes. Furthermore, the current study considered a limited spectrum of seven input and five output parameters, specifically related to cardiac mechanics. Future studies should include a wider range of parameters, particularly those associated with biochemical alterations. These additions would enhance the relevance of the findings to real physiological variations observed in chronic alcoholism.

6. Conclusion

This study utilized MRI-based 3D electro-mechanical modelling to analyse cardiac performance in chronic alcoholic versus control hearts, with a particular focus on biomechanical sensitivities. Global sensitivity analysis revealed key physiological parameters with the highest impact on cardiac outputs. Notably, LV end-diastolic pressure was identified as having the highest overall impact in both heart models. Systemic resistance found to be more influential than pulmonary resistance, especially in the alcoholic heart model. The findings highlight a distinct difference in how chronic alcoholism may affect heart performance, with LV stiffness being more significant than atrial stiffness.

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