# MODELING THE DYNAMICS OF VICIOUS CYCLES INVOLVED IN HEART-RESPIRATORY FAILURE

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**Keywords:** heart failure, acute heart failure, medical modeling, dynamic system simulation

**Funded by** Boğaziçi University Research Grant No. 13100

Heart failure is a syndrome when the heart is damaged permanently and loses its full functionality. In this case, the tissues cannot be fed sufficiently with blood and oxygen, and compensatory mechanisms are triggered. These mechanisms are the Sympathetic Nervous System, Renin-Angiotensin-Aldosterone, Antidiuretic Hormone, and Natriuretic Peptides, which help a healthy human body to reach a homeostatic balance. When the balance is impaired, they work as negative feedback loops that seek equilibrium levels (Schrier, 2006).

Compensatory mechanisms are beneficial in the short run due to increased hemodynamic parameters provided by sodium and water retention and vasoconstriction. However, heart failure patients have damaged and dilated hearts. Therefore hemodynamic parameters never reach their target levels. Water and sodium retention damages the cardiac system in the long run, as elevation in blood pressure results in excessive tension in the heart and respiratory problems occur due to fluid accumulation in the lungs. These problems increase myocardial dysfunction and result in an irreversible deterioration in the condition of the already damaged heart. (Teichman et al., 2015). This positive feedback mechanism that causes permanent deterioration in the heart is a “vicious cycle”.

The relationships of positive and negative feedback loops discussed above are shown in the causal loop diagram in Figure 1. In this study, we construct a simulation model of acute heart failure syndrome with cardiogenic pulmonary edema, by considering these feedback loops using system dynamics methodology. Our aim is to model the acute decompensated heart failure (ADHF) and investigate alternative treatment options. Our model has five sectors: hemodynamic sector, hormonal compensatory mechanisms sector, sodium and water sector, cardio-respiratory sector, and treatment sector. The period between hospitalization and discharge of a patient who is admitted with pulmonary edema and low cardiac output symptoms is the focus of simulation. The time unit is in hours and the total time horizon of the model is around one month. The time step is selected as 0.02 hours. Stella software version 9.0.3 is used. The variables are defined for both a healthy average person (male, 70kg) and C-stage heart failure patients.

In the model validation phase, four different validation experiments are analyzed. These experiments are: i) equilibrium run, ii) setting an initial fluid volume of 41 liters, iii) non-cardiogenic pulmonary edema, and iv) pharmacokinetic behaviors of drugs. The results of all validation tests are found to be consistent with literature. In the study, two main scenarios are defined. The first one simulates the

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disease without treatment while the second one considers two different treatment methods that aim to minimize pulmonary edema excretion time and time of the stabilization of the variables.

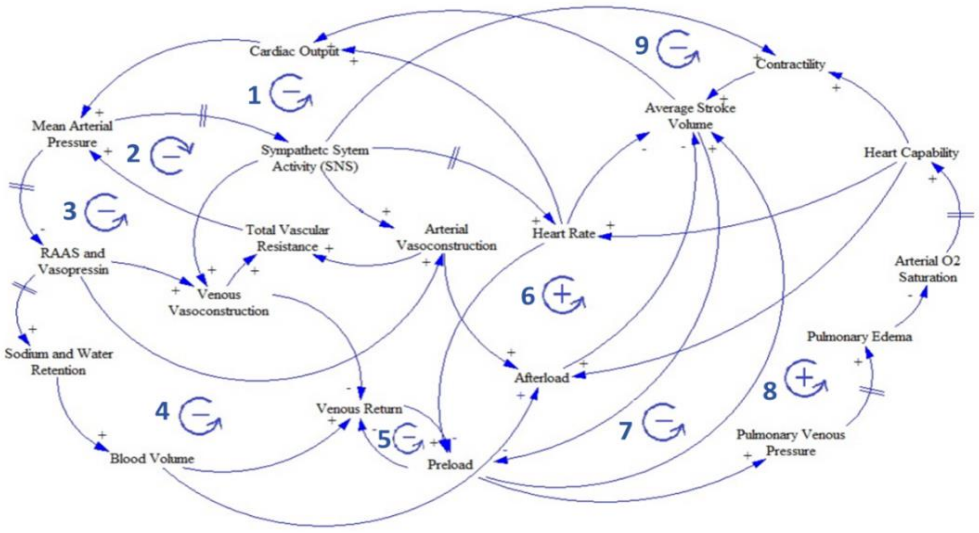


Figure 1: Causal Loop Diagram

The first scenario is constructed using the parameter values of a C-stage systolic heart failure patient.. As shown in Figure 2, hemodynamic variables collapse following a stable period. Compensatory mechanisms work to increase their values since hemodynamic parameters are lower than the values of a healthy individual.. Simultaneously, pulmonary edema occurs because of blood accumulation in the heart. Pulmonary edema decreases oxygen supply resulting in the gradual deterioration of heart performance. Decreased heart performance results in a permanent loss in heart's capability. This cycle eventually results in death if no treatment is applied.

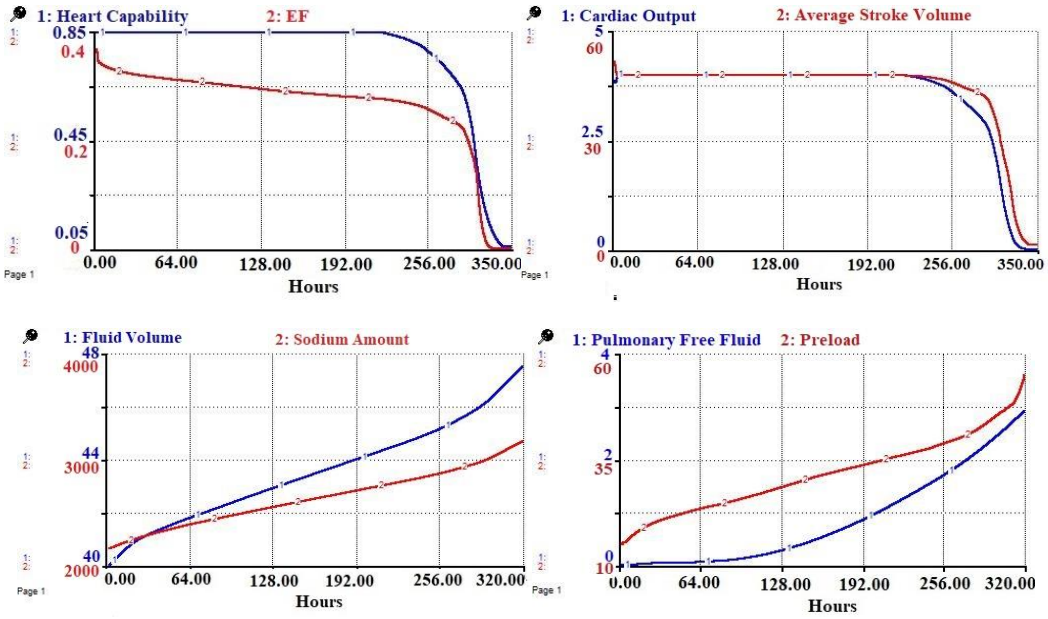


Figure 2: Dynamics of important hemodynamic variables and accumulation of fluid and sodium in periphery and lungs for C Stage Systolic HF Patient without treatment

In the second part of the scenario analysis the period between hospitalization and discharge of a patient who is admitted with pulmonary edema and low cardiac output symptoms is simulated. The time of admission to the hospital is considered as t = 180, where oxygen saturation is between 90% and 85% since most heart failure patients go to the hospital when their oxygen saturation level is in this range. In this scenario, two different treatment strategies are applied.

In the first treatment strategy, 80 mg Furosemide is given to the patient every 12 hours until pulmonary edema is completely excreted. After that, treatment is continued with 40 mg Furosemide every 12 hours, 10 mg Bisoprolol, and 16 mg Candesartan every 24 hours. In the second treatment strategy, at the beginning of the hospitalization, 10 mg Bisoprolol and 16 mg Candesartan are given every 24 hours while 80 mg Furosemide is administered every 12 hours. After the pulmonary edema dissolves, Furosemide is reduced from 80 mg to 40 mg and is continued every 12 hours.

In the first treatment strategy, the patient's pulmonary edema disappears at t = 195. Stabilization of the patient's fluid volume and sodium amount is achieved after t = 220 as seen in Figure 3. In the second strategy, the patient's pulmonary edema disappears at t = 218. Stabilization of the patient's fluid volume and sodium amount is achieved after t = 390 as seen in Figure 4. For both strategies, hemodynamic parameters are improved and their values stabilize at the same levels.

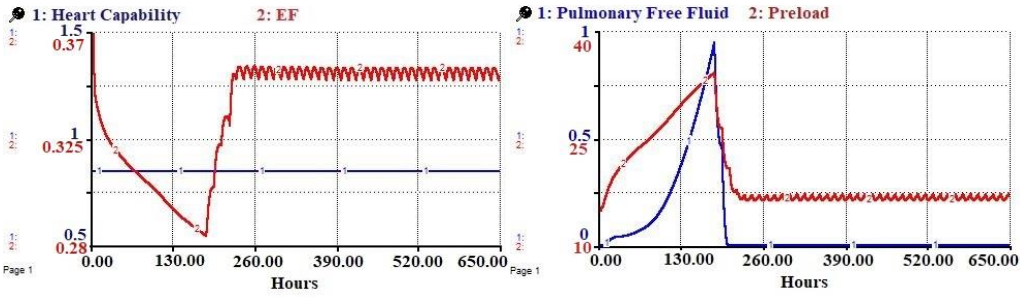


Figure 3: Dynamics of important variables when treatment strategy 1 is applied

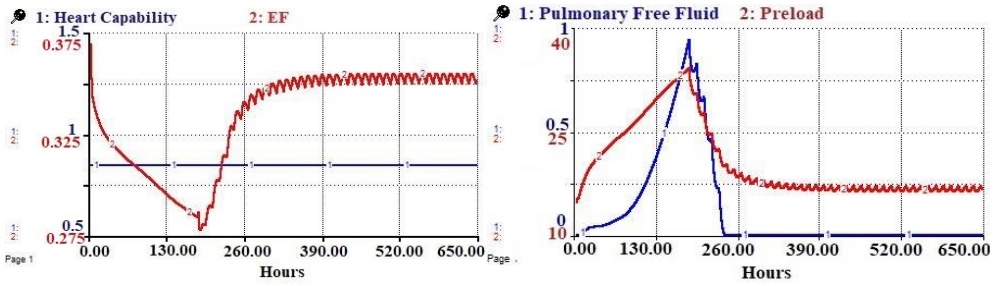


Figure 4: Dynamics of important variables when treatment strategy 2 is applied

This study has achieved the goal of modeling the dynamics of C-stage systolic acute heart failure, testing progress of the disease, and generating a test bed for analyzing the effectiveness of various treatment methods. The model is verified and validated using quantitative data in the medical literature and the expertise of doctors in the field. Then two alternative common treatment methods are analyzed. An immediate future avenue to explore would be to test alternative novel treatment methods, using different drug combinations and doses. The model can also be further developed by working

with multidisciplinary groups of physicians and physiologists to explore better strategies for treatments and to use such simulation models for the education of medical students.

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