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Research Article

A Multistate Markov Model for the Progression of Congestive Heart Failure Using Kolmogorov Differential Equation

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Abstract. The reliability of individuals and human activities are vital for the new complexity of life, work and medication improvement. Markov models are grounded strategies for assessing paces of progress between phases of chronic illnesses. This paper is mainly focused on the survival analysis of a heart patient with Congestive cardiac failure. The objective of the paper is to describe the progression process of chronic heart failure (CHF), to estimate the life expectancy of patient suffering from congestive Heart failure. Explicit expression for Availability is also derived in this paper by using Kolmogorov differential equations. Graphs have been plotted to determine the behaviour of life expectancy of patient and availability analysis.

Keywords. Congestive Heart Failure, CTMC, Kolmogorov differential equations, Life expectancy/ Mean time to absorption, Availability

Mathematics Subject Classification (2020). 90b35, 62P10, 60J25

1. Introduction

Heart failure is a common clinical syndrome and a global health priority. The burden of heart failure is increasing at an alarming rate worldwide as well as in India. Heart failure not only increases the risk of mortality, morbidity and worsens the patient's quality of life, but also puts a huge burden on the overall healthcare system. The management of Heart failure has evolved over the years with the advent of new drugs and devices [13]. One of the strategies of defeating any chronic disease is to detect it early side by side with the national planning for insuring sufficient treatment of patients. The earlier the chronic disease is detected the easier to keep the patients in their primary stages and delaying their transition to more severe stages using suitable treatments and suitable lifestyle regime [3].

Heart failure can sound very scary. But that does not imply that your heart has quit working totally as opposed to this implies that the heart is not functioning just as in the past. Heart failure is a major health problem in India as well as in other countries and leading cause of hospitalization in people older than 65.

Heart failure can be of two types depending on the time, acute and chronic. The development of acute heart failure is sudden and its initial symptoms are very severe. Acute heart failure can lead to a heart attack due to which damage has been occurred to any part of the Heart. Often the initial symptoms of acute heart failure are severe, but they are short lived and recover fast. In this case prompt treatment and timely medication is required. On the other hand, in chronic heart failure initial symptoms appear gradually over time and get worse as time progresses.

Congestive heart failure is a complex clinical syndrome that can result from any functional or structural cardiac disorder that impairs the ventricle's ability to fill with or eject blood. Since there is no definitive diagnostic test for heart failure, it remains a clinical diagnosis that is largely based on a careful history and physical examination and supported by ancillary tests such as chest radiograph, electrocardiogram and echocardiography [6]. The administration of patients with Heart failure contains a few significant steps: determination, ID of causes or reversible elements, and mediation. An early and complete clinical evaluation of all new patients with heart failure is basic to perceive conceivable foundational and cardiovascular causes that may be reversible.

Our objectives of treatment are to improve quality and amount of life by soothing side effects and improving activity resistance. Treatment depends upon the seriousness and reason for the infection. In individuals with chronic stable mild heart failure, treatment ordinarily comprises of way of life adjustments like halting smoking, actual exercise, and dietary changes as well as medications. Sometimes depending upon the reason, an implanted device like pacemaker or an *implantable cardiovascular defibrillator* (ICD) might be suggested or periodically heart transplantation might be suggested in those with serious sickness that persists despite all other measures. Heart transplantation is the replacement of a failing heart with a heart from an appropriate donor.

The American college of Cardiology/American Heart Association (ACC/AHA) [4] staging system is defined by the following four stages:

Stage A: High risk of heart failure, but no symptoms of heart failure.

Stage B: Structural heart disease but no symptoms of heart failure.

Stage C: Structural heart disease & symptoms of heart failure.

Stage D: Refractory heart failure requiring specialized interventions.

In this paper, Figure 1 shows a multistate Markov model where states shows the chronic stages of congestive heart failure. Such types of models demonstrate the progressive stages of more degradation in chronic diseases. In the event of a serious illness worsening, the patient can either recover completely or enter the next level of the disease. This paper described a multistate model which is based on transition intensity matrix Q. Kolmogorov differential equation is used to solve the explicit expression taken for life expectancy and availability of the system. Many researchers have used these types of models with various number of transient states in the treatment of many diseases such as cancer, HIV, diabetes and chronic diseases etc. [3–6, 11, 13]. A multistate Markov model is created by Grover *et al*. [7] for endurance information investigation for patient experiencing chronic liver disease. Anthwal *et al*. [2] introduced a Mathematical model for beginning of Alzheimer infection through Markov Process.

2. Assumptions

The following assumptions have been used while doing this work:

- The patient goes through a few levels of disease as per Markov chain model and states S_i, $i = \{0, 1, 2, 3, 4, 5\}$ of countable states.
- State 0 addresses sickness free state and states $1, 2, \dots, 5$ address the distinctive adverse disease state of the patient and bigger the value, the more serious is the condition.
- States of the model are representing the successive stages of congestive heart failure.
- States S_5 is considered as absorbing state.
- A recovered unit works as good as healthy state i.e., S_0.

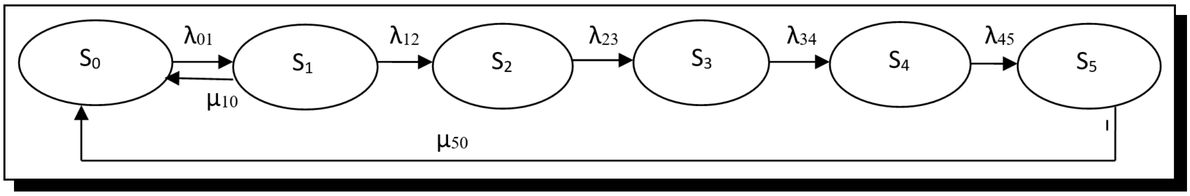


Figure 1. State transition diagram

In this paper, a multistate markov model is described where the state S_0 represent disease free state while state S_1, S_2, S_3, S_4 indicate the progressive stages of chronic heart failure according as AHA/ACC [4] and in state S_5 the patient goes under cardiac replacement therapy. With the help of Kolmogorov differential equation, explicit expressions for life expectancy and availability analysis are derived.

Table 1. All the notations used throughout the work are explained

Notations	Explanation
λ_{01}	Deteriorating rate from S_0 to S_1
λ_{12}	Deteriorating rate from S_1 to S_2
λ_{23}	Deteriorating rate from S_2 to S_3
λ_{34}	Deteriorating rate from S_3 to S_4
λ_{45}	Deteriorating rate from S_4 to S_5
μ_{50}	Recovery rate from S_5 to S_0
μ_{10}	Recovery rate from S_1 to S_0
$P_i(t)$	Probability of the state S_i, $i = 0, 1, 2, 3, 4, 5$

3. Reliability Assessment

The mean time to absorption for the proposed framework was assessed utilizing the accompanying technique of linear first order differential equations. Let $p(t)$ be the probability row vector at time t, the underlying conditions for this issue are introduced in condition (3.1):

$$P(0) = [P_0(0), P_1(0), P_2(0), P_3(0), P_4(0), P_5(0)] = [1,0,0,0,0,0]. \tag{3.1}$$

By employing the method of linear first order differential equations and for Figure 1, the set of differential eqn. (3.2) can be obtained.

$$\left.\begin{aligned}
\frac{d}{dt}P_0(t) &= -\lambda_{01}P_0(t) + \mu_{10}P_1(t) + \mu_{50}P_5(t) \\
\frac{d}{dt}P_1(t) &= \lambda_{01}P_0(t) - (\lambda_{12}+\mu_{10})P_1(t) \\
\frac{d}{dt}P_2(t) &= \lambda_{12}P_1(t) - \lambda_{23}P_2(t) \\
\frac{d}{dt}P_3(t) &= \lambda_{23}P_2(t) - \lambda_{34}P_3(t) \\
\frac{d}{dt}P_4(t) &= \lambda_{34}P_3(t) - \lambda_{45}P_4(t) \\
\frac{d}{dt}P_5(t) &= \lambda_{45}P_4(t) - \mu_{50}P_5(t)
\end{aligned}\right\} \tag{3.2}$$

The above system of differential equation (3.2) can be written in matrix form as

$$\dot{P} = TP, \tag{3.3}$$

where

$$V = \begin{bmatrix} -\lambda_{01} & \mu_{10} & 0 & 0 & 0 & \mu_{50} \\ \lambda_{01} & (\lambda_{12}+\mu_{10}) & 0 & 0 & 0 & 0 \\ 0 & \lambda_{12} & -\lambda_{23} & 0 & 0 & 0 \\ 0 & 0 & \lambda_{23} & -\lambda_{34} & 0 & 0 \\ 0 & 0 & 0 & \lambda_{34} & -\lambda_{45} & 0 \\ 0 & 0 & 0 & 0 & \lambda_{45} & -\mu_{50} \end{bmatrix}. \tag{3.4}$$

4. Life Expectancy/Mean Time to Absorption

It is difficult to evaluate the transient solutions, hence we follow [5, 8]. To calculate the Life Expectancy, the transpose matrix of T is taken and rows and columns are deleted for the absorbing states. The new matrix is called A. The expected time to reach an absorbing state is calculated from eqn. (4.1).

$$\text{Life expectancy} = E[T_{P(0)} \to P(\text{absorbing})] = P(0)(-A^{-1})\begin{bmatrix}1\\1\\1\\1\\1\end{bmatrix} \tag{4.1}$$

where the initial conditions are given by

$$P(0) = [P_0(0), P_1(0), P_2(0), P_3(0), P_4(0)] = [1,0,0,0,0]$$

and

$$A=\begin{bmatrix}-\lambda_{01} & \mu_{10} & 0 & 0 & 0\\ \lambda_{01} & -(\lambda_{12}+\mu_{10}) & 0 & 0 & 0\\ 0 & \lambda_{12} & -\lambda_{23} & 0 & 0\\ 0 & 0 & \lambda_{23} & -\lambda_{34} & 0\\ 0 & 0 & 0 & \lambda_{34} & -\lambda_{45}\end{bmatrix}$$

The explicit expression for Life Expectancy is given by

$$\text{MTSF}=\frac{N_1}{D_1}, \tag{4.2}$$

$N_1=(\lambda_{12}+\mu_{10})\lambda_{23}\lambda_{34}\mu_{45}+\lambda_{01}\lambda_{23}\lambda_{34}\lambda_{45}+\lambda_{01}\lambda_{12}\lambda_{34}\lambda_{45}+\lambda_{01}\lambda_{12}\lambda_{23}\lambda_{45}+\lambda_{01}\lambda_{12}\lambda_{23}\lambda_{34}$, and

$D_1=\lambda_{01}\lambda_{12}\lambda_{23}\lambda_{34}\lambda_{45}$.

5. Availability Analysis

The initial conditions for this problem are the same as for the reliability case: $P(0)=[1,0,0,0,0,0]$, the differential equations form can be expressed as shown in eqn. (5.1).

$$\begin{bmatrix}P_0'(t)\\ P_1'(t)\\ P_2'(t)\\ P_3'(t)\\ P_4'(t)\\ P_5'(t)\end{bmatrix}=\begin{bmatrix}-\lambda_{01} & \mu_{10} & 0 & 0 & 0 & \mu_{50}\\ -\lambda_{01} & -(\lambda_{12}+\mu_{10}) & 0 & 0 & 0 & 0\\ 0 & \lambda_{12} & -\lambda_{23} & 0 & 0 & 0\\ 0 & 0 & \lambda_{23} & -\lambda_{34} & 0 & 0\\ 0 & 0 & 0 & \lambda_{34} & -\lambda_{45} & 0\\ 0 & 0 & 0 & 0 & \lambda_{45} & -\mu_{50}\end{bmatrix}\begin{bmatrix}P_0(t)\\ P_1(t)\\ P_2(t)\\ P_3(t)\\ P_4(t)\\ P_5(t)\end{bmatrix}. \tag{5.1}$$

In the steady state, the derivative of the state probabilities become zero as presented in eqn. (5.2).

$$\begin{bmatrix}-\lambda_{01} & \mu_{10} & 0 & 0 & 0 & \mu_{50}\\ -\lambda_{01} & -(\lambda_{12}+\mu_{10}) & 0 & 0 & 0 & 0\\ 0 & \lambda_{12} & -\lambda_{23} & 0 & 0 & 0\\ 0 & 0 & \lambda_{23} & -\lambda_{34} & 0 & 0\\ 0 & 0 & 0 & \lambda_{34} & -\lambda_{45} & 0\\ 0 & 0 & 0 & 0 & \lambda_{45} & -\mu_{50}\end{bmatrix}\begin{bmatrix}P_0(t)\\ P_1(t)\\ P_2(t)\\ P_3(t)\\ P_4(t)\\ P_5(t)\end{bmatrix}=\begin{bmatrix}0\\0\\0\\0\\0\\0\end{bmatrix}. \tag{5.2}$$

To obtain the availability, equation (5.2) must be solved by using the normalising condition as presented in equation (5.3).

$$P_0(\infty)+P_1(\infty)+P_2(\infty)+P_3(\infty)+P_4(\infty)+P_5(\infty)=1 \tag{5.3}$$

The steady state availability is given by

$$A_v(\infty)=P_0(\infty)+P_1(\infty)+P_2(\infty)+P_3(\infty)+P_4(\infty)=\frac{N_2}{D_2}$$

where

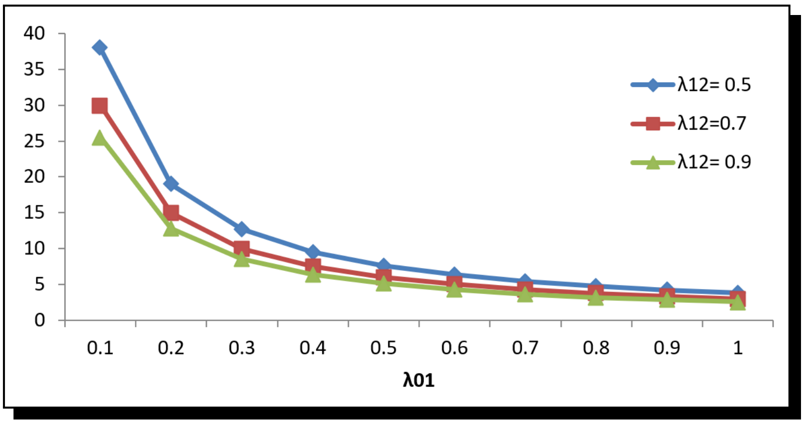
$$N_2=\lambda_{23}\lambda_{34}\lambda_{45}\mu_{50}(\lambda_{01}+\lambda_{12}+\mu_{10})+\lambda_{01}\lambda_{12}\lambda_{45}\mu_{50}(\lambda_{23}+\lambda_{34})+\lambda_{01}\lambda_{12}\lambda_{23}\lambda_{34}\mu_{50}$$

$$D_2=\lambda_{23}\lambda_{34}\lambda_{45}\mu_{50}(\lambda_{01}+\lambda_{12}+\mu_{10})+\lambda_{01}\lambda_{12}\lambda_{45}\mu_{50}(\lambda_{23}+\lambda_{34})+\lambda_{01}\lambda_{12}\lambda_{23}\lambda_{34}(\mu_{50}+\lambda_{45})$$

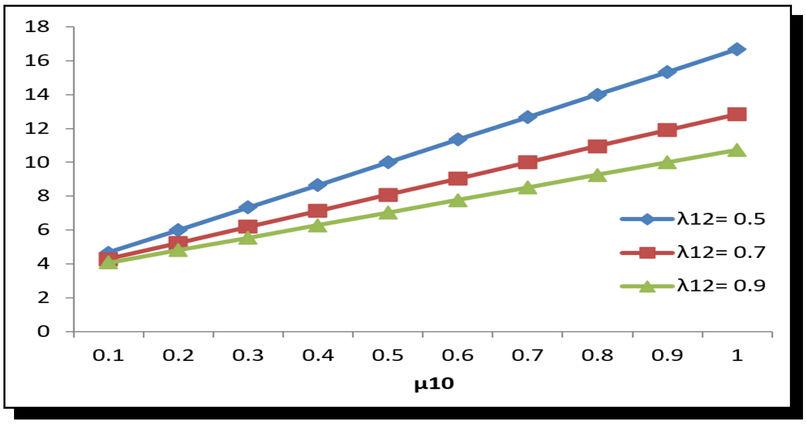
6. Graphical Analysis

Numerical examples are introduced to show the conduct of deteriorating rates and recovery rates on Life Expectancy and availability of the system dependent on given values of parameters.

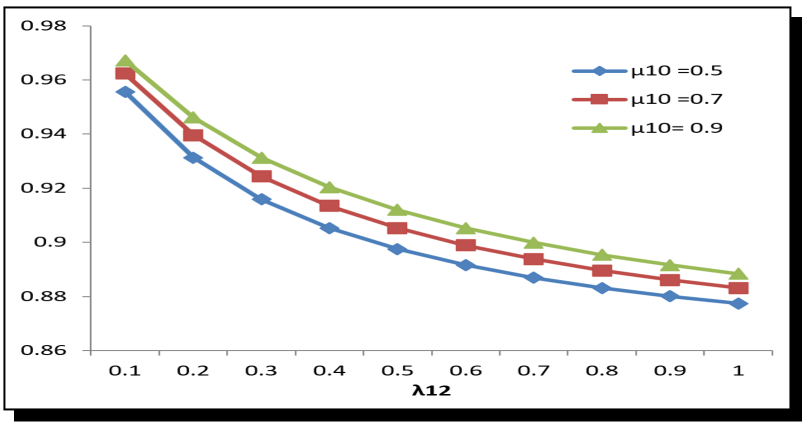
For Graphs 1–3, following parameters are used: $\lambda_{01} = 0.3$, $\lambda_{12} = 0.4$, $\lambda_{23} = 0.5$, $\lambda_{34} = 0.4$, $\lambda_{45} = 0.7$, $\mu_{50} = 0.6$, $\mu_{10} = 0.7$.



Graph 1. Life Expectancy vs. deteriorating rate λ_{01} against different values of λ_{12} $(0.5, 0.7, 0.9)$



Graph 2. Life Expectancy vs. Recovery rate μ_{10} against different values of λ_{12} $(0.5, 0.7, 0.9)$



Graph 3. Availability vs. Deteriorating rate λ_{12} against different values of μ_{10} $(0.5, 0.7, 0.9)$

7. Discussion

Chronic infections address an ailment to the well being status of a patient to be described by number of disease states. Markov models give an advantageous system to such kind of examination. Such models help to understand the mechanism of diseases and progression of diseases. Chronic diseases are the major causes of morbidity and mortality. It becomes a challenge which affects a substantial part of the population in developing countries. CTMC is important while dealing with progressive diseases. Kolmogorov differential equations play remarkable role.

Present paper deals with 5 state model in which state 0 represent disease Free State while state S_1, S_2, S_3, S_4 shows the chronic stages of Congestive Heart Failure and in state S_5 transplant process occur. We have presented illness stages of Congestive Heart Failure according as AHA/ACC. We presented explicit expression of life expectancy and availability analysis. We provide graphical analysis for our results. Graphical results show that as the deteriorating rates increasing then life expectancy as well as availability is decreasing and as the recovery rates increases then life expectancy also increases. Thus, the main goal of this article has been to make awareness about these challenging problems.

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Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

All the authors contributed significantly in writing this article. The authors read and approved the final manuscript.

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