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STOCHASTIC MODEL TO FIND THE TESTOSTERONE THERAPY ON FUNCTIONAL CAPACITY IN CHF PATIENTS USING STOCHASTIC ANALYSIS

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Abstract:

Heart failure is a serious cardiovascular condition leading to life threatening events, poor prognosis, and degradation of quality of life. According to the present evidences suggesting association between low testosterone level and prediction of reduced exercise capacity as well as poor clinical outcome in patients with heart failure, we sought to determine if testosterone therapy improves clinical and cardiovascular conditions as well as quality of life status in patients with stable chronic heart failure. The purpose of this study was to examine the testosterone therapy on functional capacity in congestive heart failure patients using the stochastic analysis of the departure and quasi input processes of a Markovian single server queue with negative exponential arrivals and repeated attempts.

Key Words: Testosterone Therapy, Congestive Heart Failure, Markovian Single Server Queue, Departure Process & Normal Distribution.

1. Introduction:

A noticeable evolution of therapeutic concepts has taken place with a variety of cardiac and hormonal drugs with the aim of improving patient's survival, preventing sudden death, and improving quality of life [7] & [9]. In a significant proportion of heart failure patients, testosterone deficiency as an anabolic hormonal defect has been proven and identified even in both genders [5]. This metabolic and endocrinological abnormality is frequently associated with impaired exercise tolerance and reduced cardiac function [16]. For this reason, combination therapy with booster cardiovascular drugs and testosterone replacement therapy might be very beneficial in heart failure patients. The physiological pathways involved in these therapeutic processes have been recently examined. First, elevated level of testosterone following replacement therapy is major indicator for increase of peak VO_2 in affected men with heart failure explaining improvement of exercise tolerance in these patients [6]. Furthermore, testosterone replacement therapy can reduce circulating levels of inflammatory mediators including tumor necrosis factor $\alpha\,(TNF-\alpha)$ and interleukin $(IL)-1\beta$, as well as total cholesterol in patients with established simultaneous coronary artery disease and testosterone deficiency. According to the present evidences suggesting association between low testosterone level and prediction of reduced exercise capacity as well as poor clinical outcome in patients with heart failure, we sought to determine if testosterone therapy improves clinical and cardiovascular conditions as well as quality of life status in patients with stable chronic heart failure.

Our queueing system is characterized by the phenomenon that a customer who finds the server busy upon arrival joins an orbit of unsatisfied customers. The orbiting customers form a queue such that only a customer selected according to a certain rule can reapply for service. The intervals separating two successive repeated attempts are exponentially distributed with rate $\alpha + j\mu$, when the orbit size is $j \geq 1$. Negative arrivals have theeffect of killing some customer in the orbit, if one is present, and they have no effect otherwise. Since customers can leave the system without service, the structural form of type M/G/1 is not preserved. We study the Markov chain with transitions occurring at epochs of service completions or negative arrivals. Then we find and use the moments of the random variable i.e., the first two moments under ergodicity are used to investigate the androgen deprivation therapy and congestive heart failure outcomes in a cohort of non metastatic prostate cancer patients.

3. Description of the Mathematical Model:

Queueing systems with repeated attempts have wide practical use in designing packet switching networks and telecommunication systems. The main characteristic of a single server queue with repeated attempts is that a customer who finds the server busy upon arrival is obliged to leave the service area, but some time later he comes back to reinitiate his demand. Between trials a customer is said to be "in orbit". Most papers assume that each orbiting customer has probability $\mu dt + o(dt)$ of reapplying for service in $(t, t + dt)$, independently of each other customerin orbit at time t. In what follows, we call this retrial policy as classical retrial discipline.For a review of the literature on this topic see [1]. Nevertheless, there are other types of queueing situations, in which the retrial rate is independent of the number of customers in orbit i.e., the retrial rate is α if the orbit is not empty at time $t$and zero if the orbit is empty. Thissecond retrial policy will be called constant retrial discipline. A detailed discussion of situations where such discipline arises can be found in [2]. In related work [8] examined the $M/G/1$ with two types of customers and constant retrial discipline.

Recently, [4] studied an $M/M/1$ queue with "negative" arrivals. Any arriving customer joins the system with the intention of getting served and then leaving the system. They are treated in the normal way by the server and are taken from the queue according to a specified queueing discipline. At a negative arrival epoch, the system is only affected if customers are present. Then, a customer is removed from the system i.e., each negative arrival reduces the total customers count by one unit. Several practical applications justify the study of these queueing models. In multiprocessor computer systems, negative arrivals represent commands to delete some transaction. In neural networks, primary and negative arrivals represent excitatory and inhibitory signals, respectively.

The purpose of the present work is to study the departure and quasi input processes of a versatile single server queue allowing the simultaneous presence of classical and constant repeated attempts, and negative arrivals. Our queueing model was introduced in [3], where the classification of states, stationary distribution, waiting time and busy period were studied. Thus, this paper completes the investigation initialed in [3].

To allow the presence of both types of repeated attempts we will assume that intervals between two successive repeated attempts are exponentially distributed with rate $\alpha\left(1 - \delta_{o_j}\right) + j\mu$, when the orbit size is j. δ_{o_j} denotes Kronecker's function. This retrial policy will be called linear retrial discipline. The main characteristic of our model is its versatility so, in this section, we discuss concrete interpretations of the systems associated with some specific choices of the parameters. Nevertheless, the queueing system under consideration has also an intrinsic interest to model some situations in packet switching networks. Consider a computer network which consists of a group of processors connected with a central transmission unit (CTU). If a processor wishesto send a message it first sends the message to the CTU. If the transmission medium is available, the CTU sends immediately the message; otherwise the message will be stored in a buffer and the CTU must retry the transmission some time later. For mathematical convenience we assumethat this random time is exponentially distributed; then we construct a retrial rate of the simplest possible type by assuming that there are two contributions to the retrial intensity. The first one α is fixed and intrinsic with the network design, whereas the second one $j\mu$ depends on thenumber of units in the buffer. In addition, the CTU sends negative signals to the buffer in order to remove one of the unsatisfied units. This mechanism guarantees a moderate level of internal congestion in the buffer.

It should be pointed out that the presence of a stream of negative arrivals has a profound influence on the system. This is revealed by the fact that the structural form of the $M/G/1$ queueis not preserved. We also observe that, due to the existence of negative arrivals, the limiting probability distribution of the continuous time process describing the number of customers in the system is not equal to the distribution of the embedded process describing the state of the system just after service completion epochs.

The rest of the paper is organized as follows. In this section we describe the mathematical model. The study of the embedded Markov chains at service completion and killing epochs and their corresponding factorial moments are carried out in next section. In last section, we obtain the Laplace Stieltjes Transform(LST) of the interdeparture times and its factorial moments.

We consider a single server queueing system with two independent Poisson streams with rates $\lambda > 0$ and $\delta \geq 0$, corresponding to primary and negative arrivals, respectively. If the server is free, an arriving primary customer begins to be served and leaves the system after service completion. Any primary customer finding the server busy upon arrival must leave the service are a immediately and seek service again at subsequent epochs until he finds the server free. He is then said to be "in orbit". These unsatisfied customers form a pool such that only one customer selected according to a certain rule can access to the server. The time intervals describing the repeated attempts are assumed to be independent and exponentially distributed with rate $\alpha\left(1-\delta_{o_j}\right)+j\mu$, when there are j customers in orbit. Negative arrivals have the effect of deleting one customer ofthe orbit, if there are any, who is selected according to some specified killing strategy. Service times are independent exponential random variables with rate v. The streams of primary andnegative arrivals, intervals separating successive repeated attempts and service times are assumed to be mutually independent.

We now discuss some particularizations which can be obtained with specific choices of the parameters α, μandδ. First, the case $\delta = 0$ leads to a retrial queue with linear retrial discipline which generalizes the classical and constant retrial queues described in the literature. The case$\mu = 0$ and $\delta = (1-H)\alpha, H \in (0,1)$, corresponds to the constant retrial queue where the customer at the head of the orbit is non persistent. Finally, the single server Markovian queue with classical waiting line and negative arrivals is obtained by letting $\alpha \to +\infty$ and $\mu \to +\infty$.

The state of the system at time t can be described by the bivariate process $X = \{X(t), t \geq 0\} = \{(C(t), Q(t)), t \geq 0\}$, where $Q(t)$ represents the number of customers in orbitand $C(t)$ is equal to 1 or 0 according as the server is busy or free, respectively. Note that theprocess X takes values on the semi strip $S = \{0,1\} \times N$.

We shall consider that the process X is in the ergodic case, which exists if and only if one of the following conditions is verified

(i) $\mu = 0$ and $\gamma < 1$

(ii) $\mu > 0$ and $\rho < 1$

Where $\gamma = \frac{(\lambda-\delta)(\lambda+\alpha)}{v\alpha}$ and $\rho = \frac{\lambda}{\delta+v}$

We also define the limiting probabilities

$$P_{ij} = \lim_{t\to+\infty} P\{C(t) = i, Q(t) = j\}, (i,j) \in S$$

Which are positive if and only if (i) or (ii) is satisfied.. The probabilities P_{ij} and the partialgenerating functions defined as $P_i(z) = \sum_{j=0}^{\infty} P_{ij} z^j$, for $i \in \{0,1\}$, can be expressed in terms of hyper geometric series. Since our model has a Poisson input, the stationary distribution is equal to the equilibrium state distribution just prior to arrival epochs.

Finally, we introduce some notation used in the rest of the paper. Let us consider the generalized hyper geometric series defined as follows

$$F_k\begin{pmatrix} a_1, a_2, \dots, a_{k+1}; z \\ b_1, b_2, \dots, b_k \end{pmatrix} = \sum_{n=0}^{\infty} \frac{(a_1)_n (a_2)_n \dots (a_{k+1})_n}{(b_1)_n (b_2)_n \dots (b_k)_n} \frac{z^n}{n!}$$

where $(x)_n$ is the Pochhammer symbol

$$(x)_n = \begin{cases} 1, & n = 0 \\ x(x+1)\dots(x+n-1), & n \geq 1 \end{cases}$$

As is usual, we denote $F_1\begin{pmatrix} a_1, a_2; z \\ b_1 \end{pmatrix}$ by $F(a_1, a_2; b_1 z)$

3. The Departure Process:

The departure process is defined as the sequence of the times $\{\eta_i\}_{i\geq 0}$ at which customersleave the queueing system after their service completion epochs. The study of $\{\eta_i\}_{i\geq 0}$ is equivalent to the study of $\{\tau_i = \eta_i - \eta_{i-1}\}_{i\geq 1}$ It should be noted that the interval τ_i can be expressed as $\tau_i = R_i + S_i$ for $i \geq 1$, where $R_i$is defined as the server idle period until the arrival of the i[th] customer and S_i is the corresponding service time. We assume that the system is stable, consequently $\tau_1, \tau_2, \dots$ are identically distributedrandom variables. For convenience of notation we will denote the interval under consideration asτ_1. We next give the joint distribution of (R_1, S_1) in terms of its Laplace Stieltjes transform (LST).

3.1 Theorem:

If the queueing system is ergodic, then the Laplace Stieltjes transform

$\varphi(\theta, \omega) = E[exp\{-\theta R_1 - \omega S_1\}]$ is given by

$$\varphi(\theta,\omega) = \frac{v}{\omega+v}\left(1 - \frac{\theta}{\theta+\lambda+\alpha}\bar{\pi}_0\left(\frac{\alpha}{\theta+\lambda} + F_2\begin{pmatrix} 1, 1+\frac{\lambda+\alpha}{\mu}, \frac{\theta+\lambda+\alpha}{\mu}; \rho \\ 1+\frac{\alpha+\delta\rho}{\mu}, 1+\frac{\theta+\lambda+\alpha}{\mu} \end{pmatrix}\right)\right) \quad (1)$$

For $Re(\theta) \geq 0, \mathrm{Re}(\omega) \geq 0$ where $\bar{\pi}_0 = \left(F\left(1, 1+\frac{\lambda+\alpha}{\mu}; 1+\frac{\alpha+\delta\rho}{\mu}; \rho\right)\right)^{-1}$ (2)

Proof:

Since the length of service time S_1, is independent of all the events occurred before itscommencement, the random variablesR_1 and S_1 are independent. Thus,

$$\varphi(\theta,\omega) = E[exp\{-\theta R_1\}]E[exp\{-\omega S_1\}]$$

Where $E[exp\{-\omega S_1\}] = v(\omega+v)^{-1}$

In order to find the LST of R_1, we condition on the number of customerspresent in the system at the previous service completion epoch to get

$$E[exp\{-\theta R_1\}] = \frac{\lambda}{\theta+\lambda}\bar{\pi}_0 + \sum_{n=1}^{\infty}\frac{\lambda+\alpha+n\mu}{\theta+\lambda+\alpha+n\mu}\bar{\pi}_n$$

Note that $$\sum_{n=0}^{\infty}\frac{\bar{\pi}_n}{\theta+\lambda+\alpha+n\mu} = \frac{1}{\theta+\lambda+\alpha}\int_0^1 \bar{\Pi}\left(\frac{\mu}{x^{\theta+\lambda+\alpha}}\right)dx$$

Thus $$\sum_{n=1}^{\infty}\frac{\lambda+\alpha+n\mu}{\theta+\lambda+\alpha+n\mu}\bar{\pi}_n = 1 - \frac{\lambda+\alpha}{\theta+\lambda+\alpha}\bar{\pi}_0 - \frac{\theta}{\mu}\int_0^1 t^{\frac{\theta+\lambda+\alpha}{\mu}}\bar{\Pi}(t)dt \quad (3)$$

Substitution into (3) leads, after some algebraic manipulations to (1).

Note that the generalized hyper geometric series in (1) is convergent if and only if the process $\{X(t), t \geq 0\}$ is ergodic. In the particular case $\mu = 0$ and $\alpha > 0$, the above result is reduced to a more explicit expression.

3.2 Corollary:

If $\mu = 0, \alpha > 0$ and $\gamma < 1$, then the LST of (R_1, S_1)given by

$$\varphi(\theta,\omega) = \frac{v}{(\omega+v)(\theta+\lambda+\alpha)}\left(\lambda+\alpha\left(1-\frac{\theta}{\theta+\lambda}\bar{\pi}_0\right)\right) \quad (4)$$

for$Re(\theta) \geq 0, Re(\omega) \geq 0$ where $\bar{\pi}_0$ was given in (2)

The LST of the pair (R_1, S_1)can be inverted by inspection. This yields the following result.

3.3 Corollary:

If the process $\{X(t), t \geq 0\}$ is ergodic, then

(i) If $\mu = 0$ and $\alpha > 0$,

$$f_{(R_1,S_1)}(x,y) = ve^{-vy}\left(\lambda e^{-\lambda x}\bar{\pi}_0 + (\lambda+\alpha)e^{-(\lambda+\alpha)x}(1-\bar{\pi}_0)\right)\delta(x)\delta(y)$$

Where $\bar{\pi}_0$ was given in (2)

(ii) If $\mu > 0$,

$$f_{(R_1,S_1)}(x,y) = \bar{\pi}_0 ve^{-vy}\left(\lambda e^{-\lambda x} + \frac{\lambda+\alpha+\mu}{\alpha+\mu+\delta\rho}\rho e^{-(\lambda+\alpha+\mu)x}\right)\times$$
$$\left((\lambda+\alpha)F\left(1, 2+\frac{\lambda+\alpha}{\mu}; 2+\frac{\alpha+\delta\rho}{\mu};\ \rho e^{-\mu x}\right) + \mu F\left(2, 2+\frac{\lambda+\alpha}{\mu}; 2+\frac{\alpha+\delta\rho}{\mu};\ \rho e^{-\mu x}\right)\right)\delta(x)\delta(y)$$

Where $\bar{\pi}_0$ was given in (2).

Our next objective is to obtain formulae for the moments of random variable R_1. $M_k^{R_1} = E(R_1^k), k \geq 0$

3.4 Theorem:

Under ergodicity, the moments of R_1 are given by

(i) If $\mu = 0$and$\alpha > 0$, then

$$M_k^{R_1} = k!\left(\frac{1-\bar{\pi}_0}{(\lambda+\alpha)^k} + \frac{\bar{\pi}_0}{(\lambda)^k}\right), k \geq 0 \quad (5)$$

Where $\bar{\pi}_0$ was given in (2).

(ii) If $\mu > 0$, then

$$M_k^{R_1} = k!\,\bar{\pi}_0\left(\frac{1}{(\lambda)^k} + \frac{1}{(\lambda+\alpha)^k}\left(F_k\left(\begin{matrix} 1, \frac{\lambda+\alpha}{\mu}, \dots, \frac{\lambda+\alpha}{\mu}; \rho \\ 1+\frac{\alpha+\delta\rho}{\mu}, 1+\frac{\lambda+\alpha}{\mu}, \dots, 1+\frac{\lambda+\alpha}{\mu}\end{matrix}\right) - 1\right)\right) \quad (6)$$

for $k \geq 1$, where $\bar{\pi}_0$ was given in (2).

Proof:

With the help of (4) we easily obtain the expression (5). Upon differentiation of (1) we also obtain

$$M_k^{R_1} = k!\left(\frac{1}{(\lambda)^k} + \frac{1}{(\lambda+\alpha)^k}\right)\bar{\pi}_0 - (-1)^k\frac{1}{\mu}I_k(\theta) \quad (7)$$

Where $I_k(\theta) = \frac{d^k}{d\theta^k}\left(\theta \int_0^1 t^{\frac{\theta+\lambda+\alpha}{\mu}-1}\, \overline{\Pi}(t)dt\right) = \theta J(\theta,k) + kJ(\theta,k-1)$ (8)

And $$J(\theta,k) = \frac{d^k}{d\theta^k}\left(\theta \int_0^1 t^{\frac{\theta+\lambda+\alpha}{\mu}-1}\, \overline{\Pi}(t)dt\right)$$

After some algebraic manipulations we find that

$$J(\theta,k) = (-1)^k k! \frac{\mu}{(\theta+\lambda+\alpha)^{k+1}} \bar{\pi}_0 F_{k+2}\begin{pmatrix} 1,1+\frac{\lambda+\alpha}{\mu}, \frac{\theta+\lambda+\alpha}{\mu}, \dots, \frac{\theta+\lambda+\alpha}{\mu}; \rho \\ 1+\frac{\alpha+\delta\rho}{\mu}, 1+\frac{\theta+\lambda+\alpha}{\mu}, \dots, 1+\frac{\theta+\lambda+\alpha}{\mu} \end{pmatrix} \quad (9)$$

Substituting (8) and (9) into (7), we derive (6). Finally, an application of Ratio test and Raabe's test guarantees again that the series in (6) is convergent if and only if the process$\{X(t), t \geq 0\}$ is ergodic. To find the k[th] moment of the inter departure time τ_1, $M_k^{\tau_1} = E[\tau_1^k]$ for $k \geq 0$, we use the simple observation that R_1 and S_1 are independent random variables. We thus obtain

$$M_k^{\tau_1} = \sum_{j=0}^{k} \binom{k}{j} M_j^{R_1} M_{k-j}^{S_1}$$

Where $M_j^{S_1} = j!\, v^{-j}$ for $j \geq 0$.

In applications, the mean and variance of any performance measure are perhaps the most important quantities. Thus, we give these quantities in the following.

3.5 Corollary:

(i) If $\mu > 0$ and $\rho < 1$, then

$$E[\tau_1] = \frac{1}{v} + \bar{\pi}_0\left(\frac{1}{\lambda} + \frac{\rho}{\alpha+\mu+\delta\rho} F\left(1,1+\frac{\lambda+\alpha}{\mu}; 2+\frac{\alpha+\delta\rho}{\mu}; \rho\right)\right)$$

$$Var[\tau_1] = \frac{1}{v^2} + 2\bar{\pi}_0\left(\frac{1}{\lambda^2} + \frac{\rho}{(\lambda+\alpha+\mu)(\alpha+\mu+\delta\rho)^3} F_2\begin{pmatrix} 1,1+\frac{\lambda+\alpha}{\mu}; 1+\frac{\lambda+\alpha}{\mu}; \rho \\ 2+\frac{\alpha+\delta\rho}{\mu}; 2+\frac{\alpha+\delta\rho}{\mu} \end{pmatrix}\right)$$

$$-\left(\bar{\pi}_0\left(\frac{1}{\lambda} + \frac{\rho}{\alpha+\mu+\delta\rho} F\left(1,1+\frac{\lambda+\alpha}{\mu}; 2+\frac{\alpha+\delta\rho}{\mu}; \rho\right)\right)\right)^2$$

Where $\bar{\pi}_0$ was given in equation (2).

(ii) If $\mu = 0, \alpha > 0$ and $\gamma < 1$, then

$$E[\tau_1] = \frac{v^2\alpha+\delta(\lambda+\alpha)(\lambda+v)}{\lambda v(v\alpha+\delta(\lambda+\alpha))}$$

$$Var[\tau_1] = \frac{1}{v^2} + \frac{1}{\lambda^2} + \frac{1}{(\lambda+\alpha)^2}\left(1 - \left(\frac{v\alpha+(\lambda+\alpha)(\delta+\alpha)}{v\alpha+\delta(\lambda+\alpha)}\right)^2\right) \quad (10)$$

4. Example:

A total of 50 male patients who suffered from congestive heart failure were recruited in a double blind, placebo controlled trial and randomized to receive an intramuscular (gluteal) long acting androgen injection ($1ml$ of testosterone enanthate $250mg/ml$) once every four weeks for 12 weeks or receive intramuscular injections of saline ($1ml$ of 0.9% $wt/vol\ NaCl$) with the same protocol. Comparing baseline variables and clinical parameters across the two groups who received testosterone or placebo did not show any significant difference, except for $6MWD$ that was higher in the testosterone group. During the 12 week study period, no significant differences were revealed in the trend of the changes in hemodynamic parameters including systolic and diastolic blood pressures as well as heart rate between the two groups. Also, the changes in body weight were comparable between the groups, while, unlike the group received placebo, those who received testosterone had a significant increasing trend in $6MWD$ parameter within the study period ($6MWD$ at baseline was $407.44 \pm 100.23m$

and after 12 weeks of follow up reached $491.65 \pm 112.88m$ following testosterone therapy, $P = 0.019$). According to post hoc analysis, the mean 6 walk distance parameter was improved at three time points of 4 weeks, 8 weeks, and 12 weeks after intervention compared with baseline; however no differences were found in this parameter at three post intervention time points. The discrepancy in the trends of changes in $6MWD$ between study groups remained significant after adjusting baseline variables $(mean\ square = 243.262, F - index = 4.402$ and $P = 0.045)$ [5], [7] & [9-15].

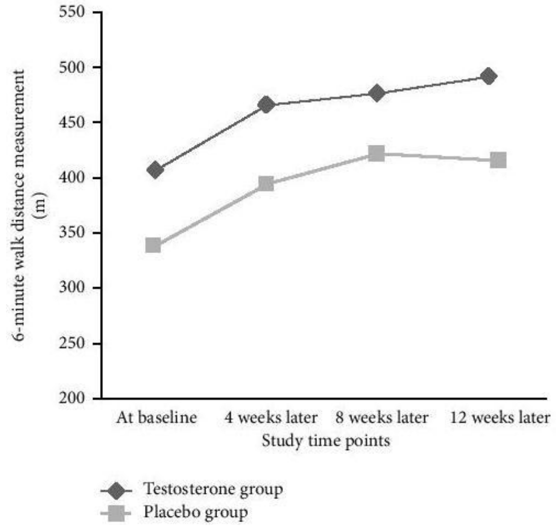
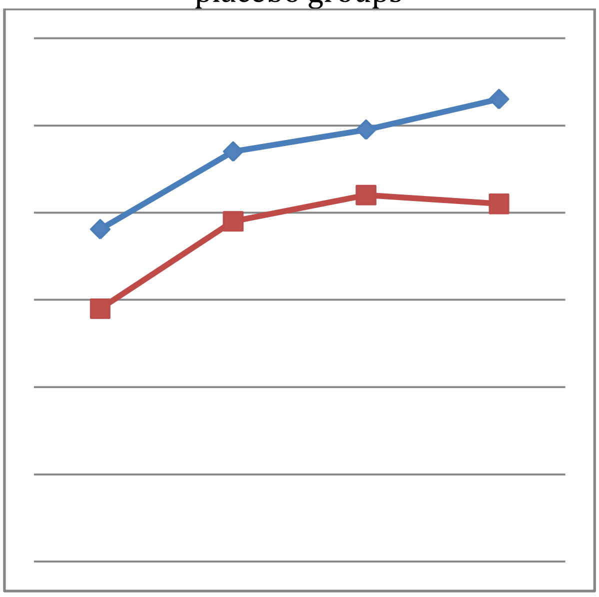


Figure 1: Trend of the changes in 6 minute walk distance parameter in intervention and placebo groups



Blue Line: Testosterone Group
Red Line: Placebo Group

Figure 2: Trend of the changes in 6 minute walk distance parameter in intervention and placebo groups using Gamma Distribution

5. Conclusion:

The changes in body weight, hemodynamic parameters, and left ventricular dimensional echocardiographic indices were all comparable between the two groups. Regarding changes in diastolic functional state and using Tei index, this parameter was significantly improved. Unlike the group received placebo, those who received testosterone had a significant increasing trend in 6 walk mean distance ($6MWD$) parameter within the study period ($P = 0.019$). The discrepancy in the trends of changes in $6MWD$ between study groups remained significant after adjusting baseline variables ($mean\ square = 243.262, F\ index = 4.402$ and $P = 0.045$). Our study strengthens insights into the beneficial role of testosterone in improvement of functional capacity and quality of life in heart failure patients. This results while using motion on Departure Process also gives the same result by using uniform distribution. The medical reports {Figure (1)} are beautifully fitted with the mathematical model {Figure (2)}; ($i.e$) the results coincide with the mathematical and medical report.

6. References:

1. Falin G I, "A survey of retrial queues", Queueing Systems, Volume 7, Page Number 127-168, 1990.
2. Farahmand K, "Single Line Queue with Repeated Attempts", Queueing Systems, Volume 6, Page Number 223-228, 1990.
3. Gomez Corral A & Artalejo J R, "Quasi Birth and Death Processes With Applications to Queues with Repeated Attempts", Advanced Applied Probability, Volume 27, 1995.
4. Harrison P G & Pitel E, "Sojourn Times in Single Server Queues with Negative Customers", Journal of Applied Probability, Volume 31, Page Number 943-963, 1993.
5. Jankowska E A, Biel B & Majda J, "Anabolic Deficiency in men With Chronic Heart Failure: Prevalence and Detrimental Impact on Survival," Circulation, Volume 114, Page Number 1829–1837, 2006.
6. Jankowska E A, Filippatos G & Ponikowska B, "Reduction in Circulating Testosterone Relates to Exercise Capacity in men with Chronic Heart Failure," Journal of Cardiac Failure, Volume 15, Page Number 442–450, 2009.
7. Malkin C J, Pugh P J, West J N & Van Beek E J R, "Testosterone Therapy in men with Moderate Severity Heart Failure: a double blind Randomized Placebo Controlled Trial," European Heart Journal, Volume 27, Page Number 57–64, 2006.
8. Martin M & Artalejo J R, "Analysis of an M/G/1 Queue With Two Types of Impatient Units", Advanced Applied Probability, Volume 27, Page Number 840-861, 1995.
9. Nieminen M S, Ohm M B & Cowie M R, "Executive summary of the guidelines on the diagnosis and treatment of Acute Heart Failure: the Task Force on Acute Heart Failure of the European Society of Cardiology", European Heart Journal, Volume 26, Page Number 384–416, 2005.
10. Senthil Kumar P, Abirami R & Dinesh Kumar A, "Fuzzy Model for the Effect of rhIL6 Infusion on Growth Hormone", International Conference on Advances in Applied Probability, Graph Theory and Fuzzy Mathematics, Page Number 246-252, 2014.
11. Senthil Kumar P, Dinesh Kumar A & Vasuki M, "Stochastic Model to Find the Effect of Gallbladder Contraction Result Using Uniform Distribution", Arya Bhatta Journal of Mathematics and Informatics, Volume 6, Issue 2, Page Number 323-328, 2014.
12. Senthil Kumar P, Dinesh Kumar A & Vasuki M, "Stochastic Model to Find the Diagnostic Reliability of Gallbladder Ejection Fraction Using Normal Distribution", International Journal of Computational Engineering Research, Volume 4, Issue 8, Page Number 36-41, 2014.

13. Senthil Kumar P, Dinesh Kumar A & Vasuki M, "Stochastic Model to find the Gallbladder Motility in Acromegaly Using Exponential Distribution", International Journal of Engineering Research and Applications,Volume 4, Issue 8, Page Number 29-33, 2014.
14. Senthil Kumar P, Dinesh Kumar A & Vasuki M, "Stochastic Model to Find the Gallbladder Dynamics with Gallstones Results Using Exponential Distribution", IFRSA's International Journal of Computing, Volume 4, Issue 3, Page Number 619-622, 2014.
15. Senthil Kumar P, Dinesh Kumar A & Vasuki M, "Stochastic Model to Find the Multidrug Resistance in Human Gallbladder Carcinoma Results Using Uniform Distribution", International Journal of Emerging Engineering Research and Technology, Volume 2, Issue 4, Page Number 278-283, 2014.
16. Tappler B & Katz M, "Pituitary Gonadal Dysfunction in Low output Cardiac Failure," Clinical Endocrinology, Volume 10, Page Number 219–226, 1979.