



MATHEMATICAL MODEL TO FIND THE TT ON FUNCTIONAL CAPACITY IN CHF PATIENTS USING UNIFORM DISTRIBUTION

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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. In the random motion on Poincare half plane, the hyperbolic distance is analyzed and also in the case where returns to the starting point is admitted. The mean hyperbolic distance in all versions of the motion envisaged and it is used to find the role of Testosterone in improvement of functional capacity and quality of life in heart failure patients.

Key Words: Testosterone Therapy (TT), Congestive Heart Failure (CHF), Poincare Half Plane (PHP), Uniform 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 [8] & [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 [10]. This metabolic and endocrinological abnormality is frequently associated with impaired exercise tolerance and reduced cardiac function [4]. 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 [11]. Furthermore, testosterone replacement therapy can reduce circulating levels of inflammatory mediators including tumor necrosis factor α ($TNF - \alpha$) and interleukin (IL) - 1β , 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. A random motion on Poincare half plane is studied. The mean hyperbolic distance in all versions especially the motion at finite velocity on the surface of a three dimensional sphere is investigated. In this case we use

$$E(t) = \frac{e^{\frac{-\lambda t}{2}}}{2} \left[\left(e^{\frac{t}{2}\sqrt{\lambda^2 - 4c^2}} + e^{-\frac{t}{2}\sqrt{\lambda^2 - 4c^2}} \right) + \frac{\lambda}{\sqrt{\lambda^2 - 4c^2}} \left(e^{\frac{t}{2}\sqrt{\lambda^2 - 4c^2}} - e^{-\frac{t}{2}\sqrt{\lambda^2 - 4c^2}} \right) \right]$$

to find the testosterone therapy (TT) on functional capacity, cardiovascular parameters (CVP), and quality of life in patients with congestive heart failure (CHF).

2. Notations:

$TNF - \alpha$	-	Tumor Necrosis Factor α
IL	-	Interleukin
TT	-	Testosterone Therapy
CVP	-	Cardiovascular Parameters
CHF	-	Congestive Heart Failure
$6MWD$	-	6 Minute Walk Distance

3. Motions with Jumps Backwards to the Starting Point:

Motion on hyperbolic spaces have been studied since the end of the Fifties and most of papers devoted to them deal with the so called hyperbolic Brownian motion [1] [6] & [7]. More recently also works concerning two dimensional random motions at finite velocity on planar hyperbolic spaces have been introduced and

analyzed. While in the corresponds of motion are supposed to be independent, we present here a planar random motion with interacting components. Its counterpart on the unit sphere is also examined and discussed.

The space on which our motion develops is the Poincare upper half plane $H_2^+ = \{(x, y) : y > 0\}$ which is certainly the most popular model of the Lobachevsky hyperbolic space. In the space H_2^+ the distance between points is measured by means of the metric

$$ds^2 = \frac{dx^2 + dy^2}{y^2} \quad (1)$$

The propagation of light in a planar non homogeneous medium, according to the Fermat principle, must obey the law

$$\frac{\sin \alpha(y)}{c(x,y)} = \cos t$$

Where $\alpha(y)$ is the angle formed by the tangent to the curve of propagation with the vertical at the point with ordinate y . In the case where the velocity $c(x, y) = y$ is independent from the direction, the light propagates on half circles as in H_2^+ .

It is shown that the light propagates in a non homogeneous half plane H_2^+ with refracting index $n(x, y) = 1/y$ with rays having the structure of half circles. Scattered obstacles in the non homogeneous medium cause random deviations in the propagation of light and this lead to the random model analyzed below.

The position of points in H_2^+ can be given either in terms of Cartesian coordinates (x, y) or by means of the hyperbolic coordinates (η, α) . In particular, η represents the hyperbolic distance of a point of H_2^+ from the origin O which has Cartesian coordinates $(0, 1)$. We recall than η is evaluated by means of (1) on the arc of a circumference with center located on the x axis and joining (x, y) with the origin O . The upper half circumference centered on the x axis represents the geodesic lines of the space H_2^+ and play the same role of the straight lines in the Euclidean plane [2] & [3].

The angle α represents the slope of the tangent in O to the half circumference passing through (x, y) . The formulas which relate the polar hyperbolic coordinates (η, α) to the Cartesian coordinates (x, y) are

$$\begin{cases} x = \frac{\sinh \eta \cos \alpha}{\cosh \eta - \sinh \eta \sin \alpha} & \eta > 0 \\ y = \frac{1}{\cosh \eta - \sinh \eta \sin \alpha} & -\frac{\pi}{2} < \alpha < \frac{\pi}{2} \end{cases} \quad (2)$$

for each value of α the relevant geodesic curve is represented by the half circumference with equation

$$(x - \tan \alpha)^2 + y^2 = \frac{1}{\cos^2 \alpha} \quad (3)$$

for $\alpha = \frac{\pi}{2}$ we get from (3) the positive y axis which also is a geodesic curve of H_2^+ . From (2) it is easy to obtain the following expression of the hyperbolic distance η of (x, y) from the origin O :

$$\cosh \eta = \frac{x^2 + y^2 + 1}{2y} \quad (4)$$

from (4) it can be seen that all the points having hyperbolic distance η from the origin O from a Euclidean circumference with center at $(0, \cosh \eta)$ and radius $\sinh \eta$.

The expression of the hyperbolic distance between two arbitrary points (x_1, y_1) and (x_2, y_2) is instead given by

$$\cosh \eta = \frac{(x_1 - x_2)^2 + y_1^2 + y_2^2}{2y_1 y_2} \quad (5)$$

In fact, by considering the hyperbolic triangle with vertices at $(0, 1)$, (x_1, y_1) and (x_2, y_2) , by means of the Carnot hyperbolic formula it is simple to show that the distance η between (x_1, y_1) and (x_2, y_2) is given by

$$\cosh \eta = \cosh \eta_1 \cosh \eta_2 - \sinh \eta_1 \sinh \eta_2 \cos(\alpha_1 - \alpha_2) \quad (6)$$

where (η_1, α_1) and (η_2, α_2) are the hyperbolic coordinates of (x_1, y_1) and (x_2, y_2) respectively. From (3) we obtain that

$$\tan \alpha_i = \frac{x_i^2 + y_i^2 - 1}{2x_i} \text{ for } i = 1, 2, \dots \quad (7)$$

and in view of (4) and (7), after some calculations, formula (5) appears. Instead of the elementary arguments of the proof above we can also invoke the group theory which reduces (x_1, y_1) to $(0, 1)$.

If $\alpha_1 - \alpha_2 = \frac{\pi}{2}$ the hyperbolic Carnot formula (6) reduces to the hyperbolic Pythagorean theorem

$$\cosh \eta = \cosh \eta_1 \cosh \eta_2$$

which plays an important role in the present paper.

The motion considered here is the non Euclidean counterpart of the planar motion with orthogonal deviations studied. The main object of the investigation is the hyperbolic distance of the moving point from the origin. We are able to give explicit expressions for its mean value, also under the condition that the number of changes of direction is known. In the case of motion in H_2^+ with independent components an explicit expression for the distribution of the hyperbolic distance η has been obtained. Here, however, the components of motion are dependent and this excludes any possibility of finding the distribution of the hyperbolic distance $\eta(t)$.

We obtain the following explicit formula for the mean value of the hyperbolic distance which reads

$$E\{\cosh \eta(t)\} = e^{\frac{-\lambda t}{2}} \left\{ \cosh \frac{t}{2} \sqrt{\lambda^2 + 4c^2} + \frac{\lambda}{\sqrt{\lambda^2 + 4c^2}} \sinh \frac{t}{2} \sqrt{\lambda^2 + 4c^2} \right\} = E e^{T(t)}$$

where $T(t)$ is a telegraph process with parameters $\frac{\lambda}{2}$ and c .

The telegraph process represents the random of a particle moving with constant velocity and changing direction at Poisson paced times.

This section is devoted to motions on the Poincare half plane where the return to the starting point is admitted and occurs at the instants of changes of direction. The mean distance from the origin of these jumping back motions is obtained explicitly by exploiting their relationship with the motion without jumps. In the case where the return to the starting point occurs at the Poisson event T_1 , the mean value of the hyperbolic distance $\eta_1(t)$ reads

$$E\{\cosh \eta_1(t) \mid N(t) \geq 1\} = \frac{\lambda}{\sqrt{\lambda^2 + 4c^2}} \frac{\sinh \frac{t}{2} \sqrt{\lambda^2 + 4c^2}}{\sinh \frac{t}{2}}$$

The next section considers the motion at finite velocity, with orthogonal deviations at Poisson times, on the unit radius sphere. The main results concern the mean value $E\{\cos d(P_0 P_1)\}$, where $d(P_0 P_1)$ is the distance of the current point P_1 from the starting position P_0 . We take profit of the analogy of the spherical motion with its counterpart on the Poincare half plane to discuss the different situations due to the finiteness of the space where the random motion develops.

We here examine the planar motion dealt with so far assuming now that, at the instants of changes of direction, the particle can return to the starting point and commence its motion from scratch.

The new motion and the original one are governed by the same Poisson process so that changes of direction occur simultaneously in the original as well as in the new motion starting a fresh from the origin. This implies that the arcs of the original sample path and those of the new trajectories have the same hyperbolic length. However, the angles formed by successive segments differ in order to make the hyperbolic Pythagorean Theorem applicable to the trajectories of the new motion.

In order to make our description clearer, we consider the case where, in the interval $(0, t), N(t) = n$ Poisson events ($n \geq 1$) occur and we assume that the jump to the origin happens at the first change of direction i.e., at the instant t_1 . The instants of changes of direction for the new motion are

$$t'_k = t_{k+1} - t_1$$

where $k = 0, 1, \dots, n$ with $t'_0 = 0$ and $t'_n = t - t_1$ and the hyperbolic lengths of the corresponding arcs are

$$c(t'_k - t'_{k-1}) = c(t_{k+1} - t_k)$$

Therefore, at the instant t , the hyperbolic distance from the origin of the particle performing the motion which has jumped back to O at time t_1 is

$$\prod_{k=1}^n \cosh c(t'_k - t'_{k-1}) = \prod_{k=1}^n \cosh c(t_{k+1} - t_k) = \prod_{k=2}^{n+1} \cosh c(t_k - t'_{k-1}) \quad (8)$$

where $0 = t'_0 < t'_1 < \dots < t'_n = t - t_1$ and $t_{k+1} = t'_k + t_1$. Formula (8) shows the first step has been deleted. However, the distance between the position P_t and the origin O of the moving particle which jumped back to O after having reached the position P_1 , is different from the distance of P_t from P_1 since the angle between successive steps must be readjusted in order to apply the hyperbolic Pythagorean Theorem.

If we denote by T_1 the random instant of the return to the starting point (occurring at the first Poisson event), we have that

$$\begin{aligned} E\{\cosh \eta_1(t) I_{\{N(t) \geq 1\}} \mid N(t) = n\} &= E\{\cosh \eta(t - T_1) I_{\{T_1 \leq t\}} \mid N(t) = n\} \\ &= \int_0^t E\{\cosh \eta(t - T_1) I_{\{T_1 \in dt_1\}} \mid N(t) = n\} dt_1 \\ &= \int_0^t E\{\cosh \eta(t - T_1) \mid T_1 = t_1, N(t) = n\} Pr\{T_1 \in dt_1 \mid N(t) = n\} dt_1 \end{aligned} \quad (9)$$

By observing that

$$\begin{aligned} E\{\cosh \eta(t - T_1) \mid T_1 = t_1, N(t) = n\} &= E\{\cosh \eta(t - t_1) \mid N(t) = n - 1\} \\ &= \frac{(n-1)!}{(t-t_1)^{n-1}} I_{n-1}(t - t_1) \end{aligned}$$

and that

$$Pr\{T_1 \in dt_1 \mid N(t) = n\} = \frac{n!}{t^n} \frac{(t-t_1)^{n-1}}{(n-1)!} dt_1$$

with $0 < t_1 < t$, formula (9) becomes

$$E\{\cosh \eta_1(t) I_{\{N(t) \geq 1\}} \mid N(t) = n\} = \frac{n!}{t^n} \int_0^t I_{n-1}(t - t_1) dt_1 \quad (10)$$

From (10) we have that the mean hyperbolic distance for the particle which returns to O at time T_1 , has the form:

$$\begin{aligned} E\{\cosh \eta_1(t) \mid N(t) \geq 1\} &= \frac{e^{-\lambda t}}{Pr\{N(t) \geq 1\}} \sum_{n=1}^{\infty} \lambda^n \int_0^t I_{n-1}(t - t_1) dt_1 \\ &= \frac{\lambda e^{-\lambda t}}{Pr\{N(t) \geq 1\}} \int_0^t e^{\lambda(t-t_1)} E(t - t_1) dt_1 \end{aligned}$$

We give here, a general expression for the mean value of the hyperbolic distance of a particle which returns to the origin for the last time at the k^{th} Poisson event T_k . We shall denote the distance by the following equivalent notation $\eta(t - T_k) = \eta_k(t)$ where the first expression underlines that the particle starts from scratch at time T_k and then moves away for the remaining interval of length $t - T_k$. In the general case we have the result stated in the next theorem.

Theorem: 3.1

If $N(t) \geq k$, then the mean value of the hyperbolic distance η_k is equal to

$$\begin{aligned} E\{\cosh \eta_k(t) \mid N(t) \geq k\} &= \frac{\lambda^k e^{-\lambda t}}{Pr\{N(t) \geq k\}} \int_0^t e^{\lambda(t-t_k)} E(t-t_k) dt_k \\ &= \frac{\lambda^k e^{-\lambda t}}{Pr\{N(t) \geq k\}(k-1)!} \int_0^t e^{\lambda(t-t_k)} t_k^{k-1} E(t-t_k) dt_k \end{aligned} \quad (11)$$

where $E(t) = e^{\frac{-\lambda t}{2}} \left\{ \cosh \frac{t\sqrt{\lambda^2+4c^2}}{2} + \frac{\lambda}{\sqrt{\lambda^2+4c^2}} \sinh \frac{t\sqrt{\lambda^2+4c^2}}{2} \right\}$

Proof:

We start by observing that

$$\begin{aligned} E\{\cosh \eta_k(t) \mid N(t) \geq k\} &= \sum_{n=k}^{\infty} E\{\cosh \eta_k(t) I_{\{N(t)=n\}} \mid N(t) \geq k\} \\ &= \sum_{n=k}^{\infty} E\{\cosh \eta_k(t) I_{\{N(t) \geq k\}} \mid N(t) = n\} \frac{Pr\{N(t)=n\}}{Pr\{N(t) \geq k\}} \\ &= \sum_{n=k}^{\infty} E\{\cosh \eta_k(t) I_{\{N(t) \geq k\}} \mid N(t) = n\} Pr\{N(t) = n \mid N(t) \geq k\} \end{aligned} \quad (12)$$

Since $T_k = \inf\{t: N(t) = k\}$, the conditional mean value inside the sum can be developed as follows

$$\begin{aligned} E\{\cosh \eta_k(t) I_{\{N(t) \geq k\}} \mid N(t) = n\} &= E\{\cosh \eta(t - T_k) I_{\{T_k \leq t\}} \mid N(t) = n\} \\ &= \int_0^t E\{\cosh \eta(t - T_k) I_{\{T_k \in dt_k\}} \mid N(t) = n\} dt_k \\ &= \int_0^t E\{\cosh \eta(t - T_k) \mid T_k = t_k, N(t) = n\} Pr\{T_k \in dt_k \mid N(t) = n\} dt_k \end{aligned}$$

Now we consider $E_n(t) = \frac{n!}{t^n} I_n(t)$ (13)

Using the above condition (13), we have that

$$\begin{aligned} E\{\cosh \eta(t - T_k) \mid T_k = t_k, N(t) = n\} &= E\{\cosh \eta(t - t_k) \mid N(t - t_k) = n - k\} \\ &= \frac{(n-k)!}{(t-t_k)^{n-k}} I_{n-k}(t - t_k) \end{aligned}$$

and on the base of well known properties of the Poisson process we have that

$$Pr\{T_k \in dt_k \mid N(t) = n\} = \frac{n!}{t^n} \frac{1}{(k-1)!} \int_0^t t_k^{k-1} dt_k$$

where $0 < t_k < t$. In conclusion we have that

$$E\{\cosh \eta_k(t) I_{\{N(t) \geq k\}} \mid N(t) = n\} = \frac{n!}{t^n} \frac{1}{(k-1)!} \int_0^t t_k^{k-1} I_{n-k}(t - t_k) dt_k$$

and, from this and (12), it follows that

$$\begin{aligned} E\{\cosh \eta_k(t) \mid N(t) \geq k\} &= \sum_{n=k}^{\infty} \frac{n!}{t^n} \frac{1}{(k-1)!} \int_0^t t_k^{k-1} I_{n-k}(t - t_k) dt_k \frac{e^{-\lambda t} (\lambda t)^n}{n! Pr\{N(t) \geq k\}} \\ &= \frac{e^{-\lambda t} \lambda^k}{Pr\{N(t) \geq k\} (n-1)!} \int_0^t e^{\lambda(t-t_k)} t_k^{k-1} E(t-t_k) dt_k \end{aligned}$$

Finally, in view of Cauchy formula of multiple integrals, we obtain that

$$\frac{e^{-\lambda t} \lambda^k}{Pr\{N(t) \geq k\} (n-1)!} \int_0^t e^{\lambda(t-t_k)} t_k^{k-1} E(t-t_k) dt_k = \frac{e^{-\lambda t} \lambda^k}{Pr\{N(t) \geq k\}} \int_0^t dt_1 \dots \int_{t_{k-1}}^t e^{\lambda(t-t_k)} E(t-t_k) dt_k$$

Theorem: 3.2

The mean of the hyperbolic distance of the moving particle returning to the origin at the k^{th} change of direction is

$$E\{\cosh \eta_k(t) \mid N(t) \geq k\} = \frac{\lambda^k e^{-\lambda t}}{\sqrt{\lambda^2+4c^2} Pr\{N(t) \geq k\}} \left\{ \frac{e^{At}}{A^{k-1}} - \frac{e^{Bt}}{B^{k-1}} + \sum_{i=1}^{k-1} \left(\frac{1}{B^i} - \frac{1}{A^i} \right) \frac{t^{k-i-1}}{(k-i-1)!} \right\} \quad (14)$$

where $A = \frac{1}{2}(\lambda + \sqrt{\lambda^2 + 4c^2})$ and $B = \frac{1}{2}(\lambda - \sqrt{\lambda^2 + 4c^2})$

for $k = 1$, the sum in (14) is intended to be zero.

Proof:

We can prove (14) by applying both formulas in (11). We start our proof by employing the first one:

$$E\{\cosh \eta_k(t) \mid N(t) \geq k\} = \frac{\lambda^k e^{-\lambda t}}{Pr\{N(t) \geq k\}} \int_0^t dt_1 \dots \int_{t_{k-1}}^t e^{\lambda(t-t_k)} E(t-t_k) dt_k \quad (15)$$

Now consider $E(t) = \frac{e^{-\lambda t/2}}{2} \left\{ \frac{\lambda + \sqrt{\lambda^2 + 4c^2}}{\sqrt{\lambda^2 + 4c^2}} e^{(t/2)\sqrt{\lambda^2 + 4c^2}} + \frac{\sqrt{\lambda^2 + 4c^2} - \lambda}{\sqrt{\lambda^2 + 4c^2}} e^{-(t/2)\sqrt{\lambda^2 + 4c^2}} \right\}$ (16)

Therefore in view of (16), formula (15) becomes

$$E\{\cosh \eta_k(t) \mid N(t) \geq k\} =$$

$$\frac{\lambda^k e^{-\lambda t}}{Pr \{N(t) \geq k\}} \int_0^t dt_1 \dots \int_{t_{k-1}}^t e^{\lambda(t-t_k)} \left\{ \frac{e^{\lambda(t-t_k)/2}}{2} \left[\frac{\lambda + \sqrt{\lambda^2 + 4c^2}}{\sqrt{\lambda^2 + 4c^2}} e^{(t-t_k)/2} \sqrt{\lambda^2 + 4c^2} + \frac{\sqrt{\lambda^2 + 4c^2} - \lambda}{\sqrt{\lambda^2 + 4c^2}} e^{-(t-t_k)/2} \sqrt{\lambda^2 + 4c^2} \right] E(t-t_k) \right\} dt_k$$

By introducing A and B as in (14), we can easily determine the k fold integral

$$\begin{aligned} E\{\cosh \eta_k(t) | N(t) \geq k\} &= \frac{\lambda^k e^{-\lambda t}}{\sqrt{\lambda^2 + 4c^2} Pr \{N(t) \geq k\}} \int_0^t dt_1 \dots \int_{t_{k-1}}^t \{Ae^{A(t-t_k)} - Be^{B(t-t_k)}\} dt_k \\ &= \frac{\lambda^k e^{-\lambda t}}{\sqrt{\lambda^2 + 4c^2} Pr \{N(t) \geq k\}} \int_0^t dt_1 \dots \int_{t_{k-2}}^t \{e^{A(t-t_{k-1})} - e^{B(t-t_{k-1})}\} dt_{k-1} \\ &= \frac{\lambda^k e^{-\lambda t}}{\sqrt{\lambda^2 + 4c^2} Pr \{N(t) \geq k\}} \int_0^t dt_1 \dots \int_{t_{k-3}}^t \left\{ \frac{e^{A(t-t_{k-2})}}{A} - \frac{e^{B(t-t_{k-2})}}{B} + \frac{1}{B} - \frac{1}{A} \right\} dt_{k-2} \end{aligned}$$

At the j^{th} stage the integral becomes

$$E\{\cosh \eta_k(t) | N(t) \geq k\} = \frac{\lambda^k e^{-\lambda t}}{\sqrt{\lambda^2 + 4c^2} Pr \{N(t) \geq k\}} \int_0^t dt_1 \dots \int_{t_{k-j-1}}^t \left\{ \frac{e^{A(t-t_{k-j})}}{A^{j-1}} - \frac{e^{B(t-t_{k-j})}}{B^{j-1}} + \sum_{i=1}^{j-1} \left(\frac{1}{B^i} - \frac{1}{A^i} \right) \frac{(t-t_{k-j})^{j-i-1}}{(j-i-1)!} \right\}$$

At the $(k-1)^{th}$ stage the integral becomes

$$E\{\cosh \eta_k(t) | N(t) \geq k\} = \frac{\lambda^k e^{-\lambda t}}{\sqrt{\lambda^2 + 4c^2} Pr \{N(t) \geq k\}} \int_0^t dt_1 \left\{ \frac{e^{A(t-t_1)}}{A^{k-2}} - \frac{e^{B(t-t_1)}}{B^{k-2}} + \sum_{i=1}^{k-2} \left(\frac{1}{B^i} - \frac{1}{A^i} \right) \frac{(t-t_1)^{k-2}}{(k-i-2)!} \right\}$$

At the k^{th} integration we obtain formula (14).

By means of the second formula in (11) and by repeated integrations by parts we can obtain again result (14).

4. Motion at Finite Velocity on the Surface of a Three Dimensional Sphere:

Let P_0 be a point on the equator of a three dimensional sphere. Let us assume that the particle starts moves from P_0 along the equator in one of the two possible directions (clockwise or counter clockwise) with velocity c .

At the first Poisson event (occurring at time T_1) it starts moving on the meridian joining the north pole P_N with the position reached at time T_1 (denoted by P_1) along one of the two possible directions.

At the second Poisson event the particle is located at P_2 and its distance from the starting point P_0 is the length of the hypotenuse of a right spherical triangle with cathetus P_0P_1 and P_1P_2 ; the hypotenuse belongs to the equatorial circumference through P_0 and P_2 .

Now the particle continues its motion (in one of the two possible directions) along the equatorial circumference orthogonal to the hypotenuse through P_0 and P_2 until the third Poisson event occurs.

In general, the distance $d(P_0P_1)$ of the point P_1 from the origin P_0 is the length of the shortest arc of the equatorial circumference through P_0 and P_1 and therefore it takes values in the interval $[0, \pi]$. Counter clockwise motions cover the arcs in $[-\pi, 0]$ so that the distance is also defined in $[0, \pi]$ or in $[-\pi/2, \pi/2]$ with a shift that avoids negative values for the cosine.

By means of the spherical Pythagorean relationship we have that the Euclidean distance $d(P_0P_2)$ satisfies

$$\cos d(P_0P_2) = \cos d(P_0P_1) \cos d(P_1P_2)$$

and, after three displacements,

$$\begin{aligned} \cos d(P_0P_3) &= \cos d(P_0P_2) \cos d(P_2P_3) \\ &= \cos d(P_0P_1) \cos d(P_1P_2) \cos d(P_2P_3) \end{aligned}$$

After n displacement the position P_t on the sphere at time t is given by

$$\cos d(P_0P_t) = \prod_{k=1}^n \cos d(P_kP_{k-1}) \cos d(P_nP_t)$$

Since $d(P_kP_{k-1})$ is represented by the amplitude of the arc run in the interval (t_k, t_{k-1}) , it results

$$d(P_kP_{k-1}) = c(t_k, t_{k-1})$$

The mean value $E\{\cos d(P_0P_t) | N(t) = n\}$ is given by

$$\begin{aligned} E_n(t) &= E\{\cos d(P_0P_t) | N(t) = n\} \\ &= \frac{n!}{t^n} \int_0^t dt_1 \int_{t_1}^t dt_2 \dots \int_{t_{n-1}}^t dt_n \prod_{k=1}^{n+1} \cos c(t_k, t_{k-1}) \\ &= \frac{n!}{t^n} H_n(t) \end{aligned}$$

Where $t_0 = 0, t_{n+1} = t$ and

$$H_n(t) = \int_0^t dt_1 \int_{t_1}^t dt_2 \dots \int_{t_{n-1}}^t dt_n \prod_{k=1}^{n+1} \cos c(t_k, t_{k-1})$$

The mean value $E\{\cos d(P_0P_t)\}$ is given by

$$\begin{aligned} E(t) &= E\{\cos d(P_0P_t)\} \\ &= \sum_{n=0}^{\infty} E\{\cos d(P_0P_t) | N(t) = n\} Pr \{N(t) = n\} \\ &= e^{-\lambda t} \sum_{n=0}^{\infty} \lambda^n H_n(t) \end{aligned}$$

By steps similar to those of the hyperbolic case we have that $H_n(t)$, $t \geq 0$, satisfies the difference differential equation

$$\frac{d^2}{dt^2} H_n = \frac{d}{dt} H_{n-1} - c^2 H_n$$

where $H_0(t) = \cos ct$ and therefore we can prove the following:

Theorem: 4.1

The mean value $E(t) = E\{\cos d(P_0 P_t)\}$ satisfies

$$\frac{d^2}{dt^2} E = -\lambda \frac{d}{dt} E - c^2 E \quad (17)$$

with initial conditions

$$\begin{cases} E(0) = 1 \\ \frac{d}{dt} E(t) \Big|_{t=0} = 0 \end{cases} \quad (18)$$

and has the form

$$E(t) = \begin{cases} e^{-\frac{\lambda t}{2}} \left[\cosh \frac{t}{2} \sqrt{\lambda^2 - 4c^2} + \frac{\lambda}{\sqrt{\lambda^2 - 4c^2}} \sinh \frac{t}{2} \sqrt{\lambda^2 - 4c^2} \right] & 0 < 2c < \lambda \\ e^{-\frac{\lambda t}{2}} \left[1 + \frac{\lambda t}{2} \right] & \lambda = 2c > 0 \\ e^{-\frac{\lambda t}{2}} \left[\cosh \frac{t}{2} \sqrt{4c^2 - \lambda^2} + \frac{\lambda}{\sqrt{4c^2 - \lambda^2}} \sinh \frac{t}{2} \sqrt{4c^2 - \lambda^2} \right] & 2c > \lambda > 0 \end{cases} \quad (19)$$

Proof:

The solution to the problem (17) and (18) is given by

$$E(t) = \frac{e^{-\frac{\lambda t}{2}}}{2} \left[\left(e^{\frac{t}{2} \sqrt{\lambda^2 - 4c^2}} + e^{-\frac{t}{2} \sqrt{\lambda^2 - 4c^2}} \right) + \frac{\lambda}{\sqrt{\lambda^2 - 4c^2}} \left(e^{\frac{t}{2} \sqrt{\lambda^2 - 4c^2}} - e^{-\frac{t}{2} \sqrt{\lambda^2 - 4c^2}} \right) \right] \quad (20)$$

so that (19) emerges.

For large values of λ , the first expression furnishes $E(t) \sim 1$ and therefore the particle hardly leaves the starting point. If $\frac{\lambda}{2} < c$, the mean value exhibits an oscillating behavior; in particular, the oscillations decrease as time goes on, and this means that the particle moves further and further reaching in the limit the poles of the sphere.

5. 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 $P = 0.045$) [8-10] & [12-13].

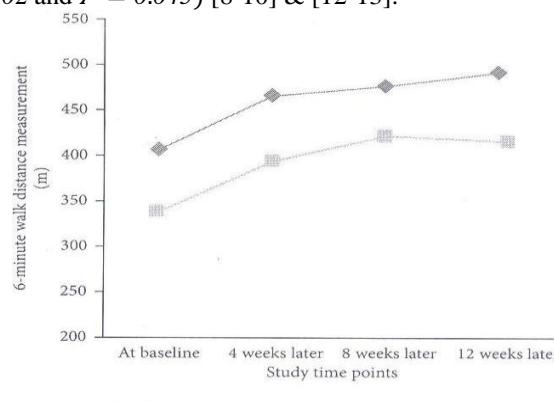


Figure 1: Trend of the changes in 6 minute walk distance parameter in intervention and placebo groups

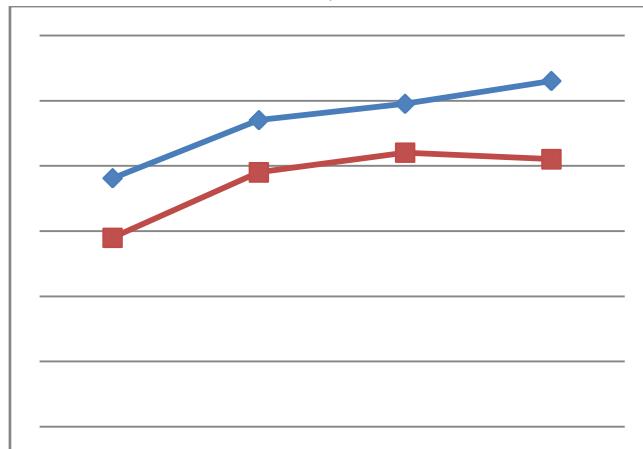


Figure 2: Trend of the changes in 6 minute walk distance parameter in intervention and placebo groups using Uniform Distribution

6. 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 Poincare half plane 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.

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