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Adult Heart Dynamics Evaluated from A Chaotic Mathematical Law

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Abstract

Aim: to confirm the diagnostic capacity in 18 hours of a methodology applied to heart dynamics in the frame of a chaotic exponential mathematical law previously applied in 21 hours based on dynamical systems theory and fractal geometry. *Materials and Methods*: a blind study was developed with 100 Holter registries, 30 normal and 70 pathological, with lengths of at least 18 hours up to 21 hours. The values of heartbeats, as well as minimal and maximal heart rates, were taken to build attractors and quantify their fractal dimension and its occupation space with the Box-Counting method. A comparison between the values obtained for both 18 and 21 hours was made as well as a comparison with the clinical diagnostic Gold Standard. *Results*: the values obtained for the spaces of occupation in the grid Kp of 18 hours were between 202 and 374 and between 43 to 195 for the pathological ones. Sensitivity and specificity were 100% and the Kappa coefficient was 1 for 18 and 21 hours. Conclusion: the diagnostic capacity of a chaotic exponential mathematical law applied to Holter registries in 18 hours was confirmed. This reduction can be useful in order to obtain earlier diagnostics about heart dynamics in contexts such as in the Intensive Care Unit.

Keywords: Nonlinear dynamics; Heart rate; Diagnostic

Introduction

The study of nonlinear dynamics deals with the states and evolution of dynamical systems based on the analysis of the behavior of variables along time [1]. This evolution can be represented in the phases space through attractors that highlight tendencies of the system and whose trajectory can be predictable or unpredictable, and for the latter, fractal geometry can be applied given its approach to irregularity [2,3]. Fractals can be abstract, statistical, or wild. Chaotic attractors are wild fractals and their fractal dimension can be measured through the Box-Counting method.

In the first decade of the 21st century, cardiovascular diseases have positioned as one of the main issues of public health between noncommunicable diseases. In 2008, about 17 million people died from that cause, and it is estimated that for 2030 this value augments to 30 million [4]. It is worth noting that cardiovascular disease is mostly presented in countries with low or middle income, with an incidence of 80% [5].

One of the most used devices in cardiovascular dynamics is Holter monitors, which allow to identify transient or abrupt significative alterations of heart rhythm, or ischemic lesions, among other abnormalities. The study of the RR interval, one of the main intervals studied in Holter monitors, has been included in different diagnostic guidelines in the clinical aspect given its relationship with cardiovascular mortality [6-8].

On the basis of dynamical systems theory [1], chaos and fractal geometry [2, 9], it has been established that heart dynamics is a phenomenon of irregular nature. Goldberger [10] has conducted a novel interpretation of the concepts of normality and disease, showing that, when relying on dynamical systems theory, highly random or irregular patterns as well as excessive regularity are characteristics of disease while normality is found halfway between both ends [10]. From this point of view, new predictive indexes of mortality from the analysis of RR intervals have been incorporated in patients that have suffered from acute myocardial infarction, finding better parameters of evaluation [11]. However, its clinical applicability is not yet determined and discussed.

Following this perspective and line of investigation, methodologies that evaluate Holter registries have been developed applying the theory of probability, allowing to establish significative distinctions between disease and normality [12]. This methodology was applied to patients with arrythmias, allowing to detect minor alterations that could be related to disease [13], which is useful in the clinical field to detect disease earlier. Then, a chaotic exponential mathematical law of heart dynamics was established from the analysis of continuous heart rate registries in 21 hours, generating objective parameters between normality and disease. Besides, all the possible heart attractors were deduced, including those that belong to acutely or chronically sick dynamics or normal as well as those in evolution towards disease [14].

The purpose of this study was to confirm the diagnostic capability of an exponential mathematical law to evaluate 100 Holter registries with a reduction of time from 21 to 18 hours.

Material and Method

Selection and Description of Participants

Holter registries with a length of at least 18 hours of patients older than 21 years of age were included, considering both normal and pathological cases. The diagnostics for each case were established by an expert cardiologist according to clinical history, physical examination and Holter results. The registries come from research databases of Insight Group developed with data of patients that consulted at Clínica del Country in Bogotá, Colombia, between 2016 to 2017. Registries with a length inferior to 18 hours or patients younger than 21 or patients with unclear clinical diagnostics were excluded.

Definitions

Phases space: geometrical space of at least two dimensions in which, through the graphical representation of ordered pairs of the same dynamical variable along time, the dynamics of a system are geometrically observed.

Fractal dimension through Box-Counting method: fractal dimension of an attractor in the phases space found through Equation 1, as follows:

$$D = \frac{LogN(2^{-(K+1)}) - LogN(2^{-K})}{Log2^{K+1} - Log2^{K}} \quad (1)$$

where D: fractal dimension, N: number of squares occupied in the grid by the chaotic attractor; K: grade of partitioning of the grid.

Simplified Box-Counting equation: equation 1 is simplified through Equation 2, considering grids with a proportion of ½ with respect to its dimensions, as follows:

$$D = Log_2\left[\frac{K_p}{K_g}\right] \quad (2)$$

where Kp is the number of squares occupied in the small grid and Kg the big grid.

Exponential law of chaotic heart dynamic: obtained when clearing Equation 2 in terms of Kp, obtaining:

$$K_p = 2^D K_g \quad (3)$$

where D: fractal dimension.

Technical Information

In principle, the clinical diagnostics were masked. That is, the clinical diagnostic consideration whether the registry was normal or abnormal was hidden during the application of the methodology and obtaining the mathematical diagnosis for each case; these clinical diagnostics were revealed only when the statistical analysis was developed [14]. Next, a pseudo-aleatory sequence of heart rates, that is, a simulation of the heart rate dynamics for both 21 and 18 hours, was conducted in order to perform calculations with the methodology in the two scenarios. This sequence is generated with a previously developed software that considers the values of minimal and maximal heart rate and heartbeats for each hour [14]. With this sequence, it was possible to build chaotic attractors in the phases space through the graphing of ordered pairs of one heart rate with respect to the following one, consecutively. Later, the fractal dimension of the attractors was calculated, using Equation 2, through the overlapping of Kp and Kg grids of 5 beats/min and 10 beats/min respectively for each of the attractors.

Statistics

The conventional diagnosis of Holter registries for normal and pathological cases was taken as Gold Standard against the physical-mathematical diagnosis in 21 and 18 hours. When comparing both results, a contingency table of 2×2 was used to discriminate false positive, false negatives, true positives, and true negatives. Then, values of sensitivity, specificity, and Kappa coefficient were calculated in order to determine the concordance between the conventional and mathematical diagnostics.

For the developing of these calculations, the following was considered. False-positive (FP) were defined as mathematically pathological but clinically as normal; false negatives (FN) were those cases that were cataloged clinically as pathological while remaining mathematically normal. True positives (TP) were the cases clinically and mathematically considered as pathological and true negatives (TN) were the cases diagnosed as normal within mathematical and clinical limits.

Cohen's coefficient (K) was evaluated through Equation 4:

$$K = \frac{Co - Ca}{Tt - Ca} \tag{4}$$

where Tt the totality of cases; Co is the value of observed concordances between the mathematical evaluation and Gold Standard, while Ca is the value of concordances attributed to randomness. To calculate Ca, the cases evaluated as normal with the mathematical methodology were called f_1 while the pathological ones were called f_2. Also, the conventional evaluation is taken, being C_1 the number of cases evaluated as normal while the pathological ones were called C_2. These values were taken into the Equation 5 which is as follows:

$$Ca = \left[\frac{f_1 x C_1}{Tt}\right] + \left[\frac{f_2 x C_2}{Tt}\right] \tag{5}$$

Results

100 Holter registries with a length of at least 18 hours of patients older than 21 years were obtained, among them, 30 within boundaries of normality and the remaining 70 registries presented some pathology according to the diagnosis of an expert clinical cardiologist. The 29 most representative Holter registries of the 100 registries analyzed in the study were highlighted in Table 1 as well as the values obtained with the methodology in Table 2.

Table 1. Clinical diagnostic for some representative heart dynamics of the study

Case no.	Clinical information
1	Acute myocardial infarction, auricular fibrillation, 12 events of bigeminy and trigeminy
2,3,4,8, 10, 11, 14, 16, 17, 19, 22, 26, 29	Normal
5	Medical control for pre-surgery
6, 24	Arrhythmia in study
7	Syncope in study
9	Tachycardia in study
12	Dilated myocardiopathy
13, 23, 25	Palpitations in study
15	Obstructive myocardiopathy
18	Arterial hypertension
20	Stroke
21	Coronary cardiopathy
27	Pre-syncope in study
28	Bundle Branch block. Extrasystoles. Frequent supraventricular extrasystoles with episodes of atypical auricular flutter or auricular tachycardia with rapid ventricular response

The fractal dimensions of the attractors were between 0.81 and 1.99 for the normal dynamics while the pathological one had values between 0.81 and 1.95 in the case of dynamics evaluated in 21 hours. On the other hand, for the dynamics evaluated in 18 hours, values between 0.85 and 1.99 corresponded to normal dynamics and between 0.83 and 2.05 to pathological dynamics (Table 2).

The values of the occupation spaces of dynamics in 21 hours for Kp grid were between 200 and 378 for normal dynamics and the pathological ones between 46 and 195. The values of the occupation spaces of dynamics in 18 hours for Kp grid were between 202 and 374 for normal dynamics and the pathological ones between 43 and 195 (Table 2).

Table 2. Values of spatial occupation for the Kp, Kg grids and fractal dimension of each dynamic both in 18 and 21 hours, from the registries of Table 1

Case	**21 hours**			**18 hours**		
	Kp	**Kg**	**DF**	**Kp**	**Kg**	**DF**
1	47	16	1.55	43	15	1.52
2	360	169	1.09	364	169	1.11
3	290	94	1.63	290	93	1.64
4	341	98	1.80	343	99	1.79
5	157	83	0.92	158	81	0.96
6	156	46	1.76	159	48	1.73
7	135	75	0.85	137	77	0.83
8	242	74	1.71	243	74	1.72
9	175	74	1.24	173	75	1.21
10	255	145	0.81	259	144	0.85
11	235	60	1.97	234	61	1.94
12	57	22	1.37	57	23	1.31
13	193	67	1.53	193	67	1.53
14	200	57	1.81	202	58	1.80
15	159	52	1.61	155	53	1.55
16	337	142	1.25	333	144	1.21
17	307	126	1.28	304	128	1.25
18	195	55	1.83	195	53	1.88
19	286	72	1.99	287	72	1.99
20	144	82	0.81	144	81	0.83
21	128	36	1.83	133	37	1.85
22	287	136	1.08	292	138	1.08
23	173	46	1.91	178	45	1.98
24	146	59	1.31	147	61	1.27
25	151	58	1.38	148	56	1.40
26	277	75	1.88	279	73	1.93
27	181	47	1.95	186	45	2.05
28	46	15	1.62	49	16	1.61
29	378	98	1.95	374	96	1.96

For the Kg grid, the values of the occupation spaces of dynamics were between 57 to 169 for normal dynamics while the abnormal ones had values between 15 and 83 in 21 hours. The values of the occupation spaces of dynamics in 18 hours were between 58 to 169 for normal dynamics while the abnormal ones had values between 15 and 81 in 18 hours. In all cases, the mathematical diagnostics in 21 and 18 hours matched.

The statistical analysis was conducted to compare the mathematical diagnostics with respect to the clinical Gold Standard, highlighting that for both in 21 and 18 hours, the values of specificity and sensitivity were 100%. Regarding the diagnostic concordance of the applied method and the clinical diagnostic, a Kappa coefficient of 1 was obtained.

In figure 1, the size difference between an attractor of a normal dynamic against an acute dynamic can be noted, showing that for normality, the spaces of occupation of the attractor a significantly bigger than for the case of an acute dynamic.

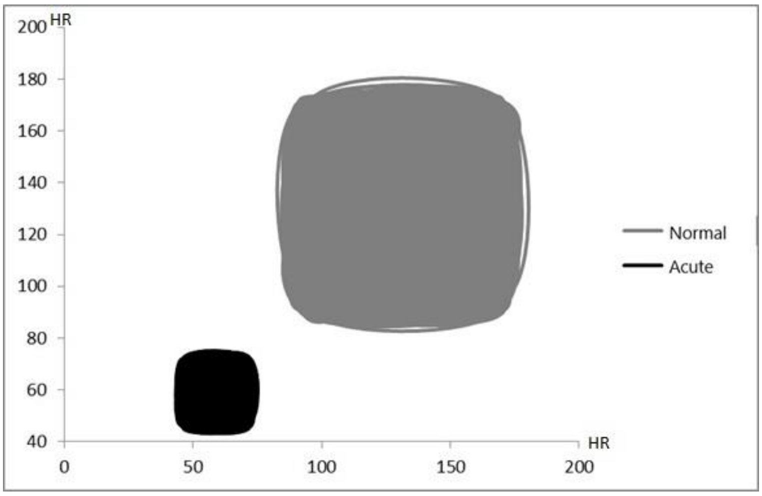

Figure 1. Attractors for two dynamics evaluated in 18 hours corresponding to the case 28 and 29 which correspond to normal and acute states with spaces of occupation of Kp = 374 and 49 as well as Kg = 96 and 16, respectively. Both Y and X axes are heart rates (HR)

Discussion

This is the first paper where the diagnostic capacity and clinical utility of a chaotic exponential mathematical law in the context of dynamical systems and fractal geometry through the application to Holter registries in 18 hours is demonstrated. It should be noted that the values of fractal dimension do not allow to obtain any difference between normality and abnormality of chaotic heart dynamics (Table 1), however, through the values obtained in Kp grids for both 18 and 21 hours (see table 1) this is accomplished with sensitivity and specificity of 100% and exhibiting concordances between both the mathematical and the clinical traditional diagnostics with a Kappa coefficient of 1. Besides, the geometric patterns of attractors for normality and abnormality are distinguishable (see Figure 1).

It is worth noting that the possibility of obtaining numerical and geometrical objective, reproducible and reliable distinctions, between normality, disease and the evolution between both states, can be obtained through methodologies such as this chaotic model. This methodology could be useful in the clinical setting given that it would allow physicians to rely on objective measures to diagnose whether a patient is presenting acute cardiac disease and treat it accordingly or if the patient is evolving towards an acute episode in order to make preventive measures with greater certainty in critical contexts such as the Intensive Care Unit, independent of the expertise of the physician, the semiology or the results of diagnostic tests such as heart rate variability that depend on epidemiological measures that confuse the interpretation of the clinical contexts.

The classical thinking of physiology about the human body has been based in concepts of regularity and periodic behaviors of dynamics [15,16]; however, with the rise of applications of theoretical physics and mathematics in different areas of knowledge, this thinking has been discussed and, in some aspects, it has changed. In the frame of said mathematical perspective, this chaotic exponential law was developed. The findings of this methodology are limited since there is a need to confirm their validity in further applications with different clinical contexts such as prospective studies or involving different cardiac pathologies, backgrounds or ages including pediatrics; more drastic reductions in time in order to obtain earlier diagnostics and more importantly, it is necessary to develop an automatization through software with real time patients to be easily applicable in the clinical context.

It is clear how an adequate diagnosis and control of cardiovascular pathologies is relevant as well as the establishment of measurements in the clinical aspect that facilitate the conjoint work by the different professionals involved that is, nurses, cardiologists, physicians, internists, among others since it is estimated that near 15% of strokes are secondary to arrhythmias [17]. The arrhythmical events such as tachycardia or bradycardia [18] or acute ischemic heart diseases could seriously compromise life, that is why methodologies that perform more timely diagnostics of heart dynamics alterations are necessary in order to provide earlier treatments.

On the basis of the evaluation of physiological signals of human body, methodologies have been developed to characterize its behavior. Particularly, the area that occupies greater concern with respect to is clinical implications is heart dynamics [18]. Nevertheless, reading, interpreting and evaluating these signals can represent a pivotal challenge when establishing basic differences such as normality and abnormality [19]. Currently, the methods used have been focused towards changes in heart rate such as heart rate variability in patients who suffered acute myocardial infarction [20-23] stroke [24] and even to predict all-cause mortality [25]. However, these methodologies are attached to a model of causal thinking, using populational lineal statistical methods and based in the principle of regularity, periodicity and stability, that is, classic homeostasis. On the contrary, the laws derived from the physical and mathematical thinking have risen and applied in cases as this exponential law to characterize and differentiate heart dynamics [14].

The chaotic heart system presents a self-organization that can be observed through the acausal thinking and reasoning of contemporary theoretical physics, highlighted in fields as chaos theory [1, 2, 9, 26], quantum mechanics [27] and statistical mechanics [28, 29], where phenomena are simplistically comprehended and generalizations are possible to establish relying on a few cases away from causal relationships. Following this line of thinking in the medical field, theories that predict the binding of peptides to the human leukocyte antigen (HLA) class II [30], predictions of mortality from sets theory [31] and $CD4^+$ counts from complete blood count have been developed [32].

Conclusions

The capacity of the established exponential mathematical model was proven to diagnose the heart dynamics in 18 hours, exhibiting the maximal diagnostic concordance between the conventional clinical parameters and the physical-mathematical diagnosis when evaluated with measures of sensitivity, specificity and Kappa coefficient. This methodology could be fully applicable in the clinical context with a computational integration such as software integrated to monitoring devices in the intensive care unit or general wards in hospitals, allowing mathematical and computational diagnostics in less time.

Ethical Issues

The developed study is aligned with the ethical principles of the World Medical Association Declaration of Helsinki. Besides, it includes Resolution 8430 of 1993 emitted by the Ministry of Health in Colombia and its declared as an investigation of minimal risk since physical-mathematical calculations are performed over registries and non-invasive tests previously prescribed. The data and integrity of the participants were protected.

Conflict of Interest

The authors declare that they have no conflict of interest.

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