Application of An Exponential Mathematical Law of Cardiac Dynamics In 16 Hours

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Abstract

Introduction and objectives: nonlinear dynamics and fractal geometry have allowed the advent of an exponential mathematical law applicable to diagnose cardiac dynamics in 21 hours, however, it would be beneficial to reduce the time required to diagnose cardiac dynamics with this method in critical scenarios, in order to detect earlier complications that may require medical attention. The objective of this research is to confirm the clinical applicability of the mathematical law in 16 hours, with a comparative study against the Gold Standard.

Methods: There were taken 450 electrocardiographic records of healthy patients and with cardiac diseases. A physical-mathematical diagnosis was applied to study cardiac dynamics, which consists of generating cardiac chaotic attractors based on the sequence of heart rate values during 16 hours, which were then measured with two overlapping grids according to the Box-Counting method to quantify the spatial occupation and the fractal dimension of each cardiac dynamic, with its respective statistical validation.

Results: The occupation spaces of normal dynamics calculated in 16 hours were compatible with previous parameters established, evidencing the precision of the methodology to differentiate normality from abnormality. Sensitivity and specificity values of 100% were found, as well as a Kappa coefficient of 1.

Conclusions: it was possible to establish differences between cardiac dynamics for 16 hours, suggesting that this method could be clinically applicable to analyze and diagnose cardiac dynamics in real time.

Introduction

The theory of dynamic systems allows analyzing the state and evolution of systems, which can be predictable or unpredictable. Its analysis has been possible through mathematical procedures that evaluate the changes of its dynamic variables over time [1]. The evolution of the systems can be represented graphically in the phase space from attractors. According to the trajectories of the dynamics [2], the different attractors originate; if the trajectories exhibit a predictable character, punctual or cyclic attractors are obtained and if the trajectories have an unpredictable character, the chaotic attractors, characterized by their irregularity, originate. This characteristic means that its quantification is done using fractal geometry, developed by Benoit Mandelbrot [3, 4].

Cardiovascular diseases are consolidated as one of the most important health problems of the century. According to estimates by the World Health Organization, the number of deaths from this cause is projected to increase to 25,000.00 in the year 2030[5], with low- and middle-income countries being the most affected [6]. Considering the impact of these diseases on public health, it is necessary to develop and improve methods that allow the timely detection of cardiovascular diseases. The Holter is a diagnostic tool, with which it is possible to detect alterations of the cardiac rhythm [7]; in Intensive Care Units, continuous electrocardiographic recordings are made through monitors.

The analysis of the RR interval guides the clinical experts in the differentiation of normality and disease [5, 8, 9]; however, there are still limitations in its clinical application, given that its evaluation is made from the homeostatic notions, according to which, normality is related to regular patterns, while in aging or abnormality there is a decrease in capacity to maintain the heart rate [10]. Some studies show that this perspective presents limitations and has established new forms of analysis based on theories and methods of physics and mathematics, such as dynamic systems, the law of chaos, fractal geometry, among others [11–14].

Goldberger et al., Have conducted studies based on the theory of dynamic systems; these investigations allowed the establishment of a new conception of normality and illness, according to which the disease is associated with very irregular or very periodic dynamics and normality is found between these two behaviors [15]. From this line of thought, Huikuri et al, established new predictive mortality rates in patients with acute coronary syndrome such as acute myocardial infarction and severely decreased ejection fraction [16].

From this same perspective, Rodríguez and Cols [17] developed an exponential mathematical law based on dynamic systems and fractal geometry, with which it was possible to make precise diagnoses, determine the severity of cardiac dynamics, differentiate normality, disease and evolution towards exacerbation in 21 hours; Likewise, it was possible to establish the totality of possible cardiac dynamics. Its clinical usefulness was corroborated in different investigations, including a blind study with 115 Holters [18], evidencing sensitivity values, 100% specificity and a Kappa coefficient of 1. This methodology was applied in subjects enrolling with arrhythmias [19–20], a study was also developed where the ability of this exponential mathematical law to perform diagnoses in 18 hours was demonstrated [21]. The purpose of the present investigation is to confirm the clinical applicability of the aforementioned law in 16 hours.

Materials And Methods

Definitions

Space of phases: Space of 2 or more dimensions, in which the dynamics of a system is represented geometrically, by means of the graphic representation of ordered pairs of values of a dynamic variable consecutive in time.

Fractal Dimension of Box-Counting: It is defined from the following equation:

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

Equation 1

D is the fractal dimension; N is the number of frames occupied by the object in the grid with partition degree k.

Simplified Box-Counting equation: Obtained by Equation 1, applied to two squares with a proportion of ½ in its dimensions, obtaining the formula:

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

Kp represents the number of squares occupied in the smallest grid and Kg those corresponding to the large grid.

Exponential law of cardiac chaotic dynamics17-20 It is obtained after a clearing of Equation 2 and is expressed as follows:

$$K_p = 2^D K_g \quad \text{Equation 3}$$

Population

450 continuous electrocardiographic and Holter records were taken, evaluated in 21 hours by an expert cardiologist, of subjects older than 21 years, 100 corresponded to cases diagnosed as normal by the clinician and 350 corresponded to patients with cardiac pathologies. The records came from databases of previous investigations of the Insight group, which allowed for a retrospective study.

Procedure

The clinical diagnoses established by the expert were masked. The maximum and minimum values of the heart rate were taken every hour and the beats per hour, in 21 and 16 hours. With these data, a quasi-random sequence of heart frequencies was generated by an equiprobable algorithm. Then, the cardiac attractors were constructed, plotting one frequency against the next in time in the phase space. The fractal dimension was calculated with the Box-Counting method (Equation 2) through the superposition of two grids, with which the spatial occupancy in Kp and Kg of the attractors was determined.

From Equation 3, the mathematical diagnosis of the records was determined, according to the previously developed law17-20, according to which, the dynamics of acute cardiac pathologies exhibit occupation spaces in the Kp grid below 73, normality it presents occupation spaces in this grid over 200, and the evolution towards the disease presents occupation spaces between 73 and 200. The mathematical diagnosis was compared in 16 and 21 hours, with which the agreement between both was established.

Statistical analysis

The diagnoses established by the clinical expert were taken as Gold Standard, according to conventional clinical parameters and were compared with the mathematical diagnosis in 16 hours, once the agreement of the diagnoses established by the mathematical law was confirmed at 16 and 21 hours. For the purposes of the statistical analysis, cases with acute and normal disease were taken. False negatives, false positives, true positives and true negatives were calculated. From a 2x2 contingency table, sensitivity and specificity were determined. Also, the Kappa coefficient was calculated.

Ethical aspects

This research is governed by the ethical, technical and scientific principles set forth in the Declaration of Helsinki of the World Medical Association. According to the provisions of Resolution 8430 of 1993 of the Colombian Ministry of Health, it is defined as a minimum risk investigation, since physical-mathematical calculations are made from non-invasive and non-invasive reports and tests requested and performed according to conventionally established protocols. protecting the information and integrity of patients.

Results

The diagnosis established by clinical parameters of the different continuous and ambulatory electrocardiographic records is shown in Table 1. For the cardiac dynamics evaluated in 21 hours, the fractal dimension of the normal attractors was found between 0,9170 and 1,9068, and for the Abnormal dynamics were found between 0,8113 and 1,9349. The fractal dimensions of the normal cardiac chaotic attractors in 16 hours showed values between 0,9251 and 1,8744, while in the case of abnormal dynamics they presented values between 0,8212 and 1,9926. This is in line with previous findings, which show that the fractal dimension does not establish objective distinctions between the different cardiac dynamics, neither for 16 nor for 21 hours (see Table 1). There was agreement between the mathematical diagnosis in 16 and 21 hours in all the cases of the study.

Table 1
Clinical diagnosis of some continuous electrocardiographic records and Holters of the investigation.

No.	Clinical diagnosis	No.	Clinical diagnosis
1	Atrial fibrillation in the studio	15	Cardiac arrhythmia
2	Normal	16	Normal
3	Dizziness, ventricular tachycardia, frequent EV with dupletes and trigeminism	17	Ventricular extrasystoles, moderate decrease in HR variability
4	Ventricular extrasystole	18	CIA, dizziness, chest pain
5	Tendency to the sinus tachycardia in the registry that must be correlated with the clinical picture of the patient. Infrequent headphone extrasystoles.	19	Normal
6	Arrhythmia control. The QTC interval is normal.	20	Normal
7	Arrhythmia in study	21	Normal
8	tachycardia and atrial fibrillation with rapid ventricular response	22	Normal
9	Normal	23	Primary dilated cardiomyopathy
10	Normal	24	Mobitz 2 atrioventricular block
11	Supraventricular ectopia Syncope	25	precordial pain supraventricular extrasystole. Moderate decrease in HR variability.
12	Normal	26	precordial pain
13	Normal	27	Normal
14	Normal	28	Frequent extrasystolia, frequent atrial extrasystole with short and frequent salves of nonsustained atrial tachycardia. Frequent monomorphic ventricular extrasystole with bigeminism.

The occupation spaces for normal cardiac chaotic dynamics evaluated in 21 hours in the Kp grid were between 209 and 398, and for abnormal dynamics between 22 and 195. The occupation spaces for normal cardiac dynamics evaluated in 16 hours in the Kp grid were they found between 211 and 400, and in the case of the pathological dynamics between 22 and 195 (look Table 2).

Table 2. Spaces of occupation of the cardiac attractors evaluated in 16 and 21 hours corresponding to the ambulatory and continuous electrocardiographic records of Table 1. Kp represents the values for the grid of small squares, Kg represents the values for the grid of large squares and DF corresponds to the fractal dimension.

No.	21 hours			16 hours		
	Kp	Kg	DF	Kp	Kg	DF
1	166	50	1.731	167	51	1.7113
2	273	85	1.683	269	83	1.6964
3	183	89	1.040	187	88	1.0875
4	165	62	1.412	160	64	1.3219
5	136	52	1.387	132	51	1.3720
6	99	39	1.344	103	41	1.3289
7	122	52	1.230	124	51	1.2818
8	195	51	1.935	195	49	1.9926
9	338	179	0.917	338	178	0.9251
10	312	152	1.037	317	152	1.0604
11	116	32	1.858	120	31	1.9527
12	347	145	1.259	351	143	1.2955
13	371	104	1.835	369	104	1.8270
14	218	101	1.110	220	100	1.1375
15	175	80	1.129	170	80	1.0875
16	210	77	1.447	213	76	1.4868
17	149	48	1.634	154	48	1.6818
18	179	102	0.811	182	103	0.8213
19	209	67	1.641	211	66	1.6767
20	315	98	1.684	317	99	1.6790
21	225	60	1.907	220	60	1.8745
22	238	92	1.371	242	91	1.4111
23	22	8	1.459	22	6	1.8745
24	107	38	1.494	109	36	1.5983
25	158	46	1.780	162	44	1.8804
26	133	36	1.885	134	34	1.9786
27	398	188	1.082	400	188	1.0893

28	153	58	1.399	152	56	1.4406

Regarding the grid Kg, the occupation spaces in 21 hours for the dynamics without alterations were between 60 and 188, while for the abnormal dynamics were between 8 and 102. The occupation spaces for the dynamics in the grid Kg in 16 hours they presented values for normality between 60 and 188, and for abnormality between 6 and 103 (see Table 2).

Figure 1 shows three attractors, corresponding to normality, acute disease and evolution towards exacerbation. This figure shows the decrease in the spatial occupation of the chaotic attractor when the dynamics approaches the acute disease, which confirms the previously mentioned findings.

Discussion

This is the first work in which the clinical applicability and the diagnostic capacity of the exponential chaotic mathematical law are corroborated, in the context of a reduction of the evaluation time to 16 hours in a blind study with 450 cases, evidenced that the methodology allows establish precise quantitative differences between normality and disease, with values of sensitivity and specificity of 100% and a Kappa coefficient of 1, after a comparison between the mathematical and conventional diagnosis. This mathematical method objectively quantifies the severity of the pathologies, establishing itself as a predictive and diagnostic methodology capable of differentiating normal and pathological states, by decreasing the occupation spaces of the attractors in the fractal space of Box Counting.

The mentioned mathematical exponential law, developed from an inductive reasoning coming from the theoretical physics, allowed to establish the totality of possible cardiac dynamics. This method could be automated for its wide use in the clinic, given its objectivity and reproducibility. He has shown his ability to make mathematical distinctions between cardiac dynamics [18], even in patients taking arrhythmias [19, 20, 22]. In the present work, the evaluation time of cardiac dynamics was reduced, which would be important at the clinical level due to the greater opportunity in the establishment of the diagnoses.

Classical physiology has been governed by homeostatic conceptions, according to which normality is evidenced by regular or periodic behaviors [22]. However, this approach has been controverted by studies carried out from the theory of dynamic systems [15]. These investigations have proposed new routes in the analysis of heart rate variability, which is usually evaluated based on pre-established homeostatic notions. With the work done on the basis of dynamic systems, partial results have been obtained, associating the decrease in the variability of the heart rate with disease [23]. On the other hand, the mathematical law applied in this research allows the realization of precise diagnoses and the detection of evolution towards disease, based on the self-organization of the cardiac system, establishing clear numerical limits.

The theory of chaos [1, 13, 24], quantum mechanics [25] and statistical mechanics [26, 27] have been the starting point for predictions in science, regardless of causal relationships. This acausal perspective, typical of modern theoretical physics, is the substratum of the exponential mathematical law object of this work, for which, it makes independent diagnoses of statistical, population or other considerations.

Physical and mathematical theories have led to diagnoses and predictions of cardiac systems, based on the Zipf / Mandelbrot law [28, 29], the probability theory and entropy [30]. Likewise, diagnoses have been established at the cellular level [31, 32, 33] and arterial [34]; Predictions of malaria have been made in Colombia [35] and the population of CD4 T lymphocytes has been determined in patients seropositive for HIV [36]. Predictions have also been developed in immunology [37] and mortality in the Intensive Care Unit [38].

Conclusions

In this work, the clinical and diagnostic utility of the exponential mathematical law was confirmed. It was evidenced that he could adequately differentiate the normal cardiac pathological dynamics, depending on the occupation spaces of the chaotic attractors, showing their predictive character.

Declarations

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Conflicts of interests

None

Availability of data and material

Data will be made available upon reasonable request.

Ethics approval

This study was approved by Universidad del Magdalena ethics committee.

Consent to participate

Not applicable.

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Figures

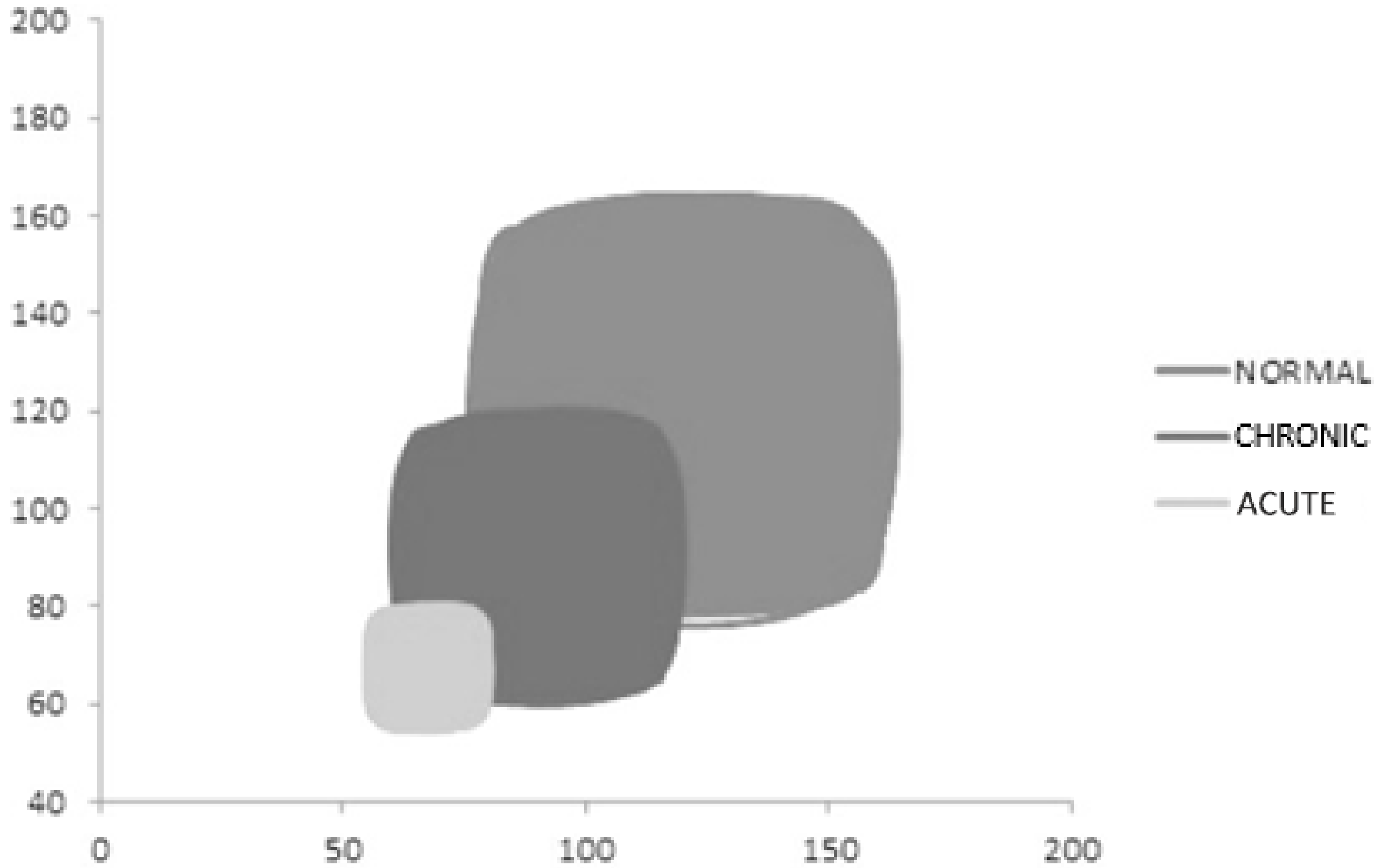

Figure 1

Cardiac chaotic attractors exhibiting evolution from normality towards chronic and acute disease.