Fractal Diagnostic Generalization of the Left Ventricular Cardiac Morphology: Moderate and Severe Abnormalities from Ventriculogram

Generalización diagnóstica fractal de la morfología cardiaca ventricular izquierda: anormalidades moderadas y severas a partir del ventriculograma

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ABSTRACT

Introduction: Cardiac irregularity is adequately described by means of fractal geometry, which was the basis for the development of a diagnosis of the left ventriculogram. **Methods**: All possible permutations of similarity degrees from fractal dimensions were simulated for the ventricle in systole, diastole and the totality. Permutations were defined between the previously established minimum and maximum values of similarity degrees for moderate and severe abnormality. **Results**: The total number of ventricular prototypes between moderate and severe abnormality was established. The total number of possible ventricular structure prototypes is 1614: 794 ventricles with moderate abnormality

and 820 with severe abnormality. Previous measurements of ventricles with a diagnosis of moderate and severe abnormality were found within the generalization. **Conclusions**: An objective geometric methodology was developed, which is of diagnostic aid in the clinical practice. It determined all possible left ventricular structures with moderate and severe abnormality, independently of clinical classifications.

Keywords
left ventriculogram; diagnosis; ejection fraction; fractal dimension.

RESUMEN

Introducción: La irregularidad cardiaca es adecuadamente descrita mediante geometría fractal, la cual fue base para el desarrollo de un diagnóstico del ventriculograma izquierdo. **Métodos**: Se simularon la totalidad de permutaciones posibles de grados de similitud de las dimensiones fractales del ventrículo en sístole, diástole y totalidad, definidas entre los valores mínimos y máximos de los grados de similitud para anormalidad moderada y severa previamente establecidos. **Resultados**: Se estableció el número total de prototipos ventriculares entre anormalidad moderada y severa. El número total de prototipos de estructura ventricular posibles fue de 1614: 794 ventrículos con anormalidad moderada y 820 con anormalidad severa. Medidas previas de ventrículos con diagnóstico de anormalidad moderada y severa se encontraron incluidas dentro de la generalización. **Conclusiones**: Se desarrolló una metodología geométrica objetiva y de ayuda diagnóstica a nivel clínico, que determinó todas las posibles estructuras ventriculares izquierdas con anormalidad moderada y severa, independientemente de clasificaciones clínicas.

Palabras clave
ventriculograma izquierdo; diagnóstico; fracción de eyección; dimensión fractal.

Introduction

The ventricular shape and function can be altered both in acute and chronic heart pathologies, such as acute or chronic heart failure (1,2), which, among others, has coronary disease as one of its main causes. In this sense, diagnostic images of the ventricle obtained from the ventriculogram or the echocardiogram have been used to determine morphological and functional alterations. The ventriculogram is not used as much as before, due to the fact that the echocardiogram is more practical and less invasive. However, the ventriculogram became one of the methods that allow to accurately assess the ventricular silhouette at the end of diastole

and systole, to determine possible morphological alterations and to estimate the left ventricular volumes and the ejection fraction (3).

The morphological measurement of the left ventricle and its respective cavities has conventionally been carried out through linear Euclidean geometrical measurements that have allowed to classify the ventricular form as normal or with mild, moderate or severe abnormality (4). The cut-off points that define normality and abnormality apply both to measurements made in ventriculograms and in echocardiograms. In the morphological evaluation, Euclidean measurements of the diastolic and systolic diameter are taken into account, as well as the thickness of the septum and the posterior wall. For the functional evaluation, the ejection fraction is mainly evaluated, which may correspond to the aforementioned classification, so that a normal ventricle will have an ejection fraction greater than 55%; a ventricle with mild abnormality will have an ejection fraction between 45% and 54%; moderate, between 30% and 44%; and severe, less than 30% (5).

The forms of nature are irregular. However, they are usually evaluated with Euclidean measures with which paradoxical or inadequate results have been reached, since Euclidean geometry is designed to measure regular objects (6). Fractal geometry was developed to adequately measure the irregularity of objects found in nature (7,8). The dimensionless numerical measurement that characterizes these objects is the fractal dimension, and the method used to measure the irregularity of wild fractals, such as objects of nature, is Box Counting (8,9). Among the wild fractals of the human body and its components are the coronary and bronchial branching, the convolutions, brain neurons and others that have been analyzed in various studies (10,11).

In medicine, fractal geometry has served as the basis for developing methodologies with which to differentiate between normal and disease states. For example, Landini and Rippin (12) established a scale of fractal values that are associated with the lesion degrees until carcinoma in the epithelial connective tissue of the oral mucosa

interface. Similarly, Gazit, Baish, and Safabaksh (13) established fractal values characteristic of normality and disease of the tumor architecture and physiology in androgen-dependent tumors of mice. However, several studies have shown that, in many cases, the use of fractal measurements evaluated in isolation does not provide enough information for a later diagnosis. From this fact, concepts have been developed for the analysis of fractal dimensions that make it possible to establish diagnostic differences. Such is the case of a methodology based on the concept of *intrinsic mathematical harmony*, which allows the comparison of the fractal dimensions of the parts and the totality, differentiating between normality and restenosis of coronary arteries in an animal experimentation model (14); also, through the concepts of variability and net difference of the fractal dimensions, the levels of severity of occlusive arterial disease evaluated in angiographies were mathematically differentiated (15).

In the specific case of the study of the ventricular shape measured from the ventriculogram, Rodríguez et al. (16) designed a new methodology based on fractal geometry that includes the creation of the concept of *degrees of similarity*, which allows the comparison of the fractal dimensions of the ventricular contours in systole, diastole and totality from images with a diagnosis of cardiac ventricular normality and severe abnormality. This study served as the basis for the development of a diagnostic methodology for clinical application for ventriculograms classified as normal and with mild, moderate and severe abnormality, while achieving differentiation from the degrees of similarity, with clinical implications for any heart pathology that has repercussions on ventricular geometry.

In this research, a generalization was made to obtain a complete spectrum of all the possible ventricular prototypes that can be established between the classifications of moderate to severe abnormality based on theoretical simulations generated from the results of a previous study (16), useful as an objective and reproducible method of diagnostic aid in clinical practice.

Materials and methods

Definitions

Fractal: Irregular object. Term that indicates as an adjective, irregular, and as a noun, irregularity.

Unit and significant figure: In a decimal number, the unit corresponds to the figure(s) that are to the left of the comma; while those to the right of the comma are called significant figures.

Box Counting Fractal dimension:

$$D = \frac{LogN(2^{-(K+1)}) - LogN(2^{-K})}{Log2^{k+1} - Log2^k} = Log_2 \frac{N(2^{-(k+1)})}{N(2^{-k})}$$

Where N is the number of boxes occupied by the object; K is the degree of partition of the grid; and D is the fractal dimension (5).

Regions: These correspond to the left ventricle images obtained from the ventriculogram, observed as described below:

Systole (S): the region corresponding to the image in systole.

Diastole (D): the region corresponding to the image in diastole.

Totality (T): corresponds to the sum of the values measured in systole and diastole.

Procedure

The generalization developed was based on a previous study (16) in which 36 cases were selected where the ventricular form was evaluated from the left ventriculogram, which were divided into 4 groups according to the ejection fraction: 9 normal, 9 with ejection fraction slightly decreased, 9 moderately decreased and 9 severely decreased. These cases were selected to have the full spectrum of the different possible alterations of the ventricle and compare them with the proposed mathematical methodology. This study was carried out by specialists of the Department of Hemodynamics of the Fundación CardioInfantil-Instituto de Cardiología, and the images of the ventriculogram were obtained from the ACOM-

TOP Siemens system. Technically, the femoral artery was canalized percutaneously for cardiac catheterization, inserting 5 or 6 French catheters. Subsequently, 30 to 45 mL of contrast medium were injected in the left ventricular cavity at a speed of 10 to 12 mL/s.

The diagnostic methodology of the left ventriculogram developed by Rodríguez et al. (16), which supports the present study, established the definition of degrees of similarity between the fractal dimensions of three regions: systole, diastole and totality (see definitions), to establish the mathematical diagnosis. According to this methodology, to establish the degrees of similarity between the fractal dimensions of the parts and the totality, a value is assigned to each significant figure as follows: the units are given a value of 1; to the tenths, 10; to the hundredths, 100; and to the thousandths, 1000. Next, the fractal dimensions are compared, looking, from left to right, for the first significant figure that is different. Once this figure is identified, one is subtracted from the other and the result of this subtraction is multiplied by the value assigned to this significant figure. An example of how to calculate these values is found in the Appendix.

Likewise, in this study it was established that the state of moderate disease is characterized by degrees of similarity with values between 1 and 900, with the presence of at least one value between 100 and 900. Severe disease is characterized by values between 1 and 9000, where at least one of these values must be between 100 and 9000. The degrees of similarity were grouped according to four sets established as follows: A = {x | 1 ≤ x ≤ 9}, B = {x | 10 ≤ x ≤ 90}, C= {x | 100 ≤ x ≤ 900} y D = {x | 1000 ≤ x ≤ 9000}. In this way, moderate disease is characterized by presenting values within sets A, B, or C, and at least one value within set C while severe disease is characterized by values between 1 and 9000, with at least one value within sets C or D.

In order to find all the possible prototypes of ventricular structure with moderate and severe disease, the maximum and minimum extremes of the degrees of similarity were taken for the ventricles with moderate and severe disease

previously found (16). Based on the degrees of similarity of the fractal dimensions, a numerical simulation was developed from the calculation of all the possible permutations between the limit values for both moderate disease and severe disease, where each combination obtained was termed as a ventricular fractal prototype.

Next, the total number of prototypes obtained for each state was quantified. These prototypes were compared with values of degrees of similarity of prototypes measured in previous studies (16), in order to determine if these were included by the generalization developed. Due to the mathematical nature of the methodology developed, it does not require the use of statistical analysis.

The type of methodology described here did not affect any treatment or clinical decision; therefore, it did not affect the patients. This research complied simultaneously with the ethical, scientific and technical standards, and with the health research ethical guidelines of Article 11 of Resolution 008430 of 1993, of the Ministry of Health of Colombia. This methodology is classified within the category of risk-free research, since the mathematical calculations were performed based on test results of clinical practice that had been medically prescribed, protecting the integrity and anonymity of the participants (17).

Results

In total, we found 794 possible theoretical permutations of degrees of similarity that are associated with ventricular geometric shapes with moderate abnormality, and 820 for severe abnormality. Thus, a total of 1614 prototypes were obtained for moderate and severe disease. Tables 1 and 2 provide examples of the ventricular prototypes obtained for the two degrees of lesion evaluated. Given the characteristics of the mathematical diagnosis, we excluded the possibility of finding prototypes whose degrees of similarity are, for example: [10 10 10] or [1 1 1], as well as [1 100 100] and [30

1 80], or other possible combinations equivalent to these.

Table 1. *Prototypes of ventriculograms with moderate disease*

Prototypes	Fd			Degrees of similarity		
	S	D	T	S-D	S-T	T-D
M1	0.1429	0.4857	0.4286	30	30	600
M2	0.0769	0.3750	0.0625	30	100	30
M3	0.0476	0.0714	0.0385	300	100	400
M4	0.9348	0.9231	0.8462	100	10	10
M5	0.1765	0.1471	0.5652	300	40	40
M6	0.6190	0.6316	0.6875	200	700	500
M7	1.2501	1.2857	0.9091	300	1	1
M8	1.2727	1.1667	1.1538	10	10	100
M9	1.0625	1.0588	1.0000	100	600	500
M10	1.0714	0.9286	1.0833	1	100	1

Fd: fractal dimension; S: systole; D: diastole; T: totality.

Table 2. *Prototypes of ventriculograms with severe disease*

Prototypes	Fd			Degrees of similarity		
	S	D	T	S-D	S-T	T-D
S1	0.1667	0.1629	1.7143	4000	1	1
S2	0.1176	1.2163	1.2108	1	1	6000
S3	0.7059	0.7222	0.7647	200	600	400
S4	0.8947	0.8821	0.8804	100	100	2000
S5	1.1875	1.2667	1.1429	10	400	10
S6	1.3067	1.3079	0.9529	1000	1	1
S7	1.4714	1.3750	1.4250	10	500	10
S8	0.8333	0.8750	0.4615	400	40	40
S9	0.7692	1.0882	1.0667	1	1	200
S10	0.2609	0.2692	0.2847	9000	200	200

Fd: fractal dimension; S: systole; D: diastole; T: totality.

The measurements made to ventricles in previous studies were found within the prototypes obtained, which evidenced that the measures made in practice are included within the generalization developed.

Discussion

This is the first study that establishes the totality of the prototypes of ventricular fractal structures with moderate and severe abnormality, based on a theoretical simulation generated from the results found in a previous study that allowed to establish differentiations between normality and abnormality of the left ventricular structure (16). The mathematical relationships of the ventricular contours in the states of systole, diastole and the union of both, quantified by the concept of degrees of similarity, make it possible to establish a finite number of possible structures for both moderate abnormality and severe abnormality, so they are verifiable with conventional diagnoses.

This new methodology is useful as a diagnostic aid tool, by establishing in an objective and reproducible manner all the possible geometric shapes of the left ventricle that vary between moderate and severe abnormality, regardless of the specific type of cardiac disease. The use of this generalization would facilitate the application of the diagnosis developed in both surgery-type and pharmaceutical-type interventions, because having all the possible fractal ventricular structures, one could count on all the possible evolution routes from normality to disease, useful for monitoring in the clinical practice.

Other studies have sought to establish ventricle measurements based on Euclidean measurements. For example, Kappenberger (18) demonstrated by means of a simulation how the geometry and the anatomy of the heart correlate to each other, which evidenced that these influence the electrical stability of the heart. Other methodologies developed with this same perspective have studied the left ventricle by means of geometric analogies and mathematical analyzes, applying also Euclidean rules. The object of study of these methodologies is to quantify the ejection fraction and to model the right anterior and left anterior ventricle projected in an oblique space, in order to calculate the volume. For example, Brogan et al. (19) resembled the symmetry of the ventricular cavity applying the Simpson's method of discs; in another research they found the volume of the left ventricle by an approximation of the ventricular structure to that of an ellipsoid.

Among the computational methods, a methodology has been designed that traces several lines from the contour of the ventricle, which converge in a single central point that serves for the analysis of ventricular dynamics. However, it is a theoretical methodology that does not cover the differences of the thickening in the different segments of the wall. In a study related to this, a methodology was designed that more correctly reflects the

movement of the ventricular cavity from an artificial line superimposed at the same distance from the ventricular edge in systole and diastole, which allows to differentiate between normality and different heart pathologies. In contrast, this methodology achieves an objective mathematical characterization of the irregularity of the ventricle, making it unnecessary an approximation to regular shapes, such as those performed in the aforementioned studies, also establishing the totality of possibilities that may be found in clinical practice, together with a diagnosis for each particular case, regardless of the epidemiological and statistical methods.

One of the limitations of the ventriculogram is that, in addition to being an invasive diagnostic test, it has the limitation that from the conventional evaluation methodologies, not always a normal ventricular diagnosis implies an absence of pathology and, in turn, not always the identification of a ventricular thickening implies an altered ventricular function (20). This study shows how the applied methodology clarifies the diagnosis of the heart ventricle beyond classifications by using fractal geometry that allows to establish objective measures appropriate to the irregularity of this type of anatomical structures. Its use has also allowed the development of diagnoses applied to coronary angiography (15) and pediatric echocardiography (21), since it exceeds conventional methods.

Likewise, through mathematical methods theoretical simulations of all the particular cases of moderate and severe alterations of the ventricular form can be obtained. The statistical methods used in medicine today can only establish inferences about population groups, but cannot obtain generalizations from which particular cases can be deduced. The type of generalization developed in this study allows to establish with few particular cases all the possibilities of a phenomenon, and makes it possible to mathematically diagnose all the possible states that may occur in practice.

From this line of research other experimental and clinical applicability studies have been developed. This is the case of a methodology with which the totality of arterial prototypes was determined in an experimental restenosis model (14) and differences were established between normality and disease. A generalization was also developed that establishes the total of possible preneoplastic and neoplastic cells of cervical squamous epithelium and obtains a diagnosis that differentiates between normality and disease, mathematically clarifying the indeterminate state of ASCUS cells (22). Based on the theory of dynamic systems and fractal geometry applied to cardiology, it was achieved—by means of an exponential law—to determine all the possible normal cardiac dynamics, with acute disease, and the evolution between those two states, a study whose clinical applicability as a diagnostic aid tool was recently confirmed (23).

The approach in which this methodology has been developed is analogous to the way in which physical phenomena of chaos theory (24), quantum mechanics (25), and statistical mechanics (26) are studied, in the sense that the mathematical orders underlying the irregularity and apparent unpredictability of phenomena are established from an acausal perspective. From this conception and from the form of inductive reasoning characteristic of theoretical physics, methodologies have been developed that are useful in other fields of medicine. Among them is a diagnostic method of cardiac dynamics, which allows differentiation between normality and different degrees of evolution to acute disease, which make it possible to also predict the evolution of patients even in the absence of other clinical signs evaluated in a conventional manner (27). Predictions have also been made in the areas of infectology (28), immunology (29), molecular biology (30), and erythrocyte morphology (31). In the area of the prediction of epidemics, a predictive methodology for malaria outbreaks was recently developed in 820 municipalities, with a success rate of 99.86% (32). Like the present study, these studies demonstrate the relevance of using physical and mathematical theories to solve problems in all medical fields.

It is necessary to highlight that the present study corresponds to a theoretical generalization, and that it is based on mathematics and

the inductive method of theoretical physics, according to which it is possible to establish generalizations with few cases studied and regardless of causal considerations such as type of pathology, risk factors, among others, since the epicenter are the underlying mathematical relationships. To continue the research process, in subsequent studies we will consider the establishment of the validation of the model according to the reference method or other aspects.

Conclusions

The present study optimally characterized the structure of the ventricle with moderate and severe abnormal diagnosis, based on a new methodology based on fractal geometry and the definition of degrees of similarity. Furthermore, the establishment of the total number of prototypes for the ventricular structure helps to reduce errors attributed when considering the left ventricle as a geometric object measurable from regular shapes in two and three dimensions; it can also be applied in the future to any computer system.

Acknowledgements

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Appendix

The method of calculating the degrees of similarity between the fractal dimensions of the M1 prototype of Table 1 is: for the S-D the values of the first different figure between the fractal dimension values of systole and diastole are taken, which in this case is in the tenths, having in the systole a value of 1; while in the diastole it has a value of 4. Both values are subtracted, and 3 is obtained, which is multiplied by the value assigned to this significant figure, which is 10. The result of this is that the degree of similarity is 30. We proceed in the same way for the S-T.

For the calculation of T-D the same procedure is followed: in this case the different figure between the fractal dimensions of totality and diastole is the second. The value of this figure for totality is 2, for diastole is 8, and the subtraction of these values is 6 that, when multiplied by the value assigned for this significant figure, which is 100, it is obtained that the T-D degree of similarity is 600.