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ORIGINAL RESEARCH

Theoretical geometric generalization of left ventriculogram during cardiac dynamic of clinical application

Generalización geométrica teórica del ventriculograma izquierdo durante la dinámica cardíaca de aplicación clínica

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Ventriculogram, fractal, left ventricle.

Palabras clave:
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ABSTRACT

Fractal geometry has proven to be adequate for mathematical description of irregular objects such as the human body. Based on this geometry, an objective and reproducible representation of a left ventricle was previously developed. The aim of this research was to develop a simulation based on this methodology that allows establishing all possible left ventricular dynamics from normality to severe disease. All possible combinations for each state were determined from maximum and minimum values of similarity degrees previously found for normal ventricular structures with mild, moderate and severe disease. The whole spectrum of ventricular dynamics between normality and disease during cardiac dynamic was quantified. There were found out 2,165 possible prototypes of ventricular structure: 551 of healthy states, 794 of mild and moderate disease, and 820 of severe disease. It was found that the similarity degrees of ventricle measures observed in previous studies were included within the identified prototypes. Thus, a generalization that establishes all possible ventricular fractal prototypes that may be found in clinical practice was developed, which is able to differentiate a normal state from several degrees of disease.

RESUMEN

La geometría fractal ha probado ser adecuada para la descripción de objetos irregulares tales como el cuerpo humano. Con base en esta geometría, se desarrolló previamente una representación objetiva y reproducible de un ventrículo izquierdo. El objetivo de esta investigación fue desarrollar una simulación basada en esta metodología que permita establecer todas las dinámicas posibles del ventrículo izquierdo desde la normalidad hasta la enfermedad severa. Todas las combinaciones posibles para cada estado se determinaron a partir de los valores máximos y mínimos de los grados de similitud previamente encontrados para las estructuras ventriculares normales con enfermedad leve, moderada y grave. Se cuantificó todo el espectro de la dinámica ventricular entre la normalidad y la enfermedad durante la dinámica cardíaca. Se encontraron 2,165 posibles prototipos de estructura ventricular: 551 de estados sanos, 794 de enfermedad leve y moderada y 820 de enfermedad severa. Se encontró que los grados de similitud de las medidas de ventrículo observadas en estudios previos se incluyeron dentro de los prototipos identificados. De esta manera, se desarrolló una generalización que establece todos los posibles prototipos de ventrículo fractal que se pueden encontrar en la práctica clínica, que es capaz de diferenciar un estado normal de varios grados de enfermedad.

INTRODUCTION

Mandelbrot in 1975 developed Fractal Geometry from impossibility to perform Euclidean measurements in irregular objects, defining the concept of fractal dimension with the purpose of describe by right way.[1-3] In actual medicine, fractal geometry have been used with success in cellular, tissue and dynamics characterization and diagnosis, such as cardiac dynamic.[4-9]

Ventriculography is used for visualizing cardiac internal morphology. It is an invasive process where cardiac size and movement

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are observed, through a colorant injection inside left or right ventricle cavity for taking X-ray images. This procedure is an undirected measure of cardiac physiology, which allows observing ventricular shape of final systole and diastole, calculating ejection fraction (EF) of ventricle, as well as establishing motility anomalies of ventricular wall.[10] However, its actual evaluation exhibit problems since that it depends on evaluator's experience. With the aim of improve the diagnostic, it has emerged the necessity to develop methodologies which be useful as tools of diagnostic support for differentiating objectively several pathologies in clinical practice.

Different methodologies based on fractal geometry had allowed establishing differences between normal and sick states in a physiologic and morphologic level. For example, Polhman & cols,[11] and Lefebvre & Benali[12] decreased the false positive found in digital mammography evaluation. Other works like Luzi & col[13] achieved to detail tumors of different histological types. Also, normal tissues and with tumor growing in mouse eyes have been mathematically differenced,[14] and a fractal growing model of transition from a normal vasculature to a tumoral one has been developed through a combination that allows seeing the percolation invasion and a simulation of autocrine mechanism.[15]

However, it is not always possible to find ranges that allow establishing characteristic values of normality and sickness; therefore, the isolated evaluation of fractal dimensions not always provide enough diagnostic information for characterizing disease-normality states and their evolution. Inside this context, investigations in different areas of medicine have been developed which provide methodologies and concepts for obtaining of diagnostics based on analysis of theses dimensions.

For instance, Rodríguez & cols.[16] observed that different cardiac pathologies produce changes in geometric structure of the whole ventricle that cannot be perceptible from conventional methodologies, differentiating normality from severe cardiac involvement. Based on that work, a mathematical methodology was developed that allows establishing mathematical differences from concept of similarity degrees between fractal dimensions of left ventricular contours during cardiac dynamic. This methodology is applied in systole, diastole and totality of left ventriculograms evaluated clinically as normal, mild, moderate and severe with regard to conventional clinical diagnosis. The concept of similitude degree allows comparing fractal dimensions of ventricle in systole, diastole and totality, and allows differentiating normality from several disease. This concept also establishes that mild and moderate disease are not mathematically differentiable, providing to clinical practice an objective and reproducible method of diagnostic support that allows evaluating quantitatively such evolution. This methodology provides diagnostic geometry quantification with implications for each cardiac pathology that have repercussions in ventricular geometry.[17]

This investigation has the purpose of generalizing these results through permutations of similarity degrees for every state, which allows determining the whole set of possible ventricular prototypes of normality and abnormality, meaning all possible ventricular fractal structure combinations in systole, diastole and totality that can be obtained in clinic practice for every state.

Definitions

1.1. Fractal: Irregular object or irregularity of an object.
1.2. Box-counting dimension fractal: Numeric measure for evaluating the irregularity of an object.
In this case N: is the number of squares filled by the object, K: is the partition degree of the grid and D: the fractal dimension.

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

1.3. Regions measured with fractal:
Systole (S): region corresponding to the image of ventricle in systole.
Diastole (D): region corresponding to the image of ventricle in diastole.
Totality (T): addition of the measured values in systole and diastole.

MATERIALS AND METHODS

The present mathematical research of clinical application started from similitude degrees between fractal dimensions of left ventricle images. This similarity degrees were obtained in a previous work in which a mathematical diagnosis of left ventriculography of clinical application was developed.[17] Ventriculograms evaluated as normal, and with mild, moderate and severe disease were used. Five ventriculograms were chosen for the generalization development, one of each classification were selected.

For obtaining similarity degrees, fractal dimensions from two of the measured mathematical regions were compared. A value for each digit of fractal dimension was defined: for the units a value of 1, for the tenths a value of 10, for the hundredth a value of 100, and for the thousandth a value of 1,000 was assigned. Next, the first digit from left to right was located, which is different among compared fractal dimensions and its values are subtracted. The result of the subtraction is multiplied by the assigned value to the digit.[17] For instance, for calculating T-D similitude degree of vetriculogram number 4 with severe lesion *(Table I)*, the first significant figure different between the numbers of fractal dimension of the objects in question (totality and diastole) must be found. Thus, the first different figure is in thousandths that for totality is 0, while in diastole is 3. Then, the absolute value of this subtract is 3, which in turn is multiplies with 1,000 that is the assigned value to this significant figure obtaining a similarity degree of 3,000. Also happens with similarity degree S-D and S-T. So, for finding S-D, the different figure which is in the hundredths is 4 for systole and 3 for diastole. Subtract of these values is multiplied by the assigned value for hundredths that is 100, thus the similarity degree is 100. For finding S-T, the different figure is in the hundredths too, with a value of 4 for systole and 3 for totality, so its value of similarity degree is also 100.

According to previously developed methodology, the similarity degree between the fractal dimensions for a ventricle with normal ejection fraction is less or equal to 90, while for

Table I. Examples of some obtained prototypes based on simulation, where FD is fractal dimension for each one of diagnosis.

Prototypes	Normal						Mild-moderate						Severe					
	FD			Similarity degrees			FD			Similarity degrees			FD			Similarity degrees		
	S	D	T	S-D	S-T	T-D	S	D	T	S-D	S-T	T-D	S	D	T	S-D	S-T	T-D
1	1.000	0.9231	0.8462	1	1	10	1.8333	1.6923	1.6154	20	20	800	1.0000	1.0526	1.1667	500	10	10
2	1.000	1.4286	1.1667	40	10	30	1.2500	1.2353	0.9000	200	1	1	1.7500	1.7273	1.0556	300	70	70
3	0.7500	0.8000	1.3846	10	1	1	1.0667	1.1579	1.1222	10	10	300	1.1000	1.1765	0.9474	700	1	1
4	0.8750	0.9440	0.6250	10	20	30	1.5714	1.5330	1.5238	400	500	100	1.1429	1.1333	1.1308	100	100	3000
5	1.2857	1.4286	0.6364	20	1	1	1.2500	0.9474	1.1765	1	10	1	0.7645	0.8125	0.8670	10	10	500

severe illness the values are from 1 to 9,000, with a minimal value from 100 to 900. For mild and moderated illness the values are from 1 to 900, with a minimal similarity degree from 100 to 900.[17] Every found possible similarity degrees are grouped in the next four sets:

$$A = \{x \in R \mid 1 \leq x \leq 9\}$$
$$B = \{x \in R \mid 10 \leq x \leq 90\}$$
$$C = \{x \in R \mid 100 \leq x \leq 900\}$$
$$D = \{x \in R \mid 1.000 \leq x \leq 9.000\}$$

In that way, normal ventricles exhibit values within the sets A and B, ventricles with mild and moderate injury exhibit values that belong to sets A, B and C, presenting at least a value from set C. While ventriculograms with severe injury present values included at the A, B, C and D sets, presenting at least a value within the C or D set. The maximum and minimum similarity degree values were taken for each considered lesion grade (normal, mild, moderate and severe) for the five initial prototypes chosen with the aim of defining the mathematical limits of the generalization.

Starting from the case in which the three measured regions have similarity grades of [1, 1, 10] [SD ST DT], and changing consecutively this three values until the greatest values found in the experience,[17] all possible combinations of similarity grades were obtained. It corresponds to the whole ventricular prototypes existent. Each different set of three measures of similarity degree describes different ventricular prototypes. And each ventricular prototype collects different ventricular structures that are characterized by this prototype, so the whole of ventricular structures existents are included in the generalization.

This kind of study doesn't affect any treatment or decision in a clinical level; therefore it wouldn't affect the patients. It is a research that follows simultaneously the ethic, scientific and technical norms; and with the ethic guidelines of the 11th article of the resolution 008430 of 1993, of the Health Ministry of Colombia, for research in health. This methodology can be classified on the research category with no risk, thanks to mathematic calculations based on test results of clinical practices that had been medically prescribed protecting the integrity and anonymity for the participants.[18]

Mathematical analysis

Finally, fractal dimension values of the studied ventriculograms of previous research were taken (see definitions).[16,17] The similarity degree within three mathematical regions of each ventriculogram was taken too, and these values were compared with the obtained theoretical prototypes for confirming the correspondence with developed generalization.

According to this methodology, the result is always the same, without take into account the experiment repetitions. It allows dispensing of statistical methodologies and of using of large samples for proving the correspondence of any particular ventriculogram.

By mathematical definition of similarity degree, some combinations of similarity degree [SD ST DT] were excluded, such as: [20 20 20], [1 1 1], [1 200 200], [40 1 90] and similar. For example, in the case [1 200 200], the difference between fractal dimensions of diastole and systole is 1 within units. The difference between fractals dimensions of systole and totality is of 2 and it occurs in the second decimal cipher, but this condition does impossible that the similarity degree D-T (diastole-totality) was 200, because this meaning that fractal dimension of diastole and the fractal dimension of totality are equals until the first decimal cipher. And as the totality is equal to systole until the first decimal cipher (ST = 200), then by the trichotomy principle, the diastole and systole should be equal until the first decimal cipher too, but it is known that it is no longer such, because those fractals dimensions are different in the unit, and its similarity degree (SD) is 1.

Other example is the case where the three similarity degrees are equal. This case is impossible to found in the practice by the same arguments exposed above. That is why the simulation of similarity degrees doesn't stars by [1 1 1], but by [1 1 10]. This show that not all mathematical possibilities have correspondence in experience, for this reason, some mathematical permutations are not taken into account for totality of ventricular prototypes.

RESULTS AND DISCUSSION

This is the first work in which a theoretical generalization of a diagnostic methodology of clinical application based on fractal measures and similarity degrees of left ventricle, determining all ventricular prototypes. This methodology is based on calculating fractal dimensions and their relations, which were evaluated through concept of similarity degrees which allows simultaneously assessing of ventricular contour in systole, diastole and both states. This methodology is useful as a tool of diagnostic support since that allows quantifying evolution between normality and severe disease including any cardiac pathology that have repercussions in ventricular geometry.

It was found in this generalization that, there are a total of 2,165 possible combinations of ventricular structures between normality and disease; 551 are normal ventricles, 794 are ventricles with moderate and mild lesions, and 820 with severe lesion. *Table I* shows 5 of all prototypes obtained for each one of the evaluated states.

Noteworthy that although mathematically is possible to realize a larger number of combinations of similarity degree, within obtained outcomes are not taken into account the cases that do not satisfy specific conditions of previously developed diagnosis because they are meaningless in the experience. However, overall measures of ventricles examined in previous studies[16,17] are included within generalization. So that, although not all mathematical possibilities have experimental sense, all experimental possibilities are included within those obtained mathematically.

Previously established diagnosis pointed out that ventricles with mild and moderate lesions do not exhibit mathematical features for differentiate it, showing that these classifications are based on qualitative observations. The developed generalization allows mathematically establishing the evolution state of any ventriculogram independent of these classifications. This is why the presence of increasing values of similarity degrees is associated with a greater pathological involvement, as the previous diagnosis had demonstrated,[17] showing the clinical applicability of this methodology.

This methodology simultaneously assesses and relates cardiac function and form. This requires not only measurement of ventricle in systole and diastole but a mathematical abstraction that accounts of the whole which is set by the sum of the occupancy states of ventricles in systole and diastole. By this is possible the establishment of comparisons and generalization of all measures of ventricular structure that can occur during cardiac dynamic.

Another works have been shown the relationship between morphological disturbances and the changes in cardiac behavior, such as the case of Kappenberg who developed a simulation that showed how geometry and anatomy affect cardiac electric stability.[19] Other research developed with the aim of improvement the left ventricle measures are focused on mathematical analysis and geometric projections based on notions as area, surface and volume. For calculating the ventricular volume, several methodologies have been designed. One of these allows making a right anterior oblique projection and a left anterior one, which resembles the symmetry of ventricular cavity.[20] Other uses the Simpson disks that resembling the ventricle form to an ellipsoid.[21,22] Regard to the above, a need has arisen of doing methodologies that not only calculate ventricular volume but analyze the movement of each point of ventricular contour. In this scope, a mathematical model was designed with the aim of reflexing more correctly the movement of ventricular cavity from an artificial line superposed to the same distance of ventricular border.[23,24]

Opposite to the mentioned works, based on different Euclidean measures of the ventricular geometry, the methodology proposed in this research is based on the irregularity characteristic of the object, and the way in that the relations between the parts and the whole change with regard to normality and disease. It allows obtaining an objective and reproducible methodology of clinical application that evaluates any ventricle independent of conventional classifications. Also, the generalization developed can be

applied to the future in development of computer simulations which model the geometric changes of ventricular dynamic in systole and diastole, and its evolution from normality to disease.

Following this thought form; other generalizations of experimental and clinical application had been developed. Such is the case of a law of exponential geometric character with which all possible cardiac chaotic atractors related with normality and disease estates are deduced.[25,26] Based on fractal measures of arteries in a restenosis experimental model, all possible normal and sick arterial prototypes were found.[27] Also, a generalization which establishes all possible uterine cervical cells was developed, allowing diagnosing normality and disease and mathematically clarifying the state of ASCUS cells.[28] All these methodologies are done in the context of theoretical methods of physics,[29-31] making unnecessary the using epidemiologic and statistical methods, like is stated in this work.

This work is based on a kind of acausal reasoning of the studied phenomenon, as a consequence variables such as sex, age, medical history or specific pathologies does not take into account. The application of theories based on an acausal conception of the nature as quantum mechanics,[32,33] chaos theory[34,35] and statistical mechanics[36,37] allows the establishment of mathematical orders underlying the irregularity and apparent unpredictability of phenomena.

From this scope, objective and reproducible methodologies of diagnostic support and clinical application useful for all fields of medicine have been developed, such as a diagnosis based on proportional entropy that differentiates normality, chronic and acute disease and evolution between them.[38] The predictive power of this approach was confirmed in the Coronary Unit Care.[39] From this acausal perspective, different methodologies have been developed of predictive character in immunology and molecular biology,[40] in dengue and malaria epidemics[41,42] and in cellular morphophysiology.[43,44] In infectology, methodologies for predicting CD4 T cells based on values of lymphocytes and leukocytes[45] obtained from the complete blood count (CBC) have been developed. These works, just as this investigation, highlight the significance and practicality of using physical and mathematical theories for solving various medical problems.

CONCLUSIONS

A theoretical generalization of clinical application was developed useful as a tool for diagnostic assessment of left ventriculography that unifies evaluation of ventricular structure and physiology during evolution between normality and disease.

From this methodology, there is a finite quantity of ventricular prototypes from normality to severe disease, showing that the previously developed diagnostic methodology simplifies the evaluation of ventriculogram. This constitutes an objective and reproducible method of clinical application.

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