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Arterial Pressure Fractality is Highly Dependent on Wave Reflection

Ricardo L. Armentano, *Senior Member IEEE*, Leandro J. Cymberknop, Walter Legnani, Franco M. Pessana, Damian Craiem, Sebastian Graf and Juan G. Barra

***Abstract*— Wave reflection is an important factor that influences pressure wave morphology and becomes more significant with aging, when cardiovascular risk increases. A pressure wave, measured at any location in the arterial tree, can be decomposed into its forward and backward components and depends on the corresponding amplitude and shifting time delays. Fractal dimension (FD) quantifies the time series complexity defined by its geometrical representation. Objective: The aim of this study was to evaluate the arterial pressure and diameter time series in order to assess the relationship between wave reflection and arterial pressure fractal dimension (FD). Methods: Simultaneous aortic pressure and diameter were measured in 14 conscious dogs. A pair of ultrasonic crystals, a pressure microtransducer and a pneumatic cuff occluder were positioned in the upper third of the descending aorta. Results: Total reflection induced by the occlusion maneuver decreased FD concomitant to the aortic stiffening. Conclusion: Arterial pressure fractality is highly dependent on wave reflection.**

***Key words*— Wave reflection, Fractal dimension, Arterial Blood pressure**

I. INTRODUCTION

The arterial system is the result of a complex arrangement of branched segments. In this sense, it cannot be reduced to a single tube. Consequently, the non-uniform elastic properties as well as the distributed natures of the terminations play an important contributory role [1]. Arterial vascular beds can be characterized either by determination of a global parameter or by considering the arterial segments in terms of their physical properties. One of the main features of arterial beds is the tree-like structure [2]. Accordingly, the term “arterial tree” refers to the branching structure from a main conduit artery up to the capillary beds, without including the latter. These and other trees in the arterial circulation have an open structure based on repeated bifurcations, following *fractal* rules [3]. A fractal time series behaves similarly at different degrees of magnification (observation scales), which may be deterministic or stochastic. In geometric terms, a fractal signal cannot be described or quantified by usual Euclidean measures, owing to its high irregularity [4]. Additionally, arterial wave reflection is recognized as an important phenomenon affecting pressure and flow contour from the ejecting ventricle [5]. Concerning the above, a time series complexity can be quantified in terms of its fractal characteristic. Part of the complexity arises from the basic structure of the cardiovascular system. The heart and the vasculature contain structures, which have a fractal-like appearance. The basic pattern of blood distribution is fractal, and this is imposed both by the anatomy of the vascular tree and by the local regulation of vascular tone [6]. In previous studies, a wavelet transform based technique was applied to arterial blood pressure and diameter time series, in order to reveal structures or patters that cannot be observed by usual procedures. Self-similar presence was confirmed, which is a necessary condition (but not sufficient) for a signal to be considered as a fractal [7]. As a consequence of that behavior, fractal dimension (FD) estimation was adopted, in order to quantify the loss of waveform complexity in blood pressure time series under pathological conditions [8]. In addition, these previous works suggested that stiffening is associated with a decrease in the fractal nature of the aortic pressure, but the mechanism remains unrevealed. Even more, FD can be seen as a measure of irregularity, roughness and variation [9].

To our knowledge, the effect of wave reflection on arterial pressure fractality has not been previously reported. The goal of the present work was to analyze the fractal complexity of the arterial pressure wave in basal state and during total occlusion, where multiple branching reflections are avoided.

II. MATERIAL AND METHOD

A. Experiments

Data of previous protocols performed in 14 male mongrel dogs (4.9±1.9 years, 22.2±2.9 kg) were recompiled to this study [10, 11]. In all cases, anesthesia was induced with intravenous thiopental sodium (20 mg/kg) and, after intubation, maintained with 2% enflurane carried in pure oxygen (4 L/min) through a Bain tube connected to a Bird Mark VIII respirator. Under sterile conditions, a left thoracotomy was made at the fifth intercostal space. A pressure microtransducer (Konigsberg P7, 1200 Hz frequency response) and a fluid-filled polyvinyl chloride catheter (2.8 mm OD, for later calibration of the microtransducer) were implanted in the descending thoracic aorta through a little incision in the left brachial artery. A pair of ultrasonic crystals (5 MHz, 4-mm diameter) was

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R. L. Armentano, L. Cymberknop, W. Legnani and F. M. Pessana are from Buenos Aires Regional Faculty, National Technological University, Medrano 951, (C1179AAQ), Ciudad Autónoma de Buenos Aires, Argentina (e-mail: lcymber@ieee.org).

R. L. Armentano, F. M. Pessana, , D. Craiem, S Graf and J. G. Barra are from Faculty of Engineering and Exact and Natural Sciences, Favaloro University, Buenos Aires, Argentina (e-mail: armen@ieee.org)

sutured on the adventitia of the aorta, after minimal dissection, to measure external aortic diameter. The transit time of the ultrasonic signal (1580 m/s) was converted into distance using a sonomicrometer (Triton Technology Inc.) and observed on the screen of an oscilloscope (Tektronix 465B) to confirm optimal signal quality. A pneumatic cuff occluder made from silicon rubber was implanted around the descending thoracic aorta, proximally to the pressure transducer and the ultrasonic crystals, at a distance of 150 mm from the left ventricle. Aortic arc bifurcations (carotid, subclavian and brachiocephalic trunk arteries) were not subjected to occlusive maneuvers. Before repairing the thoracotomy, all cables and catheters were tunneled subcutaneously to emerge at the intercapsular space.

At least one week after surgery, the aortic pressure was registered using the pressure microtransducer, which had been calibrated against a Statham P23-D transducer connected to the aortic fluid-filled catheter. The zero reference point was set at the level of the right atrium. The Statham transducer had been previously calibrated using a mercury manometer. The external aortic diameter signal was calibrated in millimeters using the 1-mm step calibration facility of the sonomicrometer. Aortic pressure and diameter signals were digitized every 4 ms on a computer using an analog to digital converter (National Instruments Lab PC) and digitally stored for later analysis. Instantaneous pressure-diameter loops were displayed on-line on the computer monitor. The acquisition started with approximately 20 consecutive beats in basal state (baseline state) and then the pneumatic occluder was inflated in order to obtain a total wave reflection (total occlusion state) [10, 11]. The instantaneous pressure-diameter loops were monitored and registered until stabilization was evidenced. After completion of the protocols, animals were euthanized with an intravenous overdose of thiopental sodium followed by potassium chloride; the correct position of the ultrasonic crystals was confirmed at necropsy in all cases.

All protocols were approved by the Research and Development Council of the Favaloro University, and the study was conducted in accordance with the Guide for the Care and Use of Laboratory Animals published by the United States National Research Council (National Academy Press, Washington, DC, 1996).

B. Fractal Dimension. Higuchi's method

Fractal dimension quantifies how densely a metric space is occupied by the fractal set [12]. Moreover, FD determines the time series complexity measure defined by its geometrical representation [13]. From a theoretical point of view, a fractal can be defined as an affine self-similar set, whose Hausdorff dimension (a measure of the space "filled" by the set at its point's neighborhood) is strictly larger than its topological dimension [14]. Considering a time series of one time dependent variable, its FD value is included in the interval [1,2]. While the Hausdorff dimension is the most relevant measure, on a practical level, Box counting (BCD) or Correlation dimensions (CD) are implemented more frequently [15]. The former has been selected for FD analysis, during the present study.

Assessment of FD in this study was performed by applying the method proposed by Higuchi [16]. A number of subsets based on the original temporal series (*x(t)*, of length *N*) are generated, considering an initial time value (*m*) and a temporal increment (*k*) as parameters, as follows:

$$x_k^m = \left\{ x(m); x(m+k); x(m+2k), .., x\left(m + \left[\frac{N-m}{k} \right] k \right) \right\} \qquad (1)$$

The term [(*N-m)/k*] in (1) denotes the maximal time interval (Gauss notation) that can be considered for a selected *m* value. For each experimental time series, an averaged length is calculated ($L_m(k)$), as can be observed in the following expression:

$$L_m(k) = \frac{\sum_{i=1}^{\left[\frac{N-m}{k}\right]} \left| x(m+ik) - x(m+(i-1)k \right| \frac{N-1}{\left(\frac{N-m}{k}\right)k}}{k} \qquad (2)$$

Then, the time series length function for each time increment (*L(k)*) is assessed, according to the expression:

$$L(k) = \frac{\sum_{m=1}^{k} L_m(k)}{m} \qquad (3)$$

Finally, if $L(k) \propto k^{-FD}$ is found, the time series morphology may be quantified by its FD value. The latter can be obtained by applying a linear regression method to a doubly logarithmic scale representation of *L(k)* against *1/k*. In addition, maximal value of time interval *k* (k_{max}) should be emphasized, especially if adequate accuracy is required in the FD estimation process.

Higuchi proposed a method that may be applied to any kind of time series, stationary or not. However, the obtained value lacks of information related to the system involved (deterministic, chaotic or stochastic), which is responsible for the signal being analyzed. In consequence, the method should be applied in the evaluation of variations that have occurred in the same signal (before and after significant events or different physiological states, such as those considered for this procedure) [15]. During the present study, arterial pressure time intervals acquired at a sampling rate of 250 Hz were processed by means of Higuchi's method. A value of 16 was adopted for k_{max} and was estimated by applying linear regression analysis to consecutive groups of 5 points, belonging to the doubly logarithmic graph, which remained within an error band of 5% maximum variation.

C. Signal Processing algorithms development

Signal processing algorithms were developed on MatLab platform (MathWorks INC, Massachusetts, USA) through the design and implementation of a graphic user interface (GUI). Prior to the non-linear processing, existing trends were eliminated (i.e. respiration induced fluctuations, electrical artifacts, etc.) by means of digital filtering. The latter involves the use of the de-noising method, which is implemented through the application of the wavelet transform. For this study, soft thresholding was applied based on a mixture of Stein's Unbiased Estimate of Risk and minimax rules [17].

In order to characterize non-stationary events, Higuchi's method was applied to short segments of the time series (2 beats interval). A maximal window length was selected in order to ensure, simultaneously, maximal number of samples as well as a stationary behavior of the time interval (moving window method) [15].

D. Statistical analysis

Data were expressed as mean values ± standard deviation (SD). The presence of significant differences between baseline state and total occlusion state was assessed using a paired Student's t-test. For all statistical analyses, $P<0.05$ was adopted as statistically different.

E. Aortic Stiffness Assessment

Changes in aortic wall stiffness were estimated assuming that the arterial wall is an isotropic homogeneous elastic material. Consequently, a linear elastic theory was applied, as follows:

$$E = \frac{dP}{d\varepsilon} \tag{4}$$

where E is the pressure-strain elastic modulus [18], P corresponds to the measured aortic pressure and ε is the aortic strain. The variation of ε was obtained by referring the dynamic diameter to its non-stressed value. A biphasic model was adjusted, assuming two linear regions with different elastic modulus. According to this, low pressure slope is related to the elastin elastic response while the high pressure slope indicates the recruitment of collagen fibers. Both behaviors were quantified by means of linear regression analysis.

F. Aortic Wave Separation

Wave separation was performed according to the method proposed by [19]. Arterial pressure waveform was measured before and after the occlusion, so that the forward and backward pressure waves would be equal. Under occlusion state, forward pressure was estimated as half of the measured pressure. Then, at baseline state, backward pressure was obtained from the difference between measured pressure and the previously calculated forward pressure.

III. Results

Aortic pressure and diameter measured signals may be observed in Figure 1, both at baseline state (first three beats) as well as at total occlusion state (last two beats). Forward and backward waveform separation analysis is shown in Figure 2, at baseline state, in a representative dog.

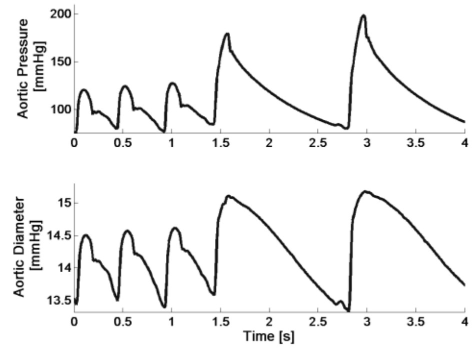

Fig. 1. Higher Panel: *In-vivo* measured aortic arterial pressure. **Lower Panel:** *In-vivo* measured aortic arterial diameter.

FD values continuous variation, during the whole procedure, are visualized in Figure 3. A significant decrease in aortic pressure waveform complexity (pointed out by a FD diminution) is observed during the occlusion interval.

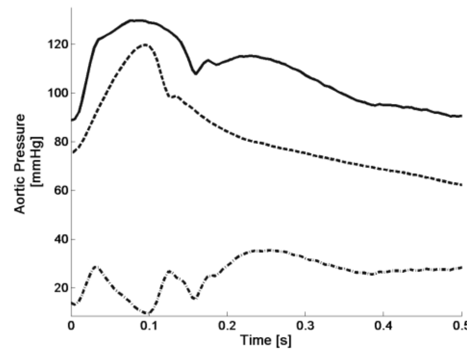

Fig. 2. Aortic pressure wave separation, baseline state. **Solid line**: Measured aortic pressure. **Dashed line**: Obtained forward traveling component. **Dashed pointed line:** Obtained backward traveling component.

FD values obtained by applying Higuchi's method, both under baseline and after the occlusion maneuver, are detailed in Table I. Corresponding values of aortic stiffness are also included.

TABLE I
AORTIC PRESSURE FRACTAL DIMENSION (FD) AND PRESSURE-STRAIN ELASTIC MODULUS (E) VALUES CORRESPONDING TO BASAL AND OCCLUSION STATES.

Parameter	Basal State	Occlusion State
Aortic E [10^6dyn/cm^2]	0.70±0.17	1.79±0.85*
Aortic pressure FD	1.07±0.02	1.02±0.01*

*$P<0.05$ was considered as significant different. Values are expressed as mean ± standard deviation

IV. Discussion

The purpose of the present study was to assess the effect of multiple branching reflections on arterial pressure fractal complexity. FD was applied, as a non-linear measure, in order to quantify arterial pressure complexity (or roughness). To this end, Higuchi's method was implemented, which is widely utilized in non-linear signal processing literature.

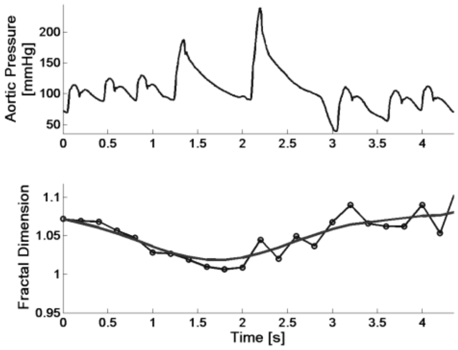

Fig. 3. Higher Panel: Aortic pressure variation, during the occlusion maneuver**. Lower Panel**: Aortic pressure fractal dimension variation, corresponding to the same interval.

Arterial wall stiffness was evaluated using the first derivative of the pressure-strain relationship. During the total reflection state, and neglecting the distance between the pressure measurement and the occlusion site, the reflected wave was considered equal to the incident wave. As a result, measured aortic pressure was treated as the composition of two incident waves. Consequently, backward waves corresponding to baseline state were calculated independently of flow time series waveform (Figure 2). Total reflection induced by pneumatic occluder decreased FD concomitant to the aortic stiffening (Figure 3). Under occlusion state, obtained aortic pressure FD values should be coincident to those calculated from forward pressure, since the latter corresponds to half the measured pressure (Newman's method). Consequently, it may be inferred that the higher FD values assessed in baseline state are the result of the presence of reflected waves. Therefore, this behavior suggests that under total reflection (only carotid, subclavian and brachiocephalic branches remained without being occluded) aortic blood pressure *unwrinkling* (pulsatility increase in conjunction with a loss of roughness) is the consequence of the absence of the fractal nature, induced by the multiple branching of the arterial tree. It is noteworthy that FD analysis was performed over short time intervals, no longer than two heartbeats. This consideration allowed the insolation of the intrinsic mechanical response, preventing the contribution of reflex regulation mechanisms (which take place around the fifth heartbeat after occlusion) whose intervention might contaminate the waveform structure. Additionally, the heart rate decrease, induced during the occlusion maneuver, constituted another intriguing result. Considering that the development of the phenomenon occurred in less than a time constant of the system, the observation clearly deserves further investigation. Moreover, it is well known that physiological process originate complex, anisotropic fluctuations, which cannot be processed properly by usual measures. In this sense, fractal based techniques provide a *nature based* approach, in order to identify the presence of multi-scale interactions [6]. The present results suggest an evident trend between arterial wall reflection and the morphology of the acquired pressure time series. In previous studies [7, 8] it was demonstrated that loss of fractal complexity was related to an increase of arterial stiffness. In this study, the influence of wave reflection from the descending thoracic aorta and its posterior successive bifurcations (the upper vascular bed was not interrupted) was also evaluated. What remains to be investigated, is if arterial stiffness can be considered as a factor in FD diminution or may be induced by the presence of reflected waves.

In conclusion, arterial pressure fractality is highly dependent on wave reflection. Further studies will be needed in order to demonstrate the role of arterial stiffness itself and its relation to wave reflection in the loss of arterial pressure fractal complexity.

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