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Energy Dissipation in the Arterial Wall Analyzed by Allometric Relationships*

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Abstract— **INTRODUCTION: Allometry describes the disproportionate changes in shape, size or function that are observed when comparing separate isolated features in animals spanning a range of body sizes. Scaling of the energy dissipation has been also observed in warm blooded animals, essentially varying as mammal's body mass (BM). Part of the energy stored in the arterial wall during elastic distension corresponding to the viscous deformation is dissipated within the arterial wall. OBJECTIVE: To elucidate the allometric existing relationship between BM and arterial wall viscosity, as a measure of energy dissipation. MATERIAL AND METHODS: Arterial viscous dissipation (W_{VD}) was assessed in dogs, sheep, and humans in terms of BM and heart rate (*HR*) variations. RESULTS: An allometric law was found between W_{VD} and *BM*, jointly with the assessment of W_{VD} in terms of *HR*. CONCLUSION. The existence of a power-law link for viscous dissipation and BM that involve different mammals was demonstrated.**

I. Introduction

Mammals have in common a great number of structural, biochemical and physiological features. Nevertheless, despite these similarities, rarely are primary functions among mammal's linear extrapolations of body size [1]. Allometry (literally 'different measure') describes the disproportionate changes in shape, size or function that are observed when comparing separate isolated features in animals spanning a range of body sizes [2]. Indeed, living beings self-regulate to persist, so the importance of allometric relationships´ lies in the fact that self-regulation processes structurally depend on the size of organisms in terms of length, volume, body mass (***BM***) and contact surface with the medium [3]. This condition implies the development of theoretical 'scaling laws' to describe the multiple interrelationships of life in any of its manifestations, from considerations of the basic physical and mechanical processes involved [1].

Previous studies have demonstrated that parameters like heart mass, total blood volume, cardiac output or the capillary volume of the respiratory system of mammals vary directly with ***BM***. [1]. The arterial decay time over cardiac cycle duration was shown to be 'similarly related' to animal size in [4] and wavelengths associated with the pressure pulses in the aorta during heart beats were shown to be proportional to aortic length (and ***BM***) [5]. Furthermore, the energy expenditure of the heart (the external mechanical work, computed from the product of the mean arterial pressure and stroke volume) presents an allometric relation. Basically, a larger ventricle will generate a greater amount of energy simply because of its larger heart size [6]. On the other hand, there are hemodynamic parameters that are invariant to ***BM***, such as blood pressure and arterial stiffness [7].

Biological tissues in general are not purely elastic, that is, they exhibit a marked viscous behavior [8, 9]. The elastic behavior of the arteries is due to the presence of elastin and collagen, while the vascular smooth muscle (***VSM***) has both elastic and viscous properties. While part of the energy stored in the arterial wall during elastic distension is completely restored, the remaining part of the energy corresponding to the viscous deformation is dissipated within its structure [10]. ***VSM*** cells behave as intelligent viscous shock absorbers, which exert a protective effect against the stretching of the arterial wall at high frequencies, adjusting the dissipation of energy to protect the parietal fibers from mechanical stress [11].

Considering the aforementioned, scaling of the energy dissipation has been also observed in warm blooded animals, where the rates heat production and oxygen and caloric consumption vary essentially as mammal's ***BM*** [1], [3]. Consequently, this condition leads to hypothesize that the dissipated energy within the arterial wall could also manifest an allometric relation.

To our knowledge, energy dissipation that takes place in the arterial wall has not been evaluated in terms of an allometric approach. Hence, this study aims to elucidate the existing relationship between a macroscopic dimension, such as ***BM***, and one of the three main mechanical properties of large arteries, arterial wall viscosity (***AWV***), as a measure of *energy dissipation*, expressed in terms of a power law.

II. Materials and Methods

Arterial wall behavior can be evaluated by studying the variation of the intra-luminal diameter (***D***) as a result of the intra-arterial pressure (***P***) exerted during the heartbeat. In time terms, there is a mismatch between pressure and distension due to viscosity. Such condition can be clearly observed when ***P*** and ***D*** variations are plotted against each other, and a hysteresis cycle known as '***P-D*** loop' is generated. The elastic component of the arterial wall can be identified in the dynamics of the ***P-D*** curve (both in the systolic and diastolic

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phases) while the viscous component is represented in the area enclosed by the cycle [10].

A. Measurement Protocol in Humans

The variations of ***P*** and ***D*** were studied in the carotid (neck) arteries of 11 normotensive male subjects (***NT*** Group) and 10 ambulatory male patients with essential hypertension (***HT*** Group), documented in classic laboratory tests and without treatment for a month. Additionally, a group of 5 hypertensive individuals between 38 and 64 years old who, concomitantly, had elevated values of cholesterol (total cholesterol ≥ 6.85 mmol/l), was studied (***HCHT*** Group). None of them had a history of heart, neurological or renal disease, or peripheral arterial disease in the limbs. The subjects were examined in a temperature-controlled room at 20 ± 1 ° C in a leaning position. After a 10-minute rest, brachial artery pressure was measured by means of a sphygmomanometric procedure, as the average of three consecutive measurements. Carotid wall displacements were then acquired with an echotracking device, that used pulsed Doppler ultrasound. An electrocardiogram trigger made it possible to detect the maximum arterial distention in relation to its initial diameter. The radiofrequency signal obtained, was digitalized and stored for subsequent processing. Finally, the instantaneous arterial diameter waveform was obtained as the difference between the far and near wall displacements every 3ms. In turn, the arterial pressure wave was registered at the same site of the distension. The noninvasive method of pressure wave measurement was based on the principle of applanation tonometry [12].

B. Measurement Protocol in Animals

In order to carry out the study in animals, the in vivo evaluation protocol included 11 mongrel male dogs aged 4.9 ± 1.9 years (Dog Group), weighing 22.2 ± 2.9 kg and 5 Merino sheep (Sheep Group, 26 ± 4.5 kg). Anaesthesia was induced with intravenous thiopental sodium (20 mg / kg) and then, a sterile thoracotomy was performed at the left fifth intercostal space [10]. A pressure microtransducer (Konigsberg 7, frequency response of 1200 Hz) was implanted and a polyvinyl chloride catheter full of liquid was inserted (external diameter, 2.8 mm, for the subsequent calibration of the microtransducer) in the descending thoracic aorta. A pair of ultrasonic crystals (5 MHz, 4 mm diameter) were stitched to the aortic adventitia, after a minimal dissection, in order to measure the external aortic diameter. The transit time of the ultrasonic signal (1580 m/s) was converted to distance using a sonometer (Triton Technology Inc, frequency response of 100 Hz), in order to determine the distance between the crystals. Two silicone rubber hydraulic cuff occluders were implanted around the descending thoracic aorta and the inferior vena cava, to carry out the analysis at high pressures (***HP***) by means of aortic maneuvers. Finally, before repairing the thoracotomy, all the wires and catheters were tunneled subcutaneously and pulled out in the interscapular space and all the animals were allowed to recover under veterinary care. This methodology made it possible to obtain accurate and reproducible ***P*** and ***D*** measurements, essentially due to the high frequency and linearity response of the sensors used [10].

C. Arterial Wall Viscous Response and Dissipated Energy Asesssment

As was previously mentioned, the clockwise rotation of the ***P-D*** loop (Fig. 1, solid line) encloses an area of 'hysteresis' (the combined effects of elasticity and viscosity determine a delay between arterial pressure and diameter time series) that represents the viscous response of the arterial wall dynamics. The parietal viscous modulus (η) was obtained according to an iterative procedure of hysteresis elimination, based on a model that considers that the pressure exerted on the wall is distributed in a representative element of elasticity (spring) and another of viscosity (cushion) (Fig. 1, dotted line) [10].

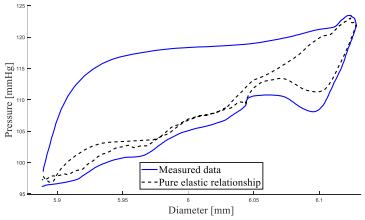

FIGURE 1. PRESSURE (P) AND DIAMETER (D) INTERACTION DELIMITS A CONTINUOUS HYSTERESIS LOOP (SOLID LINE). AFTER AN ITERATIVE PROCEDURE, HYSTERESIS CAN BE ELIMINATED (DOTTED LINE) ALLOWING THE ASSESSMENT OF THE VISCOUS PROPERTY OF THE ARTERIAL WALL

Subsequently, arterial viscous energy dissipation (W_{VD}) was calculated as follows, in terms of the obtained viscosity modulus, mean arterial diameter (D_m) and the angular pulsatility ($\omega = 2\pi HR$) [13]:

$$W_{VD} = \eta\omega\frac{D_m}{2} \tag{1}$$

D. Existing Dependences between Viscosity Index, Heart Rate and Body Mass

In animal physiology, allometry is usually expressed in the form of power-law equations relating some variable of structure or function (***Y***) as a dependent function of ***BM*** in the form:

$$Y = b \cdot BM^{\alpha} \tag{2}$$

where α (allometry coefficient) and ***b*** are both constants. The exponent α constitutes the slope of the regression line when this equation is plotted on log-log coordinates [2]:

$$\log(Y) = \log(b) + \alpha\log(BM) \tag{3}$$

If $\alpha = 0$ the physical variable is invariant of ***BM***, and when $0<\alpha<1$ there exists a geometric scaling of body length (close to 1/3) or body surface area (close to 2/3). The allometry coefficient can also be positive or negative [6]. Basically, two allometric relationships were assessed using Eq. 2 and linear regression analysis on the log-log plot: η vs ***BM*** and W_{VD} vs ***BM***. Subsequently, in order to obtain an integrated picture of the circulatory phenomenon, the already known existing allometric relationship between heart rate (***HR***) and ***BM*** was included. The analysis was then completed by the construction of a '3D graph', where the assessment of the

relationship between ***HR*** and W_{VD} (or η) arises as a natural consequence of the combination of ***HR*** vs ***BM*** and W_{VD} vs ***BM*** (a ***HR*** condition, related to a ***BM*** value, can be directly linked to a W_{VD} state).

III. Results

Table I shows the values of the hemodynamic variables and the viscoelastic properties of the different studied groups, also considering the maneuvers performed on animals. Obtained carotid artery measurements of humans are detailed in ***NT***, ***HT*** and ***HCHT*** conditions. Dogs aortic measurements at rest and ***HP*** are also included, as well as aortic measurements on sheep. The ***HR*** of studied animals was similar and higher than that of humans, showing a clear dependence on ***BM***. With regard to D_m values, sheep showed higher values than dogs in the aortic artery. In relation to the viscous properties, the arteries analyzed in humans had considerably higher values than those analyzed in animals ($p<0.05$). Viscosity values resulted to be similar between dog and sheep groups (***NS***), being slightly lower during ***HP*** maneuvers. On the other hand, when values of non-pathological humans with those with ***HT*** and ***HCHT*** are compared, an increase of η is observed in those with pathologies, being higher in ***HT*** than in ***HCHT*** with respect to ***NT*** ($p<0.05$)

In Fig. 2 (left), the 3D graph can be visualized, based on the obtained allometric relationships. Log-log regressions are presented in terms of the considered groups, constituted by dogs, sheep and humans (mean values are only shown). The obtained exponents were all different from zero ($p<0.05$, $n=66$). A direct log-log relationship was found between W_{DV} and ***BM*** (α=0.86, b=0.34 with r=0.87), showing a similar behavior (as was hypothesized) of that manifested by dissipation energy and ***BM*** in mammals. Similarly, the already known allometric law between ***HR*** and ***BM*** was obtained (α=-0.44, b=463 with r=0.97. Finally, W_{DV} showed an inverse relationship with ***HR*** (α=-1.74, b=21469 with r=0.77) and, by definition, this relationship was also present in η vs ***HR*** (α=-4.71, b=24.4×10^{10} with r=-0.82). Effectively, the combined 3D graph indicates that as ***BM*** increases; ***HR*** decreases and, simultaneously, W_{VD} increases. Therefore, an inverse relationship of W_{VD} (and the viscous modulus η) vs ***HR*** inevitably takes place, which was also confirmed by the experimental results (Fig. 2, right).

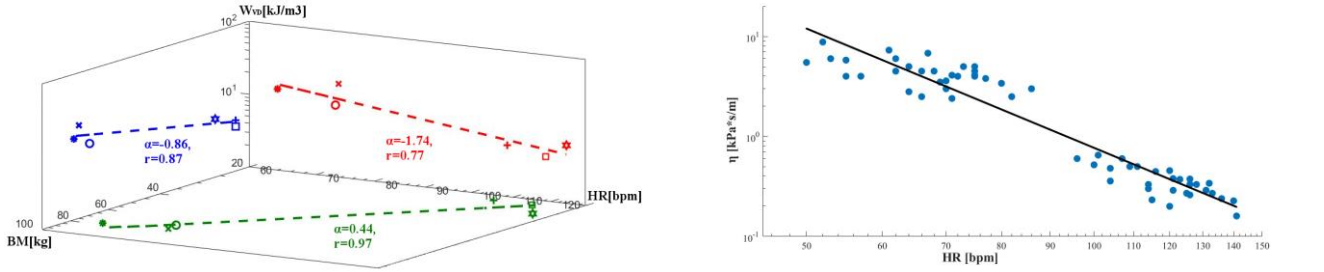

Figure 2. Left panel: a 3D graph shows the simultaneous interaction of allometric power laws (log-log regression): Dissipated viscous energy vs body mass and heart rate vs body mass. As a result, dissipated viscous energy variations in terms of heart rate is be also visualized. α constitutes the allometry coefficient. Mean values for dogs (squares, plus sign), sheep (stars) and humans (circles, asterisks and crosses) are expressed. Right panel: decrease of arterial wall viscosity (η) in terms of heart rate (α=-4.7, $b=24.4\times10^{10}$ with r=0.82), from the entire population of dogs, sheep and humans

TABLE I. Hemodynamic variables and viscoelastic properties for dogs, sheep and men. Values expressed as mean value ± SD. CA: Carotid artery; Ao: Aorta. η: arterial wall viscous property. W_{VD}: viscous energy dissipation. HP: High Pressure maneuver. NT: normotensive; HT: hypertensive; HCHT: hypercholesterolemic hypertensive.

Species	Mean Pressure	Mean Diameter	Heart Rate	Body Mass	η	W_{VD}	n=66
	[kPa]	*[10^{-3}m]*	*[bpm]*	*[kg]*	*[kPa·s/m]*	*[kJ/m^3]*	
Dog Group (Ao) Rest	13.6±0.8	15.9±1.0	108.5±17.0	22.2±2.9	56.2±15.5	5.0±0.9	11
Dog Group (Ao) HP	14.4±0.8	16.3±1.6	118.6±15.5	22.2±2.9	41.7±11.78	4.2 ±0.8	11
Sheep Group (Ao) Rest	13.5±0.7	20.4±0.2	124.4±13.4	26.0±4.5	48.4±21.6	6.2±1.9	5
Subjects NT Group (CA)	12.7±0.8	5.8±0.5	73.2±6.9	69.0±6.0	435.3±158.4	9.6±3.2	11
Subjects HT Group (CA)	16.7±0.5	7.0±0.6	73.7±11.6	75.0±9.0	786.4±243.6	18.9±3.8	16
Subjects HCHT Group (CA)	16.8±1.2	6.9±0.9	64.1±8.3	76.5±10.3	610.7±214.3	13.0±3.4	12

IV. Discussion

Much of the observed allometry in mammalian species can be explained by what seem to be scaling laws. When a physiologic parameter is regressed against ***BM***, the resultant log-log relationship demonstrates its variation as BM^{α} [2] It has been also demonstrated that power laws represented by exponents of fractional value (generally lower than 1) can be applied to the variations of aortic radius (α~3/8), aortic length (α~1/2), ***HR*** (α~-1/4), rate of oxygen uptake (α~3/4) and cardiac output (α~3/4), among others. The heart mass, the ventricles and total blood volume additionally manifest a scaling behavior in terms of ***BM*** [1]. Particularly, an allometric

relationship can be found when energy dissipation of mammals (in Watts) is evaluated in terms of mass, with allometric exponent of α~2/3, being able to reach a value of α~3/4 [3]. Taking the latter into consideration, an *in-vivo* assessment of ***AWV*** (η) and W_{VD} through different species was carried out, based on the hypothesis that the viscous property of the arterial wall could follow an allometric behavior in terms of energy dissipation. Effectively, the obtained results showed an increase of both W_{VD} and η as weight increases, represented by their corresponding power laws.

In order to develop an integrative approach that could include the circulatory aspects, the allometric relationship between ***HR*** and ***BM*** was incorporated into the study [1]. It is well-known that biological rates, such as cardiac and respiratory rates, among others, are consistently and proportionately higher in the smallest mammals, and scale with ***BM*** exponents of nearly α=-1/4 [2]. In this study, the obtained ***HR*** vs ***BM*** power law was of α=-0.44, which resulted to be higher than the expected value. However, only dogs, sheep and humans (a portion of the entire animal range) were considered for the coefficient assessment. Subsequently, a 3D graph was constructed, based on the combination of the two allometric interactions previously described (***HR*** vs ***BM*** and W_{VD} vs ***BM***). The simultaneous analysis gave rise to a third existing relationship, represented by W_{VD} vs ***HR***, which was also experimentally verified in our findings. The viscous component η and the corresponding W_{VD} were evaluated in terms of ***HR*** variations, where an inverse relationship was found, with α=-4.71 and α=-1.74 respectively. In this sense, as frequency increases, ***AWV*** decreases.

The arterial system has a self-similar geometric distribution; defined as arborescent structures whose branching levels differ in size, but not in shape. This morphological condition makes it possible to approach the problem based on the physiological invariants and the geometry of the distribution networks [3]. Consequently, since ***HR*** vs ***BM*** and W_{VD} vs ***BM*** allometric power laws coexist in arterial system, they can be simultaneously evaluated. As can be observed in the 3D graph, the W_{VD} variation in terms of ***HR*** is directly determined by the composition of both relationships, being inverse and linear in logarithmic axes. A similar behavior is observed when the viscous property η vs ***HR*** variations is evaluated. This condition resembles the behavior of thixotropic materials (those where viscosity decreases with increasing agitation, such as gelatins, honeys and some sauces) which has been extensively demonstrated in previous publications of our group [10]. The latter comprises both in vivo and in vitro experiments, in different animals, while human studies have been incorporated in the present work. More deeply, if the viscosity of the vascular-smooth muscle (hysteresis in the ***P-D*** loop) declines non-linearly with increases in excitation, then we can safely postulate an essential relation dissipation-viscosity. This behavior is represented in the dynamical mechanical property known as 'loss modulus', obtained when η is multiplied by ω. The loss modulus allows to quantify the dissipation of energy lost in the form of heat in each cardiac cycle. The loss modulus remains as an almost constant function, due to wall viscosity varies inversely when frequency increases [10]. Accordingly, ***AWV*** varies both in physiological and pathological ranges. Since hypertension causes ***VSM*** hyperplasia and hypertrophy [9], an increase in the viscous component of the arterial wall (and, consequently, in W_{VD}) is expected. This condition was verified in terms of η values in subject's evaluations, where ***HT*** and ***HCHT*** groups resulted to be higher than ***NT*** group. In addition, ***HCHT*** values were lower than those of ***HT***, suggesting that the presence of cholesterol could have an impact on ***AWV***. Finally, this study was focused on great arteries (mainly the aorta) based on the fact that animals were invasively instrumented. Due to impossibility to replicate that protocol in humans, the carotid artery was selected, which is extremely close to the aorta and could be noninvasively evaluated.

To conclude, it has to be noted that the few amount of species that was included in this study together with the conditions considered are likely to alter the value of the obtained allometric coefficients, particularly in those with similar weights. Nevertheless, it has been demonstrated the existence of a power-law link for viscous dissipation and ***BM*** that involve dogs, sheep, and humans.

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