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Gender-related differences in the excess pressure component of central aortic pressure waveform of healthy young

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Abstract—**Gender-related difference in cardiovascular diseases is one of the most investigated and still unsolved issues. Finding an explanation to this topic might have important implications for the understanding of the differences between men and women in diseases and possibly lead to the development of gender-specific strategies for its management. Recent studies have proposed that the capacitive or reservoir function of the aorta and large elastic arteries plays a major role in determining the pulse wave morphology. The pressure waveform can be explained in terms of a reservoir pressure related to arterial compliance and an "excess" or wave-related pressure associated with traveling waves. Gender-differences in the ascending aorta pressure waveform reservoir and excess components are to be characterized. The aim of this study was to evaluate, by means of a mathematical approach, gender-related differences in the central aortic pressure waveform components. Central aortic pressure waveform was non-invasively obtained in 22 healthy subjects (Age: 20 years old; 11 female). Males and females showed differences in the level and time to maximal excess pressure component, but no gender-related differences were found in the reservoir one.**

I. INTRODUCTION

GENDER differences in cardiovascular (CV) diseases (i.e. in incidence, severity and prognosis) are one of the most investigated and still uncompletly clarified issues. Finding an explanation to this topic might have important implications for understanding cardiovascular diseases. In addition, it could possibly lead to the development of a gender-specific prevention and/or treatment strategies, and could result in an improvement in CV disease management [1].

Recent studies have proposed that the capacitive or reservoir function of the aorta and large elastic arteries plays a major role in determining the pulse wave morphology. It is known that the pressure waveform can be explained in terms of a "reservoir" pressure (or component), related to the arterial system compliance and an "excess" or wave-related pressure associated with traveling waves, and local vascular properties [2].

In this context, the aim of this study was to evaluate potential gender-related differences in the reservoir and excess components of central aortic pressure, in order to improve the characterization of gender-associated CV properties.

II. MATERIAL AND METHOD

A. Study population and subjects groups

Twenty two asymptomatic subjects (age: 20 years old; 11 females), without known CV disease, consecutively referred for CV risk stratification in the CUiiDARTE Project, were considered. CUiiDARTE Project is a population-based national study developed in Montevideo, the capital of Uruguay. The latter, with an area of approximately 176,000 Km^2 (the second-smallest nation of South America), has a population of approximately 3.5 million, of which 1.8 million live in Montevideo and its metropolitan area. Most Uruguayans (88%) are Caucasian of European origin, descendants of immigrants (mainly Spanish, followed by Italian).

Subjects with history of CV, diabetes mellitus and/or renal failure were not included. Patients with traditional CV risk factors were also excluded. The study was approved by the Institutional Ethic Committee.

Subjects were studied in a single visit. Evaluation started after 9-12 hours overnight fast. Exercise, caffeine, alcohol, and vitamin C were avoided prior (at least 6 hours) to the examination. Height and weight were measured, and the body mass index (BMI) was calculated (Table 1).

B. Laboratory measurements

Venous blood samples were drawn and immediately processed using commercially available kits and/or laboratory methods. Total cholesterol (TC), serum triglycerides (TG), and high and low density lipoprotein cholesterol (HDL-C and LDL-C) were determined. Patients with one or more of the following conditions: TG≥200 mg/dL, TC≥240 mg/dL, HDL-C<40 mg/dL, LDL-C≥160 mg/dL and/or currently taking hypolipidemic agents, were excluded form the data analysis (Table 1).

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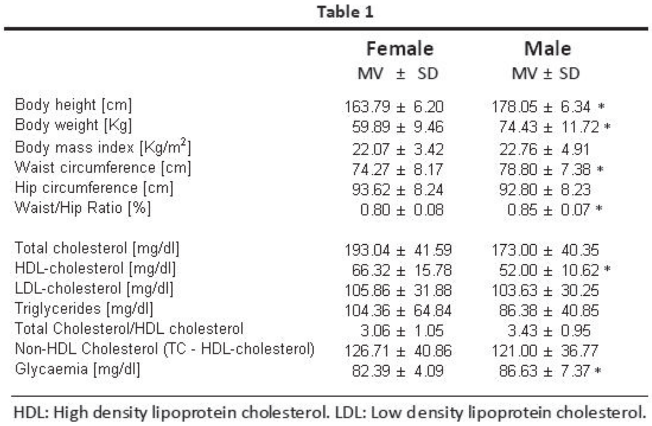

Table 1

	Female MV ± SD	Male MV ± SD
Body height [cm]	163.79 ± 6.20	178.05 ± 6.34 *
Body weight [Kg]	59.89 ± 9.46	74.43 ± 11.72 *
Body mass index [Kg/m^2]	22.07 ± 3.42	22.76 ± 4.91
Waist circumference [cm]	74.27 ± 8.17	78.80 ± 7.38 *
Hip circumference [cm]	93.62 ± 8.24	92.80 ± 8.23
Waist/Hip Ratio [%]	0.80 ± 0.08	0.85 ± 0.07 *
Total cholesterol [mg/dl]	193.04 ± 41.59	173.00 ± 40.35
HDL-cholesterol [mg/dl]	66.32 ± 15.78	52.00 ± 10.62 *
LDL-cholesterol [mg/dl]	105.86 ± 31.88	103.63 ± 30.25
Triglycerides [mg/dl]	104.36 ± 64.84	86.38 ± 40.85
Total Cholesterol/HDL cholesterol	3.06 ± 1.05	3.43 ± 0.95
Non-HDL Cholesterol (TC - HDL-cholesterol)	126.71 ± 40.86	121.00 ± 36.77
Glycaemia [mg/dl]	82.39 ± 4.09	86.63 ± 7.37 *

HDL: High density lipoprotein cholesterol. LDL: Low density lipoprotein cholesterol.

Table 1: Subjects' anthropometric and biomedical measurements. (*<0.05 with respect to Female group)

C. Central aortic pressure waveform: windkessel or reservoir and excess pressure component

Pulse wave analysis (PWA) was used to obtain the ascending aortic pressure waveform from the radial pulse (obtained by Applanation Tonometry) using customized software (SphygmoCor 7.01, AtCor Medical, Sydney, Australia) with a previously validated generalized transfer function [3]. The radial pulse wave was obtained (subject sited with the arm resting on a table) and calibrated using diastolic and mean brachial pressures (HEM-433INT Oscillometric System; Omron Healthcare Inc., Illinois, USA).

The SphygmoCor device generates an output ASCII format data matrix, consisting on a ten second snapshot of measured radial artery and the derived aortic ascending pressure signals (*P*). A set of algorithms specially developed under Matlab® platform (MATHWORKS INC, Massachusetts, USA), were used to process the data. Reservoir and Excess pressure (P_{res}, P_{exc} respectively) were calculated by applying the "only pressure known" method [4, 5] in the absence of a measured input flow (Q). A three element Windkessel model was considered, where P_{exc} consists of the difference between *P* and P_{res} and it is related to the model's characteristic impedance (z_0, a resistor considering this analysis) [Fig 1].

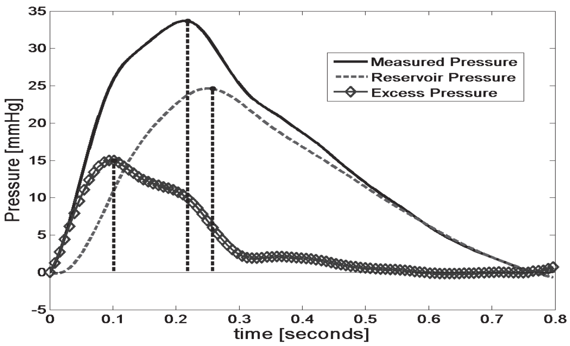

Fig. 1: Example of measured, reservoir and excess pressure (referred to its initial value). Maximal values (and time of occurrence) were calculated for the three pressures.

In consequence, P_{exc} is proportional to the flow (similar in shape). The impedance constituted by the system peripheral resistance (R) and arterial compliance (C) is related to P_{res}. Both parameters (R and C) were obtained during diastole, when the three element and the two element windkessel models behave similarly [6]. The ordinary differential equation (ODE) that governs the relationship between P_{res} and the input flow can be expressed as follows:

$$C\frac{dP_{res}(t)}{dt} = Q(t) - \frac{\left(P_{res}(t) - P_{\infty}\right)}{R} \tag{1}$$

where P_{∞} is the pressure at which the flow through the microcirculation ceases. Pressure P_{∞} is larger than zero, closer to the diastolic pressure than the venous pressure [5]. Since P_{exc} is proportional to the input flow, the Q parameter in equation (1) can be substituted by the expression *aC(P-P_{res})*, where *a* is a constant value [5]. Therefore, reservoir pressure may be obtained by finding the solution of the resulting ODE:

$$\frac{d\left(P_{res} - P_{\infty}\right)}{dt} + \left(a + \frac{1}{\tau}\right)\left(P_{res} - P_{\infty}\right) = a\left[P(t) - P_{\infty}\right] \tag{2}$$

in which τ is the time constant of the two element windkessel model (product between R and C). Time constant (τ) and P_{∞} were obtained by fitting the last third of the diastolic period [7] to an exponential decay [8]:

$$P_{dia}(t) - P_{\infty} = (P_0 - P_{\infty})e^{-\frac{t}{\tau}} \tag{3}$$

where P_{dia} is the measured pressure during last third of diastolic period whereas P_0 is the initial measured value of the time interval. The *a* component was determined by finding (iteratively) the value that minimizes the square difference between the estimated decay during P_{dia} and P_{res} expression, obtained by solving equation (2). The diastolic period beginning was assessed by finding the time at which dP/dt reaches a minimum. This point correlates better with the time the aortic valve closes [8]. Once *a* was found the resulting P_{res} was used to calculate P_{exc}, as mentioned:

$$P_{exc}(t) = P(t) - P_{res}(t) \tag{4}$$

Maximal *P*, P_{res} and P_{exc} values as well as the integral over the cardiac period (mean value) were calculated.

D. Statistical analysis

Baseline characteristics are provided as mean ± SD. Groups (Female vs. Male) were compared using a Student T Test (unpaired, two tails). A $p<0.05$ value was considered statistically significant.

III. RESULTS

Males showed higher central aortic systolic and pulse pressure levels than females [Fig 2]. Non significant differences in heart rate were found.

During the measured aortic pressure analysis, no gender-related differences were found in the reservoir or windkessel component [Fig 3]. On the other hand, the excess component of the aortic pressure showed a higher value in males (*<0.05) [Fig 4, Fig 5].

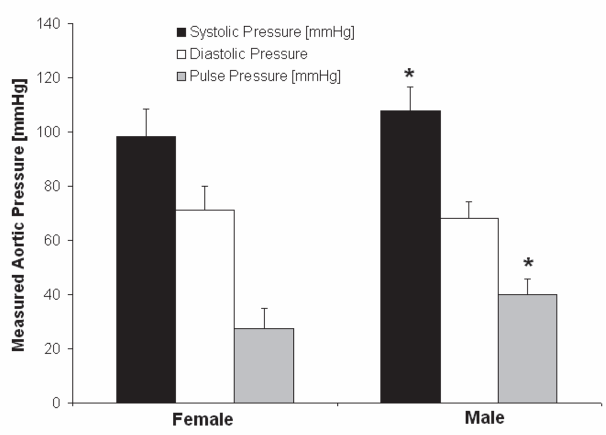

Fig. 2: Measured pressure levels (*<0.05 with respect to Female group).

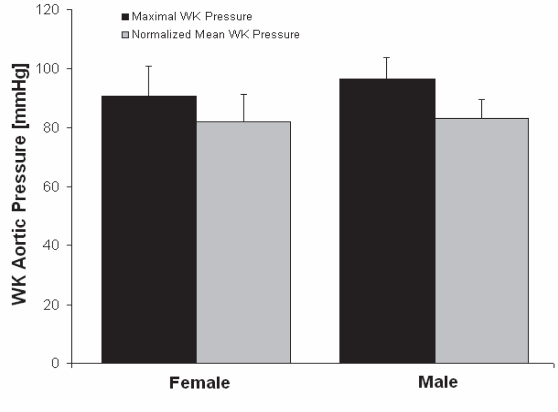

Fig. 3: Reservoir or windkessel (WK) components of the measured pressure.

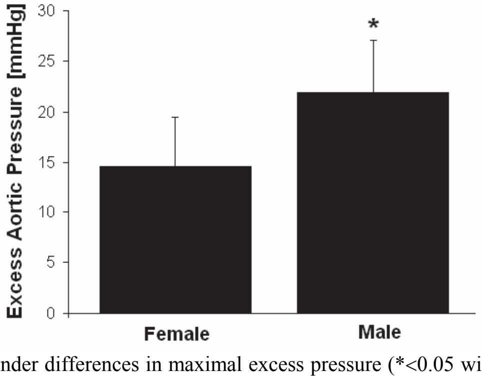

Fig. 4: Gender differences in maximal excess pressure (*<0.05 with respect to Female group)

Males and females showed significant differences in the time to the excess pressure maximal level, but no to the maximal reservoir pressure (*<0.05) [Fig. 6].

IV. DISCUSSION

In the present study, a recently proposed "wave reservoir" model was implemented, in order to analyze the central aortic pressure waveform components in humans, and to identify existing gender-related differences.

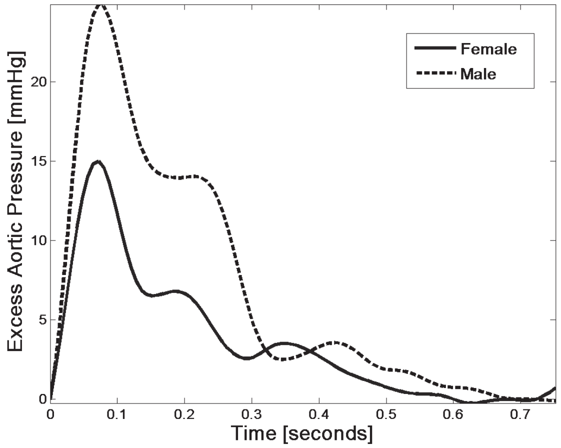

Fig. 5: Gender differences in the excess pressure waveform, for typical cases.

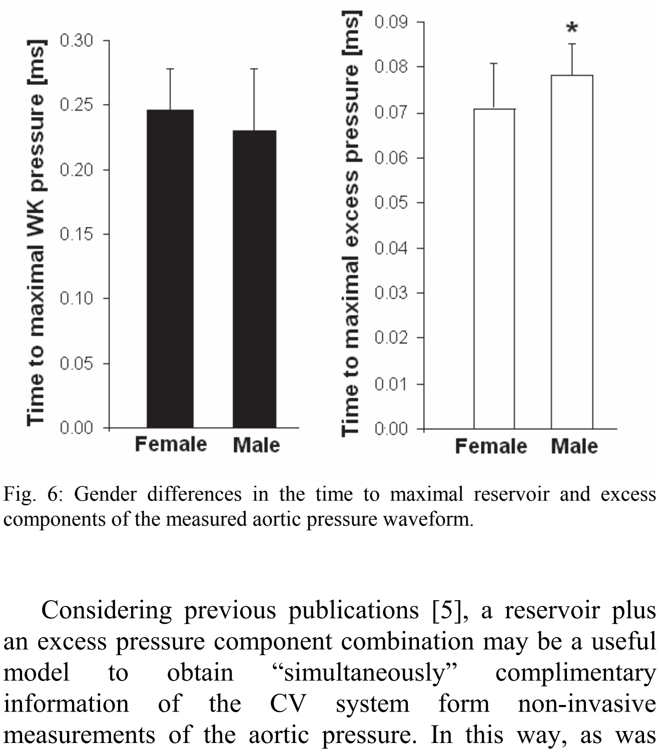

Fig. 6: Gender differences in the time to maximal reservoir and excess components of the measured aortic pressure waveform.

Considering previous publications [5], a reservoir plus an excess pressure component combination may be a useful model to obtain "simultaneously" complimentary information of the CV system form non-invasive measurements of the aortic pressure. In this way, as was stated, while reservoir pressure depends mainly on global (systemic) properties, excess pressure provides information mainly related to local behavior.

It may be mentioned that, by the first time, gender differences in aortic excess and reservoir components were assessed, being evidenced that males and females show significant differences in the excess pressure components but not in the reservoir ones. While the maximal level of the excess component is higher in males, it is earlier in females. It can be noticed that the significantly longer time in males might only be a consequence of significantly longer excess pressure. Therefore, differences in the "timing" of the excess pressure agree with previous works, witch have described that females have an earlier return of the reflected waves [9]. A shorter stature in females defines a shorter arterial tree. Consequently, a shorter time to the maximal excess pressure level could be explained by the fact that the reflecting site in females is closer to the central circulation than it is in males. For a given arterial stiffness level, the pressure wave reflected in a shorter arterial tree would reach the central aorta earlier and might tend to determine an earlier increase in the excess pressure component. To summarize, the higher maximal excess pressure levels found in males, could be explained by several factors, such as a higher stroke volume, and/or aortic stiffness (higher carotid-femoral pulse wave velocity, unpublished results). Finally, it is noteworthy that the differences in the time to maximal excess component and the differences in the excess component level might be associated In spite of the appreciations, to analyze the contribution of different variables to the timing and levels of the calculated excess pressure was beyond the main objective of the present study.

Future experimental and clinical studies are necessary, in order to perform the analysis and comparison of gender-related differences/similarities over the aortic pressure components of additional age groups. It is imperative to carefully asses the meaning of the findings, mainly in the context of gender-related differences related to CV risk profile and CV diseases characteristics.

REFERENCES

[1] Nichols WW, O'Rourke M. Chapter 3: Properties of the arterial wall: theory. Chapter 4: Properties of the arterial wall: practice. In: Nichols WW, O'Rourke M, editors. Mc Donald's Blood Flow in Arteries: Theoretical, Experimental and Clinical Principles, 4th edn. Edward Arnold Publishers, London, UK, 2005; 49–65, 67–93.

[2] J. Davies, J. Baksi, D. Francis, N. Hadjiloizou, Z. Whinnett, C. Manisty, et al. "The arterial reservoir pressure increases with aging and is the major determinant of the aortic augmentation index", Am J Physiol Heart Circ Physiol. 2010;298(2):H580-6.

[3] A. Pauca, M. O'Rourke, N. Kon, "Prospective evaluation of a method for estimating ascending aortic pressure from the radial artery pressure waveform", Hypertension. 2001;38:932-7.

[4] J. Wang, J. Flewitt, N. Shrive, K. Parke, J. Tyberg, "Systemic venous circulation. Waves propagating on a windkessel: relation of arterial and venous windkessels to systemic vascular resistance", in Am J Physiol Heart Circ Physiol. (2006).

[5] Aguado-Sierra J, Alastruey J, Wang JJ, Hadjiloizou N, Davies J, Parker KH., Separation of the reservoir and wave pressure and velocity from measurements at an arbitrary location in arteries, in Proc Inst Mech Eng H. 222(4):403-16, (2008).

[6] Westerhof N, Lankhaar JW, Westerhof BE., The arterial Windkessel, in Med Biol Eng Comput. 47(2):131-41 (2009)

[7] Stergiopulos N, Segers P, and Westerhof N. Use of pulse pressure method for estimating total arterial compliance in vivo, in Am. J. Physiol.; 276:2-2: H424-H428 (1999)

[8] Hu WC, Wang JJ, Shyu LY, Cheng HM, Chen CH, Shih, YT, Sun YJ. Evaluation of Blood Pressure Pulse Wave Velocity and Arterial Relaxation Constant, Computers in Cardiology; 36:745−748 (2009).

[9] Gatzka CD, Kingwell BA, Cameron JD, Berry KL, Liang YL, Dewar EM, et al., "Gender differences in the timing of arterial wave reflection beyond differences in body height", J Hypertens. 2001; 19(12):2197-203.